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Infectious Diseases and Tropical Medicine Research Center
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Shaheed Beheshti Medical University (SBMU)

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The Infectious Diseases and Tropical Medicine Research Center (IDTMRC)
Address: Faculty of Medicine, Shaheed Beheshti Medical University, Shaheed Chamran highway, Evin, Tehran, Iran
P.O.Box: 19615-1159 Tel: (+98)-21- 22424205-10 Fax: (+98)-21- 22424206 Email: info@ idtmrc.ac.ir Web: www. idtmrc. ac.ir
President: Ali Reza Zali (M.D.) Scientific Director: Davood Yadegarynia (M.D.) Executive Director: Reza Rafi Zadeh (M.D.)

Congress president:
Ali Reza Zali M.D.
SBMU Chancellor
Next toTaleghani Hospital, Evin Street, Shahid Chamran exp. Way, Tehran
Email:Dr_a_zali@yahoo.com Phone: +98-21- 22439900-4

The scientific Director:
Davood Yadegarynia M.D.
IDTMRC Chancellor
Faculty of Medicine Shahid Beheshti Medical
University Shahid Chamran Highway, Evin, Tehran
Email: Yadegarinia@yahoo.com Phone: (+98)21- 22439963-8

The Executive Director:
Reza Rafi zadeh M.D.
No. 5 ,Fazeli Alley ,Reihani Street ,North Majidieh , Tehran, Iran
Email: Reza.rafizadeh@gmail.com Phone: (+98)21-22 336288
Rafizadeh_reza@yahoo.com Mobile Phone: (+98)912- 345 6000

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The 1st International Congress of Infection in Transplantation and Cancer

JUNE 10-12, 2008

IN THE NAME OF GOD

It is a great honor that the Infectious and Tropical Disease Research Center of Shaheed Beheshti Medical University in collaboration with other research centers is holding 'The 1st International Congress of Infection in Transplantation and Cancer'.

I would like to extend my warmest greetings to every one in attendance.

Bearing in mind the growing reduction in infection in the world and in Iran, and consequently having diseases such as cancers as our priorities, as well as increasing organ transplantations resulting in the consumption of expensive immunosuppressive drugs and finally, the increase in opportunistic and abnormal infections, infection management in cancer and transplant patients is of vital importance which demands high experiences.

Moreover, multi drug resistant bacteria have added gravely to the problem of patients with deficient immune systems in the world and in our country.

Therefore, we have gathered here to gain from scientific experiences as well as to exchange critical information with our national and international colleagues, to be eventually capable of finding appropriate approaches to prevent infection, seek patient care, education, research, and public health.

At the end, I deeply appreciate your participation in our 3-day congress, wish you a happy and pleasant stay in this beautiful city, Tehran, as well as hope you to enjoy the warm hospitality of the people of Iran.

Davood Yadegarynia M.D.
The Scientific Director

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Review1

Bacterial Infections in the Transplant Recipients

Ali Akbar Velayati
Shahid Beheshti Medical University,Tehran, Iran
Email:aavelayati@nritld.ac.ir

The prevention and treatment of infection, especially multidrug-resistant infection, in the transplant recipient and donor remains an essential and significant part of the management of these patients.

From an immunological standpoint, current immunosuppression protocols to reduce lung transplant rejection include drugs to reduce pro-inflammatory Th1 cytokines and reduction of CD41 T-cell Th1 pro-inflammatory cytokines in peripheral blood and bronchoalveolar lavage (BAL) fluid in stable lung transplant patients, is seen after immunosuppression therapy.

Th1 pro- inflammatory cytokine production is important in host defense against microbial infection in the lungs, particularly Aspergillus and Pseudomonas spp., and it is hypothesized that excessive immunosuppression of these cytokines may also leave patients susceptible to many infections. So the art of infectious disease specialist, internist, pulmonologist and clinical immunologist in a management team, is to induce a balance between rejection and infection.

Our recent study in Masih Daneshvari hospital, as a lung-heart transplantation center, showed 52 episodes of infection in 13 lung and 3 heart transplant patients.

47 of these episodes were in lung transplant patients and 38% of all infections occurred in early phase (until one month after transplantation). The respiratory (78.8%), blood (9.6%), skin and urinary tract infections were the most prevalent infections in transplant recipients. Aspergillus (9 episodes), Pseudomonas spp (8 episodes),

Acinetobacter (6 episodes), *E.coli*, Klebsiella, Candida spp, *S. aureus*, *S.epidermidis* and viruses (CMV, VZV, adenovirus and Infuenza virus) were isolated from patients in order of frequency. All episodes of Acinetobacter infection were in lung recipients and showed resistance to third and fourth generation of cephalosporins, carbapenems, piperacillin-tazobactam, fluoroquinolones and aminoglycosides. One patient with multiresistant Acinetobacter infection died due to lack of response to antibiotic therapy. In general from seven deaths after transplantation six cases caused by infection. So our great concern in Transplantation Ward is an upsurge rate of multidrug-resistant gram negative infections and aspergillosis that need further preventive and diagnostic measures.

Review2

Kidney donation and rewarded gifting: an Iranian model

Nasser Simforoosh
Labbafinejad Hospital,Urology Nephrology Research Centre,Tehran,Iran.
Email: simforoosh@iurtc.org.ir

The shortage of kidneys for transplantation is a worldwide problem, and the gap between supply and demand is growing.1,2 Kidney transplantation is the treatment of choice for patients on dialysis, but many die before undergoing this life-saving surgery. At present, Iran is the only country in the world to have eliminated the need for a waiting list for kidney transplantation by the adoption of a rewarded-gifting model for living kidney donation.

Iran also has the largest reported experience of living unrelated-donor transplants, 1,3–5 which started with the first living unrelated kidney transplantation from a spouse, 20 years ago.1,4 Since then, 2,630 kidney trans plantations have been performed in our department alone, 2,273 of which involved living unrelated donors. The results of kidney transplantation from living unrelated donors are similar to those from living related donors, and superior to those from cadaveric donors.

These promising results have motivated other centers in Iran to use living unrelated donors as a source of kidneys for Transplantation. By the end of 2004, over 17,000 kidney Transplantations had been performed in Iran.6 In 2000, our department started to offer cost- effective2 laparoscopic donor nephrectomy (LDN). Since then, we have performed 713 LDNs—the largest number in the Middle East, and one of the largest numbers for a single center in the world. The introduction of LDN was undoubtedly a major factor that encouraged donors to take part in kidney transplantation. In the Iranian

system, however, other potential sources of kidneys—such as living related donors and particularly cadaveric donors—are also used, and are much appreciated.6

Unlike living unrelated donors, living related donors often feel immense pressure from their families to donate a kidney. Furthermore, there are risks associated with use of a donor related to the recipient, such as a family history of endstage kidney disease, that do not apply in the case of unrelated donors.

Studies have shown that over 90% of unrelated donors report satisfaction following kidney donation, to such an extent that they recommend donation to others. Interestingly, the socioeconomic status and education levels of donorsand recipients are comparable.7,8

There is an active cadaveric transplantation program in Iran: over 200 liver transplants have been performed at Shiraz University, in addition to many heart transplants and thousands of corneal transplants. Close to 1,000 cadaveric kidney transplantations have been also been performed.

The first step in development of the Iranian rewarded-gifting model was the establishment of a dedicated charitable foundation, the Society for Supporting Dialysis and Transplantation, which has branches all over Iran and over 180 transplantation clinics nationwide. The role of this society, which is run by dialysis and transplant patients and other volunteers, lies in referral of patients and donors to transplant centers and in helping patients to cope with end-stage renal disease.

The society registers the donors (mainly unrelated volunteers) and introduces them to transplant candidates. It then helps recipients with their preoperative evaluation, the costs of which are mainly reimbursed by insurance companies.

Another important feature of the Iranian model is governmental promotion of kidney transplantation. The government considers this model of rewarded gifting for living kidney donation to be socially and economically preferable to dialysis. Governmental aid covers the expenses of transplant surgery performed in public university hospitals through the insurance system. The government also pays a sum of money (currently about US$1,200) to each donor after his donation, as a gift. Donors also receive a financial reward directly from the recipient. This reward is usually coordinated by the Society for Supporting Dialysis and Transplantation, but is considered a private matter

that no one interferes with. Neither transplantation teams nor hospitals are involved in finance reward directly from the recipient. This reward is usually coordinated by the Society for Supporting Dialysis and Transplantation, but is considered a private matter that no one interferes with. Neither transplantation teams nor hospitals are involved in financial rewards fordonation. The procedure is arranged so that the majority of patients-including patients of poor socioeconomic status—can afford the operation, and many generous people and charity foundations also participate financially in this respect. Consequently, in the Iranian model, almost all patients with end-stage renal disease have the same chance to benefit from kidney Transplantation, regardless of their socioeconomic status.

We believe that the involvement of both governmental and nongovernmental organizations in providing money for the humanitarian act of unrelated kidney donation is pivotal; their efforts significantly facilitate the process of finding an appropriate kidney graft for patients with end-stage renal disease in a timely manner.In this system, pre-emptive transplantation is now a routine strategy for many patients, particularly children.9

Our transplantation teams have a crucial role in minimizing the costs of transplantation: they view this challenging surgery as a humanitarian act rather than a source of revenue. From a financial point of view, the fee for the surgeon to perform transplantation surgery is very low compared to that for other operations performed in private practice (approximately $200 for one kidney transplantation, compared with approximately $1,000 for a simple prostatectomy)—an outstanding achievement. Another important aspect of the Iranian rewarded-gifting model is the establishment of a law that regulates the process. This law states that transplantations can only be carried out between citizens of the same country; consequently, a kidney from an Iranian donor can only be transplanted into an Iranian recipient. If a patient of any other nationality wishes to undergo kidney transplantation in Iran, he or she must provide an appropriate donor (related or unrelated) from his or her own country. This restriction prevents the rampant commercialization of the organ-donation program.

The last important aspect of the Iranian model of kidney transplantation is its educational and scientific value. Over the last 20 years, 27 transplant surgeons have been trained in our department. If these young transplant surgeons had not been trained, 17,000 kidney transplants would not have been performed.

In summary, this model of rewarded gifting for living kidney donation constitutes a major breakthrough in transplant surgery that has revolutionized the transplantation process in Iran by completely eliminating waiting lists.1,2,10 The success of the Iranian organ-donation program is based on several key issues. The cornerstone of the model was the initial living unrelated organdonation arrangements between spouses.1,3 Donation is regulated by the Society for Supporting Dialysis and Transplantation, which is run by dialysis and transplant patients. The government incentive of a gift for organ donation encourages donors to articipate. Surgery is mainly performed in university hospitals, which makes Transplantation possible for patients of low socio economic status. Likewise, the very low surgeon fee makes transplantation economically feasible for both the government and patients. The law that only citizens of the same country can participate in a transplant arrangement prevents commercialization of the Iranian organ-donation program. The help of other charity foundations ensures that the system runs smoothly and securely between recipients and donors. Medical teams and hospitals are not involved in the financial rewards for donation. Finally, education of all members of the transplantation team inside Iran- including surgeons, nephrologists, and nursing staff-helps the system to run efficiently and encourages the establishment of new transplant centers nationwide.

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Review3

Infection in Solid-Organ Transplant Recipients

Laleh Solaimanizadeh,* Farzaneh Solaimanizadeh, Roya Ahmadrajabi, Sakineh Miri, Maryam Asgari.

Corresponding Auther: *

Faculty members of Bam nursing school

Email: lsolaimani@yahoo.com

Abstract:

Background & Objectives :

Increasingly immunosuppressive agents have dramatically reduced the incidence of rejection of transplanted organs while increasing patients' susceptibility to opportunistic infections and cancer. At the same time, patterns of opportunistic infections after transplantation have been altered by routine antimicrobial prophylaxis for *Pneumocystis carinii* and cytomegalovirus. These patterns have also been altered by the emergence of new clinical syndromes and by infections due to organisms with antimicrobial resistance. New quantitative molecular and antigen-based microbiologic assays detect previously unrecognized transplantation-associated pathogens such as lymphocytic choriomeningitis virus. These assays are used in the management of common infections such as those due to cytomegalovirus and Epstein–Barr virus .

Materials & Methods:

In this article, we have reviewed general concepts in the management of transplantation-associated infections and discuss recent advances and challenges.

Discussion:

It is more difficult to recognize infection in transplant recipients than it is in persons with normal immune function, since signs and symptoms of infection are often diminished. In addition, noninfectious causes of fever, such as allograft rejection, may develop in transplant recipients. Antimicrobial therapy frequently has toxic effects that may involve interactions with immunosuppressive agents. The spectrum of potential pathogens is broad, and infection often progresses rapidly. Early and specific microbiologic diagnosis is essential for guiding treatment and minimizing nonessential drug therapy. Invasive diagnostic procedures are often required for accurate and timely diagnosis. The risk of infection after transplantation changes over time, particularly with modifications in immunosuppression. Unfortunately, no assays accurately measure a patient's risk of infection. Currently, therefore, the clinician assesses a recipient's risk of infection while considering the risk of allograft rejection, the intensity of immunosuppression, and other factors that may contribute to his or her susceptibility to infection. Prophylactic strategies are based on the patient's known or likely exposures to infection according to the results of serologic testing and epidemiologic history. The risk of infection in the transplant recipient is a continuous function of the interplay between these factors. Antimicrobial prophylaxis has dramatically altered the incidence and severity of post-transplantation infections. Three general preventive strategies are used: vaccination, universal prophylaxis, and preemptive therapy. The need for immunization against MMR, DPT, HBV infection, poliomyelitis, varicella influenza, and pneumococcal pneumonia should be evaluated before transplantation. Promoting lifestyle changes after transplantation may help limit exposures to some potential pathogens. Opportunistic infections are generally absent during the first month after transplantation, since the full effect of immunosuppression is not yet present. Infections such as viremia and candidemia in this period are generally donor-derived or recipient-derived, or they are associated with technical complications of surgery. Therapy must be guided by antimicrobial-susceptibility data, making microbiologic analysis of aspirates or biopsy specimens essential. Viral pathogens and allograft rejection are responsible for the majority of febrile episodes that occur during the period from 1 to 6 months after

transplantation. Trimethoprim–sulfamethoxazole prophylaxis generally prevents most urinary tract infections and opportunistic infections such as pneumocystis pneumonia, *L. monocytogenes* infection, *T. gondii* infection, and infection with sulfa-susceptible nocardia species. The risk of infection diminishes 6 months after transplantation, since immunosuppressive therapy is usually tapered in recipients who have satisfactory allograft function. However, transplant recipients have a persistently increased risk of infection due to community-acquired pathogens. In some patients, chronic viral infections may cause allograft injury or a malignant condition such as post-transplantation lymphoproliferative disorder (PTLD) or skin or anogenital cancers.

Conclusions:

The interaction of infection and immunosuppression is the central concern. The induction of immunologic tolerance so that exogenous immunosuppression is avoided in transplant recipients, might, if successful, reduce the risk of infection after transplantation. However, two caveats would remain. First, exposures to infections subsequent to the development of tolerance might abrogate tolerance and induce allograft rejection. Second, the induction of tolerance to an allograft might induce immunologic unresponsiveness to latent organisms in that organ. More sensitive microbiologic assays, immunoassays, and genomic and proteomic markers, may provide the potential for individualized immunosuppression and prophylactic strategies. Such assays may ultimately permit a more dynamic assessment of the immune status of transplant recipients over time, allowing titration of immunosuppression and reducing deaths from infection and malignant conditions.

Keywords:
Infection, Solid-Organ, Transplant, Recipients, Prevention

Review4

Current spectrum of bacterial infections in cancer patients

Hasibi Mehrdad.
Department of Infectious Diseases,Amir-Alam Hospital,Tehran, Iran.
Email: mehrdad_hasibi@yahoo.com

Abstract:
Background & Objectives:
Infections are common cause of death and an even more common cause of morbidity in patients with a wide variety of neoplasms. Autopsy studies show that most deaths from acute leukemia and half of deaths from lymphoma are caused directly by infection. With more intensive chemotherapy, patients with solid tumors have also become more likely to die of infection. The present study seeks to elaborate on the current spectrum of bacterial infections in cancer patients.
Materials & Methods:
With a thorough review of the current literature, the article tries to find out how different factors work together to cause mortality and morbidity among patients with leukemia and lymphoma as well as the functions of catheter insertion in causing such infections.
Conclusion:
Despite all modern healthcare resources for preventing and controlling these complications, hospital-acquired bloodstream infections (BSIs) remain one of the major life-threatening infectious conditions in these patients. Also, Central venous catheters were the major source of bloodstream infection, particularly in patients with solid tumors. Direct surveillance activities with rigid adherence to antibiotic

and infection control measures in order to minimize colonization pressure and bacterial cross-transmission between patients may effectively interfere with factors associated with an infection-related unfavorable outcome.

Keywords:
Bacterial Infection; Cancer Patients; Leukemia; Lymphoma; Catheter.

Review5

Viral infections in solid organ transplantation

Majid Marjani, Masoud Shamaie, Payam Tabarsi, **Seyed Davood Mansoori** *.
Corresponding Auther:
Shaheed Beheshti University of Medical Sciences, Tehran, Iran
Email: dmansoori@yahoo.com

Abstract:

The number of solid organ transplant patients is annually on the increase. Despite preventive measures pre- & post- transplantations, infection is still on the peak of morbidity and mortality among these patients. In this respect, the viral infections play the major role. The viral respiratory infections usually follow a seasonal pattern and non produce an exclusive clinical syndrome. Adenovirus, parainfluenza virus, influenza, RSV, retrovirus, and metapnumovirus are among the most important respiratory viruses. However, pneumovirus is the most severe one among all these viruses. Moreover, infections with these viruses can act as underlying factors for secondary fungal and bacterial infections causing chronic or acute allograft rejections. HMPV is increasingly important pathogen in transplant patients. It seems that its epidemiology and clinical manifestations are similar to RSV virus. However, a reduction in immunosuppressive drugs is the basis for their treatments. CMV plays the most important role among all viruses in transplant patients as its prevalence among the normal population is 30-79 %. It can stay hidden n the human body for life. It becomes apparent in the first three months post-transplantation; yet it can be delayed due to prophylactics. CMV is an important risk factor in fungal and bacterial infections. It can play a major role in allograft rejection.

This case is speeded up in lung transplantation as Bronchiolitis obliterans and as coronary diseases in heart transplantations. It shows itself as chronic nephropathy in renal transplantations.

Infections with HCV and HBV in transplant patients are vital as they can enhance progressive liver diseases. Other viral infections which may bring about complications and cause morbidity and mortality include VZV,HSV,EBV,JC virus , BK virus, , HHV-8 , HHV-7 , HHV-6 , and Pavovirus B19.

Review6

Fungal infection in patients with immune system deficiency

Seyed Davood Mansoori *, Masoud Shammaie, Majid Marjani, Payam Tabarsi

****Corresponding Auther***
Shahid Beheshti University of Medical Sciences,Tehran,Iran
Email: dmansouree@yahoo.com

Introduction:

With the growing population suffering from decreasing immunity system due to the HIV infection, on the one hand, and advances in transplantation and therapeutic methods to prevent organ rejection, as well as well as advances in treating patients afflicted with cancer through more effective immunosuppressive drugs, pathogenic infection , especially opportunistic ones, and specifically, fungal infections in these patients have been on the increase. For example, there are 300000 annual cases of SOT transplantations in the US with a fungal infection rate of 5-59 %.

There are various fungi seen in the infections which have recipients possible. In 2-6 weeks following transplantation, both hospital-based infections and the reactivation of previous infections whether in the recipient, or in the allograft, are more prevalent. The most prevalent fungal infections are Aspergilus and Candida occurring during this period. From 1-6 months post-transplantation period, there are infections due to immunosuppressive drugs and decreasing body immunity. Endemic

Fungi such as Histoplasma, capsulatum, Coccidiosis, and Blastomyocosis, etc, as well as other opportunistic fungi such as various candidas are very prevalent. After 6 months post-transplantation period, the risk of infection by the opportunistic

infections is reduced due to a decrease in immunosuppressive drug take ups. However, some fungal infections, and especially, histoplasmosis, and criptoccoci are very prevalent. In cases of allograft rejection, which requires more effective immunosuppressive drugs, the opportunistic fungi become more active.

Recently, however, there have been advances in lung transplantation at Masih Daneshvari Hospital in Tehran which demands attention to fungi infection. There are many ways available to fight the fungi and increase the immunity systems among patients with new lungs.

In the present panel, different kinds of fungi, especially those related to lung transplantations at Masih Daneshvari Hospital in Tehran will be reviewed.

Review7

New Advances in Treatment of Invasive Fungal Infection in Patients with Cancer and Neutropenia and Bone Marrow Transplantation

Masoud Mardani M.D.
Professor of Infectious DiseasesShaheed Beheshti Medical University,Tehran ,Iran
Email: mmardani@hotmail.com

Invasive fungal infection (IFI) is a major cause of morbidity and mortality among patients with acute leukemia and receipt of an allogeneic hematopoietic stem cell transplant (HSCT). Four strategies for prevention and treatment of IFI include (1) prophylaxis, (2) empirical antifungal therapy, (3) preemptive antifungal therapy, and (4) treatment of established fungal infection. Even among highly immunocompromised patients, most will not develop an IFI. Therefore, any prevention strategy entails administering an antifungal agent to a prespecified patient population in which only a minority would be expected to benefit.

Various studies have demonstrated *Candida* species to be by far the most common fungal pathogens during neutropenia and *Aspergillus* species to be a distant second. *Candida* infections typically occur during the second or subsequent week of neutropenia, and *Aspergillus* infections typically occur later, during the third and subsequent weeks of neutropenia. Thus, fungal infections are not problematic during therapies that cause only short-term neutropenia (lasting for <1 week), but *Candida* infection is a substantial problem in neutropenic episodes lasting for >1 week. *Aspergillus* infection is mostly problematic for patients with long-term neutropenia (lasting for >2-3 weeks), such as patients treated for acute leukemia and those undergoing hematopoietic cell transplantation.

Reasons that warrant the administration of empirical antifungal therapy include the high rates of mortality and morbidity associated with fungal infections, the difficulty of diagnosing invasive fungal infections early during the course of infection, and, regrettably, the utter ineffectiveness of treatment when it is delayed.

Treatment for Candidemia

Although treatment with amphotericin B deoxycholate or lipid formulations of amphotericin B has been associated with good outcomes for patients with candidemia and other less common forms of invasive candidiasis, this approach has also resulted in significant toxicity. As a result, a series of clinical trials was undertaken initially to evaluate azole drugs as treatment of candidemia in nonneutropenic patients and, more recently, to evaluate echinocandin agents. The comparison of fluconazole with AMBd and was done by the MSG and led by Rex et al and showed, rates of efficacy, mortality, and persistent candidemia were similar for the 2 regimens, whereas the toxicity rate was significantly higher in the AMBd-treated group.

There are several effective options for the treatment of candidemia These regimens include an amphotericin B formulation, fluconazole alone (400-800 mg), caspofungin or anidulafungin, and the combination of fluconazole plus amphotericin B. The choice of initial therapy in the individual patient should be based on several factors, including prior significant exposure to fluconazole, condition of the patient (stable or life-threatening), microbiologic data about the infecting *Candida* species in the blood or (less helpful) recovered from colonized sites (e.g., urine, wound, and tracheal aspirate), and the presence of organ dysfunction that would affect drug clearance.

Effective Therapy against Invasive Aspergillosis

Invasive aspergillosis has emerged over the past 2 decades as one of the most dreaded infections complications in immunocompromised hosts, especially for patients who have sustained neutropenia, who are receiving prolonged courses of high doses of corticosteroids, or who are undergoing bone marrow or solid organ

transplantation. Amphotericin B formulations have long been the mainstay of treatment for invasive aspergillosis, but multiple studies, including retrospective case series and prospective randomized trials, have consistently shown disappointing outcomes, regardless of the specific amphotericin B agent (AMBd or a lipid formulation). Comparison of voriconazole, a second-generation azole with excellent activity against *Aspergillus* species, with AMBd as treatment for invasive aspergillosis was done. As a result of clinical trial, voriconazole has become the drug of choice of most clinicians for primary therapy of most patients with invasive aspergillosis. However, controversy has arisen about whether single-drug therapy or combination therapy (e.g., voriconazole plus an echinocandin, such as caspofungin) is optimum therapy. Recent studies provide some insights into the potential role of combination therapy. First, caspofungin has been approved for salvage treatment of invasive aspergillosis .

In conclusion three factors create the need to reevaluate older paradigms for prophylaxis and early treatment of suspected IFIs. The first is the change in the epidemiology of IFIs, in which mold infections pose a greater threat than invasive candidiasis in patients with acute leukemia and allogeneic HSCT. Among allogeneic HSCT recipients, the predominance of invasive mold infection during GVHD, rather than neutropenia, has led to recent prophylactic trials that encompass the GVHD period. Second, the availability of effective and safe mold-active agents challenges the older paradigm of using fever alone as a trigger to modify antifungal therapy. Third, chest CT findings and laboratory markers as diagnostic adjuncts for IFI may be useful as triggers to initiate or modify antifungal therapy. It is a high priority to validate the application of these tests to antifungal algorithms.

Review8

Empirical Antifungal Therapy in Treating Febrile Neutropenic Patients

Masoud Mardani M.D.
Professor of Infectious DiseasesShaheed Beheshti Medical University, Tehran, Iran
Email: mmardani@hotmail.com

Prophylactic fluconazole has led to a decrease in the frequency of invasive candidiasis among patients with leukemia and among HSCT recipients. However, invasive aspergillosis (IA) and less common molds, including zygomycetes, *Fusarium* species, and *Scedosporium* species, have become increasingly important causes of IFI-related mortality relative to invasive candidiasis among patients with leukemia and among allogeneic HSCT recipients. Some centers have noted an increased frequency of zygomycosis in patients receiving prophylactic voriconazole , it is controversial whether a causal relationship exists or whether this finding reflects a larger pool of highly immunocompromised patients. Modern prophylactic and early-treatment strategies are required that encompass the changing epidemiology of IFI, advances in antifungal agents, and improved diagnostic tools (e.g., chest CT scans and laboratory markers) that facilitate early detection of IFI.

Empirical antifungal therapy for neutropenic fever has been studied in >3000 patients and its use was justifiably supported because of the combination of inadequate diagnostic testing, the need for early antifungal drug treatment of IFI, uncertain prophylactic regimens, and high-level morbidity and mortality from IFI.

Although fever in a neutropenic patient should prompt a meticulous evaluation, we challenge the principle of using fever alone as a specific entry point for clinical decisions regarding patients receiving mold-active prophylaxis when we have

diagnostic tools that allow us to make a more precise diagnosis. Challenges and pitfalls in prevention trials involving nonneutropenic allogeneic HSCT recipients at high risk for IFI are important.

Fluconazole versus Amphotericin B

Because of its toxicity, AmB-D was more likely to be used as empirical therapy for neutropenic fever than as prophylaxis, which would entail treating a larger number of patients over a longer period. Fluconazole therapy is effective in preventing invasive candidiasis in HSCT recipients, although breakthrough fluconazole-sensitive and fluconazole-resistant infections occur. A meta-analysis of randomized studies of azole prophylaxis (fluconazole, ketoconazole, miconazole, and itraconazole) in neutropenic patients demonstrated that azoles led to reductions in the use of parenteral antifungal therapy, superficial fungal infections, IFIs, and fungal infection-related mortality. The incidence of IA was unaffected. In a meta-analysis of 16 randomized, controlled trials involving patients who did not receive HSCT and who had chemotherapy-induced neutropenia, fluconazole prophylaxis was beneficial when the incidence of IFI was expected to be >15% .

Empirical therapy for neutropenic fever initially involved initiation of AmB-D therapy to increase the spectrum of activity to include molds and azole-resistant *Candida* species. The trade-off was straightforward: early administration of a narrow-spectrum but safe agent (fluconazole), compared with later administration of a broader spectrum agent with greater toxicity (AmB-D).

There are many causes of fever in neutropenic patients (e.g., bacterial infections, transfusion reactions, drug reactions, tissue necrosis, and growth factors). IFIs are documented in ⩽5% of patients enrolled in modern empirical antifungal trials in which antifungal prophylaxis was commonly used. Indeed, 2 randomized trials showed that fluconazole was equally effective but safer than AmB-D as empirical therapy for persistently febrile neutropenic patients. Because of its lack of activity against molds, the authors cautioned that chest radiographs or CT scans be performed prior to initiating empirical fluconazole therapy .

Newer antifungal Agents

The development of newer antifungal agents with activity against yeasts and molds and with superior safety and tolerability, compared with AmB-D, raised questions about whether the older paradigm of early and safe treatment versus late and potentially toxic treatment should be continued. The improved tolerability of lipid formulations of amphotericin B, azoles, and echinocandins, compared with AmB-D, has prompted many centers to use these agents early, as prophylaxis, rather than later, as empirical therapy for neutropenic fever.

Indeed, it is common for agents within the same class and with a similar spectrum to be evaluated as prophylaxis and as empirical therapy in separate trials. The echinocandins provide an instructive example. Caspofungin was at least as effective as and less toxic than liposomal amphotericin B as empirical therapy in persistently febrile patients with neutropenia. The success rate in each arm, using a prespecified composite outcome, was only 34%, with the majority of treatment failures being driven by a lack of resolution of fever during the neutropenic period. In a prophylactic trial of autologous and allogeneic HSCT recipients that compared micafungin with fluconazole, treatment success required the absence of suspected, probable, or proven IFI through the end of therapy. Empirical modification of antifungal therapy on the basis of neutropenic fever was equated with a suspected IFI. The frequency of breakthrough candidemia was similar in both arms, but there was a trend to fewer episodes of IA in allogeneic HSCT recipients receiving micafungin. The superiority of micafungin therapy was principally driven by a lower frequency of persistent neutropenic fever requiring empirical modification of the antifungal regimen.

We suggest that modification of the antifungal regimen solely on the basis of persistent neutropenic fever should not be equated with treatment failure in either prophylactic or empirical antifungal studies.

In patients receiving no antifungal prophylaxis or fluconazole prophylaxis, empirical antifungal trials have shown that a small minority have baseline IFIs at the time of study enrollment. For example, in the empirical antifungal trial comparing

caspofungin and liposomal amphotericin B, ~5% of patients in both arms had a baseline IFI (almost 90% of these IFIs were invasive candidiasis or IA). Empirical antifungal therapy initiated prior to diagnosis of IFI would be expected to benefit this small minority of patients. Empirical treatment with caspofungin is not associated with greater toxicity than fluconazole used as prophylaxis, and it represents a viable strategy. Whether it is safe to continue fluconazole prophylaxis in neutropenic patients with persistent fever of unknown etiology who have negative chest CT findings and negative laboratory markers merits further study.

In conclusion, empirical antifungal therapy has an established role in the control of fungal infections during neutropenia. To optimize the selection of antifungal therapy, the spectrum of activity and toxicity profile of candidate antifungal agents have to be considered. With azole prophylaxis, the risk of breakthrough *Candida* infection has declined. With respect to the timing of antifungal therapy, one should consider whether the patient has received antifungal prophylaxis. Finally, the development of accurate diagnostic tests makes it possible that preemptive therapy may replace empirical therapy in the future.

Review9

B-lactamase – resistant ecsherichia coli and klebsiella species

Zohreh Aminizadeh.
Loghman Hakim hospital.Shahid Beheshti MedicalUniversity, Tehran, Iran
E.mail: zohrehaminzadeh@yahoo.com

Abstract:

B-Lactam antibiotics are among the safest and the most frequently prescribed antimicrobial agents in the world; however, emergency of B-lactam resistance in clinically important pathogens has increasingly limited their utility.

A Broad –spectrum E.coli and K.Pneumonia resistance defined an EK that determined resistance to Benzylpenicillin (penicillin G), aminopenicillins (amoxicillin and ampicillin), carboxypenicillins (carbenicillin and ticarcillin), ureidopenicillin (piperacillin), narrow-spectrum cephalosporins (cefazolin, cephalothin, cefamandole, cefuroxime, and others).

Antibiotic resistant mutants producing extended- spectrum B-lactamase (ESBL) emerged among gram-negative bacteria, predominantly Escherichia coli and klebsiella pneumonia. By 1983, ESBL- producing organism had already been isolated in Germany and were reported in the United States by 1989 with outbreaks of infections soon thereafter. In recent years, the importance of such ESBL-mediated infections has been increasingly recognized. An ESBL-E.K resistance was defined an EK that demonstrated resistance to substrates of the broad-spectrum group plus oxyimino-cephalosporins (cefotaxime, cefpodoxime, ceftazidime, and ceftriaxone) and monobactam (aztreonam) plus, for some enzymes, cefepime.

The national committee for clinical laboratory standards (NCCLS) recommends ESBL screening method and confirmatory tests, but most of microbiology

laboratories do not use an adequate screening method for ESBL-producing organism. Delay in the detection and reporting of ESBL production by gram-negative bacteria is associated with prolonged hospital stay, increased morbidity, mortality and health –care costs. Emergency of ESBL- producing isolated has important clinical and therapeutic implications. Antibiotic selection for treatment of serious infections due to ESBL- producing E.coli and K.Pneumonia is a clinical challenge because of complex nature of in vitro susceptibility testing and in vivo correlation.

Carbapenemases are a diverse group of enzymes. They are currently uncommon but are a source of considerable concern because they are active not only against oxyimino-cephalosporins and cephamycins but also against carbapenems. Worldwide, 99.9 percent of Enterobacteriaceae remain susceptible to carbapenems. For infections caused by ESBL-producing *E. coli* or klebsiella species, treatment with imipenem or meropenem has been associated with the best outcomes in terms of survival and bacteriologic clearance. Carbapenems are the surest agents for therapy, but the variety of *B*-lactamases that confer resistance to carbapenems is increasing, and overuse of any single class of antibiotic is likely to be followed by the selection of pathogens resistant to that agent. There are no *B*-lactams in development that can treat infections with organisms producing some of the new *B*-lactamases. There are also insufficient data to evaluate the benefit of combination therapy with a *B*-lactam plus a quinolone or aminoglycoside for infections due to ESBL-positive organisms. Resistance to non–*B*-lactam antibiotics is common in strains making any of these enzymes, such that alternative options for non–*b*-lactam therapy need to be determined by direct susceptibility testing. Resistance to fluoroquinolones and aminoglycosides is especially high.

Review10

Multi Drug Resistance (MDR) in cancer and transplantation infection: A solvable problem?

Hossein Goudarzi.*Roxana Khanipourroshan*
Microbiology Department,Faculty of Medicine,Shahid Beheshti Medical University, Tehran, Iran
Email: hgod100@yahoo.com

In the past 20 years, we have made substantial progress in understanding MDR and in generating the means to tackle it. The classical definition of MDR emphasizes the diversity of drug types and intra-cellular drug targets involved. We now know that two types of resistance fall under this definition:

1. Resistance due to drug pumps. This type of resistance mainly affects large amphipathic drugs, such as anthracyclines, epipodophylotoxins, and vinca alkaloids, which enter the cell rather sluggishly by passive diffusion. As entry can not be changed, all living organisms, from bacteria to human, have developed drug pumps, usually located in the plasma membrane, that extrude these drugs from the cells as soon as they enter.
2. Resistance due to interference with apoptosis. Many anti cancer & anti transplantation drugs appear to act by inducing apoptosis in the recipient cell. Decreased apoptosis can therefore lead to dug resistance, at least in cultured cells. Whether it does so in patients, remains to be seen.

Biochemical research has uncovered three types of drug pumps that may play a role in MDR. The most intensely studied is the P-glycoprotein encoded by the MDR1 gene in humans. A variety of studies have shown that this protein acts as a drug pump in the plasma membrane of tumor cells and that it can recognize an

astonishing range of cytotoxic molecules and remove them from the cell. The main role of this protein is in defence of the body against xenotoxins.

Whether the increased levels of P-glycoprotein found in some drug-resistant tumors actually contribute to resistance is still a controversial issue. I found it a periori unlikely that tumor cells would forego a perfectly fine mechanism of resistance, if available. Tumors are genetically heterogeneous and highly opportunistic. Whatever mutation is likely to allow them to continue multiplying will probably be selected for.

Compelling evidence for this type of selection has recently come from work of Fojo's group at the NCI (USA). Mickley, et al. analyzed the nature of the over expressed MDR1 allele(s) in myeloma cells from patients in which the two alleles present could be distinguished by a polymorphism. In each case in which MDR1 was over expressed, only a single allele was found over expressed. The authors modestly conclude that the results in these patient samples support the idea that MDR1 played a role in drug resistance these tumors in the course of therapy. There is no reasonable other mechanism that would consistently select for over expression of a single allele. Ongoing clinical trials in which chemotherapy is combined with an effective inhibitor of P-glycoprotein, such as the cyclosporine A analogue, PSC 833, should eventually settle whether P-glycoprotein significantly contributes to MDR of those tumors in which it is over expressed.

The multi drug resistance (associated) protein, MRP1

A second class of transporters potentially involved in MDR, is known as glutathione-drug-conjugate pumps, or GS-X pumps. The prototype is the multi drug resistance (associated) protein MRP1, discovered by Cole and Deeley. MRP1 can transport a large range of drugs conjugated to negatively charged hydrophilic ligands such as glutathione, glucuronic acid and sulphate. Indirect evidence strongly suggests that this class of pumps can also transport complexes of glutathione with cisplatin, with arsenate or with antimonite. MRP1 is also able to confer resistance to

drugs that are not known to be conjugated to any acidic ligand, such as doxorubicin or vinca alkaloids. Resistance requires the presence of glutathione, however, and all available evidence indicates that MRP1 can co-transport drug with glutathione and even (at low rate) glutathione alone. Not all hydrophobic anticancer drugs are efficiently transported by MRP1. Paclitaxel, for instance, is a good substrate for P-glycoprotein but a poor one for MRP1. The MRP1 gene is expressed in nearly all human tissue and MRP1 is found in many tumors. Although it is likely to contribute to clinical MDR, the correlation between MRP1 levels and resistance are not strong. Unfortunately there is no highly effective non-toxic inhibitor available for MRP1 yet. This is a prerequisite for the dissection of its potential clinical role.

Other MRP's

MRP1 is part of a family of transporters that now number 7 members, MRP1-7. The best characterized member thus far is MRP2, also known as the canalicular Multi specific Organic Anion Transporter (cMOAT). The major location of this transporter in the body is in the canalicular membrane of the hepatocyte where it is responsible for the excretion of conjugated bilirubin and other organic anions. There is a host of other drug transporters (or putative drug transporters) that might also contribute to MDR. Of the other MRP family members, cMOAT (MRP2) is best characterized.

In experiments with cells transfected with an MRP2 construct, transport of vinblastine and resistance to mitoxanthrone, but not to cisplatin, have been shown. So, in principle, over expression of MRP2 could contribute to MDR, in human tumors, but whether this occurs in practice remains to be determined.

Less is known about MRP3-6 and nothing yet about MRP7. We have spent considerable time on analyzing the transport activities of MRP3. By transfection studies we have shown that over expression of MRP3 can render cells resistant to etoposide and methotrexate. It is therefore probably also an organic anion pump. This pump is present in the small intrahepatic bile ducts, in the adrenal cortex

(mainly in the zona fasciculate), in colon and in the proximal tubuli of the kidney. The physiological function of MRP3 is not yet clear; we found low transport of estradiol through cells over expressing MRP3 and the protein may therefore transport steroid conjugates. Whether it can contribute to MDR in patients remains to be seen.

MRP6 is adjacent to MRP1 in chromosome 16 and its over expression in MDR lines can be fully explained by co-amplification of Mrp1 and MRP6. The same explanation holds for the Anthracycline Resistance Associated (ARA) gene found over expressed by others in resistant leukemia cells. We have shown that the putative ARA protein is almost identical to the C-terminal part of MRP6 and that partial co-amplification of MRP6 can account for the ARA RNA found in resistant cells.

IS MDR a solvable problem?

Yes and No, is the answer to this question. Yes because we can foresee the day that we can detect and understand all dug resistance mechanisms in cancer cells. The human genome project will provide us with an inventory of all human genes. Studies on drug-resistant cells will provide insight in possible resistance mechanisms. Our ability to modify the mouse genome, provides a powerful tool to unravel the function of genes in context of a living mammal, which resembles us sufficiently to allow extrapolation to humans. So yes, in 20 years or so we shall understand MDR and drug resistance in cancer and transplantation.

The other answer is No, multi drug resistance will never be completely solved, even if we understand all mechanisms involved completely, for the simple reason that cancer cells are very similar to normal cells. Mutations in five to seven genes suffice to turn a normal cell into a cancer cell. Since human cells have about 100,000 genes, the mutations that cause cancer affect only 0.01% of all genes. Obviously cancer cells may destroy their host, like invading micro-organisms, but they are still human cells with enzymatic reactions that are virtually identical to those of the

normal tissue from which the tumor was derived. Hence, all the chemotherapeutic agents that are so effective in exploiting the differences in metabolism between micro-organism and human cells are useless for tumor cells. It will then still be necessary to find drugs with sufficient for the tumor to kill all tumor cells without substantial damage to the host. We shall advance step by step on this road, but we don't expect that we are going to see the end in our lifetime.

Review11

Review of the CMV in renal transplantation

Laleh Solaimanizadeh * *Roya Ahmad Rajabi, Farzaneh Solaimanizadeh.*
****CorrespondingAuther**:*
Bam Nursing School,Bam, Iran.
Email: lsolaimani@yahoo.com

Abstract:
Background & Objectives:
Cytomegalovirus (CMV), the most important infectious complication to affect recipients of kidney transplants, is a significant cause of morbidity and mortality. In the absence of any preventative therapy, CMV infection occurs in approximately 30-75% of transplant recipients, with an incidence of CMV disease of between 8 and 80%, depending on the type of transplantation, immunosuppression and, most importantly, the donor/recipient (D/R) CMV serostatus.
Theme:
There are two general patterns of CMV infection in transplant patients. Primary infection occurs when a CMV-naive recipient is first exposed to virus. This most often occurs at the time of transplant by a virus contained within an organ obtained from a donor previously infected with CMV. Alternatively, transfusion of blood from a CMV-positive donor can result in disease. Virus already present in the recipient in a latent state can reactivate, leading to disease. Initial infection with, or reactivation of, CMV can cause direct effects, including an acute viral syndrome with fever and other constitutional symptoms; and various end-organ syndromes such as pneumonitis, enterocolitis, nephritis, and hepatitis. In the early days of transplant with older immunosuppressive agents and in the absence of effective prophylaxis, CMV infection and disease typically presented with high fever in the

first 40 days post-transplant. More recently, CMV is more insidious, occurring later after prophylaxis has been discontinued, and with reduced systemic symptoms, particularly the absence of significant fever. In addition to these primary effects, CMV infection may cause indirect effects, including allograft injury and acute and chronic rejection, increased risk of cardiac complications, diabetes, post transplant lymphoproliferative disorder (PTLD), and even death. Ultimately, it is these secondary effects that may have a greater impact on kidney survival. Because of the substantial morbidity in solid organ transplant recipients, several drugs have been developed and used for CMV prophylaxis after kidney transplantation such as valganciclovir for oral treatment. In many centers, valganciclovir has become the standard of care for CMV prophylaxis.

Conclusion:

Although valganciclovir is effective and now widely used for CMV prophylaxis in transplant patients, late CMV particularly continues to be a problem. The search for newer and better agents continues. A vaccine using DNA technology (Vical, Inc.) is entering phase 2 clinical trials attempting to immunize patients prior to transplant. Other oral agents such as maribavir (Viropharma, Inc.) have been proposed as possible replacements for ganciclovir or for use against resistant strains. These latter two technologies/drugs, if successful in the various clinical stages, are at least five years away from regulatory approval.

Keywords:
Cytomegalovirus Infection; Kidney Transplantation; Treatment.

Review12

Infection in cancer patients

Fatemeh Esfahani
Department of Oncology,Taleqani hospital,Shahid Beheshti Medical University,Tehran, Iran
Email: vass_es@yahoo.com

Abstract:

Infections are among the prevalent causes of mortality and morbidity in patients with different forms of cancers. Autopsy studies show that the mortality in most patients with acute leukemia and half of deaths in patients with lymphoma is directly due to infection. With increasing chemotherapy, the patients are more likely to die of solid infectious tumors than the underlying disease itself.

Neoplasm can make the patient physically susceptible to infection as they damage the dermis uniformity. For example, the squamous cell carcinoma can locally attack the epidermis so the bacteria can reach the underlying tissues. The blockage in a canal which is normally open can make the patient prone to infection. The urethra blockage by a tumor will cause UTI infection. Part of the host's natural defense is dependent upon constant drainage of the internal parts of the cavities. If these are not drained, the bacteria may multiply and cause diseases.

The same condition may happen in patients whose lymph nodes are interrupted due to radical surgery. One of the common problems following mastectomy is cellulitis caused by streptococcus or staphylococcus. Lymph edema or lymph insufficient drainage is the causes for such cellulitis. In most cases, local measures to prevent fluid accumulations or to stop damage to the skin will produce improvements; yet in resistant cases, antibiotic prophylaxis is required. One of the life threatening problems which is common among cancer patients is that their reticuloendothelial system to extract microorganisms is damaged. Spleenectomy is a

part of HCL, CLL, CML, and Hudgkin disease treatment. In these patients, even following absolute treatment of the underlying disease, the lack of having spleen causes the reproduction of killer infections. The same condition occurs in those who lose their spleen due to trauma. These who are otherwise healthy, will be prone to infections even 25 years following spleenectomy.

The patients undergoing spleenectomy have to be consulted for the risk of infection with the previously called DF-2 (captocynophaga canimorsos), a bacterium hosted by the animals in the mouth.

Bacteria with capsules (such as streptococcus pneumonia, hemophilus influenza, and others) are among the most prevalent organisms causing sepsis following spleenectomy. These patients have to be vaccinated against poly saccaride capsules. Since patients with spleenectomy may not refer to the physician soon after fever or other signs of bacterial infections, many physicians suggest some of the antibiotics which have been effective against such microorganisms be taken by the patients as deposits to prevent acute sepsis.

We suspect specific microorganisms when we diagnose the kind of cancer. As soon as CLL or multiple mylomia is diagnosed in a patient, the physician should become suspicious for the presence of hypo gamma globlunemia.

When the alternative immunoglubulin treatment is effective, in most cases prophylactic antibiotic is a more effective and simpler way to eradicate bacterial infection. Moreover, the patients have to take prophylactic antibiotic against pnumositosis. Patients with non-Hudgkin ALL lymphoma and other cancers treated with a high dose of gluco- corticoid, in addition to affliction with specific infections, these patients will present atypical infections.

Review13

Bone Marrow transplantation ward Taleghani hospital, Shahid Bebeheshti medical uviversity

Mahshid Mehdizadeh*,*Abbas Hajifathali, Mehdi Tabarraie, Afshin Mohamadalizadeh*
****CorrespondingAuther***
Bone Marrow transplantation ward Taleghani hospital, Shahid Behbeshti Medical Uviversity-Tehran-Iran
Email:mahshid_mehdizadeh@yahoo.com

Central venous catheters infection in bone marrow transplant patients

Central venous catheters(CVC)used in bone marrow transplant candidates in hospitals to provide secure access to the central circulation for infusion therapy, nutritional support, and apheresis..These catheters can be inserted percutaneously into the subclavian, jugularor or surgically [tunneled catheters and totally implantable venous access devices].Unfortunately central venous catheter related infections are a major cause of morbidity and mortality in the BMT setting. Coagulase-negative staphylococci, Staphylococcus aureus, aerobic Gram negative bacilli, and Candida albicans most commonly cause catheter-related infection. Management of catheter-related infection varies according to the type of catheter involved.In BMT patient with fever and neutropenia after appropriate cultures of blood and catheter, empirical IV antimicrobial therapy should be initiated on the basis of ward policy but if CVC infection is very suspicious vancomycin is usually recommended. Clinical findings of CVC infection are unreliable and BMT patients with suspected CVC infection or fever should have two sets of blood samples drawn for culture, with at least one set drawn percutaneously. Blood culture results that are positive for S. aureus, coagulase-negative staphylococci, or Candida species, in the absence of any other identifiable source of infection, should increase the suspicion for catheter-related bloodstream infection. For management of bacteremia and

fungemia from a tunneled catheter or implantable device, such as a port, the decision to remove the catheter or device should be based on the severity of the patient's illness, documentation that the vascular-access device is infected, assessment of the specific pathogen involved, and presence of complications, such as endocarditis, septic thrombosis, tunnel infection, or met static seeding. When a catheter-related infection is documented and a specific pathogen is identified, systemic antimicrobial therapy should be narrowed and consideration given for antibiotic lock therapy.In CVC infection For patients without evidence of persistent bloodstream infection, for coagulase-negative staphylococcus and for whom with no suspicion of local or metastatic complications, the CVC may be retained and antibiotics continue at least for 10 to 14 days. But in patient with complicated infections like septic thrombosis, endocarditis, osteomyelitis, or possible metastatic seeding, catheter should be removed.Some cases of CVC infections will be presented at the presentation

Review14

Fungi disease in malignancies

Abdolreza Soudbakhsh,
Department of Infectious Diseases, Imam Khomeini Hospital,Tehran University of medical Sciences,
Tehran, Iran.
Email:soudbakhsh@yahoo.com

Abstract:

In the last two decades, the cases of aggressive fungi diseases have increased, and have become the cause of mortality and morbidity in patients with deficient immune systems and malignancies. I such patients, consumption of the drugs they take, and problems such as malnutrition may underlie aggressive fungi diseases. Aspergilusis, candida, and Cryptococcus are among the most prevalent infections, while Mucor, Tricospurum, and Fusarium take the second stage. As a preliminary knowledge about fungi and their differences with microorganisms may be helpful, they are briefly explained as follows:

Fungi may be microscopic, or spherical, and reproduce by blossoming. Its colony is smooth or may be filament. It may septate as well, which is called Hypha. Its mass is called mycelium.

In fighting fungi, some information on cell wall and cell membrane is important. Fungi cell wall is made of chitin or mannan which is a carbohydrate, yet in a microbe it is lipoprotein or glycolipid. The fungi cell membrane includes sterol, while in microbes it involves glycoprotein. The drugs effective against fungi cell membrane are categorized in different groups as follows:

1) Polynes, which prevent sterol synthesis. They may cause complications in human body;

2) Azole, which attaches to the sterol and finally kills the fungi;

Other anti fungi drugs such as Grizofloin and SSIK have unknown mechanisms.

Specific Fungi in Cancer:

1) Candida: This is a natural flora in human mouth, and is increased by antibiotic consumption. Candida has different species, yet the infection severity is similar in its different forms. Most candida are sensitive to Azole and polyne, yet its C. Krusie and galabrata forms are less sensitive to floconazole.

2) Aspergilusis: This fungus is present in the environment. The most important transfer method is by respiration. White blood cell, and micro phagocytes are the best defense against aggressive Aspergilusis. Aspergilusis pneumonia may appear locally or as a progressive disease in both sides of the lungs. It may develop out of the lungs as well. In a study, there were 13 patients with Aspergilusis (7 patients with primary or metastatic cancers and 6 users of corton). 54% had positive responses to therapy.

3) Mucor mycosis: Zycomysis is usually prevalent among diabetics and patients with leukemia. In its malignant form, it appears more in the lungs. The most important defense is nutrophiles. Mucor attacks the vascular system causing necrosis and blockage with a progressive pattern. Anti fungi therapy is not effective against it.

4) Cryptococcus which becomes prevalent with pollution and pigeon and other poultry stool. Meningitis is its most visible clinical picture, yet it rarely causes pneumonia.

Review14

Pulmonary aspergillus in transplant patients: Iranian Report

Majid Marjani,* *payam Tabarsi, Katayoon Najafizadeh, Parvaneh Baqaii,Babak Sharif-Kashani, Shirin Motaharri, Mohmmad Reza Masjedi, Seyed Davood Mansoori.*

***Corresponding Author**:*

Research Center for Tuberculosis & Lung Disease Massih Daneshvari Hospital Shaheed Beheshti Medical Universit y Tehran, Iran

marjani216@hotmail.com

Abstract:

Background & Objectives:

Aspergillus is one of the most opportunistic infections following transplantations. Prompt diagnosis and proper antifungal treatments are key factors for a valuable prognosis. The present study is a report on pulmonary aspergillus in patients with heart, lung, and kidney allografts transplanted at the RCTLD Center at Massih Daneshvari Hospital, Tehran.

Materials & Methods:

In this descriptive study, transplant patient files from Dec. 2001- Jan. 2008 who were admitted due to aspergillus following transplantations were reviewed; and demographic information as well as transplantation time, probable risk factors, radiological indications, diagnostic criteria and antifungal treatment plans were extracted and analyzed.

Results:

Aspergillus was found in 8 lung transplantations, 3 renal recipients and 1 heart recipient. Mean patient age was 40.6 years. There were 7 cases with trachea bronchitis aspergillus in patients with lung transplantations all occurring in the first

6 months post-transplantations. All patients showed effective responses to antifungal therapies and bronchoscopic debridements. There was severe aspergillus in 5 patients among whom 3 patients survived through antifungal therapies. 2 patients died, though they had undergone Itrakonazole and amphotricin B. All surviving patients took variconazol

alone/or in combination with cospofungin.

Conclusion:

It seems that there are improvements among patients suffering from aspergillus, if they are treated in the first stages of the infections.

Keywords:
Infection; Organ Transplant; Aspergillus; Variconazole; Cospofungin.

Review15

Aspergillus infections in transplant recipients

Mehrnaz Rasoolinejad.
Tehran University of Medical Science, Iranian Research Center of HIV/AIDS, Tehran, Iran.
E-Mail: mehrnaz_rn@yahoo.com

Abstract:
Background & Objectives:
The number of patients undergoing transplantation has increased exponentially in recent years. Transplant recipients are among the most significant subgroups of immunosuppressed hosts at risk for invasive aspergillosis. These infections have been reported in 2 to 26% of hematopoietic stem cell transplant (HSCT) recipients and in 1to 15% of organ transplant recipients as well as in 1 to 8% of liver transplant recipients in an invasive form. They can be detected in airway sample cultures from _25 to 30% of lung transplant_recipients and in 3.3 to 14% (average, 6%) of heart transplant recipients.

The present study seeks to elaborate on the methods for the diagnosis and management of such cases among transplant recipients.

Diagnosis:
substantial delay in establishing an early diagnosis remains a major impediment to the successful treatment of invasive aspergillosis. Cultures of the respiratory tract secretions lack sensitivity. *Aspergillus* is grown from sputum specimens in only 8 to 34%, and from BAL specimens in 45 to 62%, of patients with invasive aspergillosis. Thus, confirmation of the diagnosis of invasive aspergillosis has typically required histopathologic evaluation.

Characteristic radiographic findings on high-resolution imaging studies e.g., the halo sign, have allowed earlier diagnosis of infection in neutropenic patients.

Galactomannan, for example, is a polysaccharide cell wall component of *Aspergillus* species that is released into the circulation during fungal growth in the tissues.

The double-sandwich enzyme-linked immunosorbent assay, has proven to be a potentially promising tool for the early diagnosis of *Aspergillus* infection. Aspergillosis DNA can also be detected by PCR assays where a negative test would suggest a low likelihood of invasive aspergillosis.

Management:

The FDA-approved compounds have in vitro, in vivo, and clinical activity against *Aspergillus* species and are licensed for treatment of invasive aspergillosis which include many kinds of drugs used to fight aspergillosis infections.

The number of patients undergoing transplantation has increased exponentially in recent years. Transplant recipients are among the most significant subgroups of immunosuppressed hosts at risk for invasive aspergillosis.

Aspergillus infections have been reported in 2 to 26% of hematopoietic stem cell transplant (HSCT) recipients and in 1to 15% of organ transplant recipients. Historically, the mortality rate in transplant recipients with invasive aspergillosis has ranged from 74 to 92%. An estimated 9.3 to 16.9% of all deaths in transplant recipients in the first year are considered attributable to invasive aspergillosis.

Invasive aspergillosis has been reported in 0.08 to 2.6% of autologous and 3.6 to 10.3% of allogeneic HSCT recipients,

with higher rates in those with unrelated or HLA-mismatched than in HLA-matched donors.

Neutropenia has traditionally been the predominant risk factor, with most infections occurring prior to engraftment, particularly in autologous transplant recipients. The frequency of invasive aspergillosis in autologous transplant recipients has decreased, due largely to more rapid engraftment afforded by the use of hematopoietic growth factors and of grafts with higher stem cell content.

Invasive aspergillosis has been reported in 1 to 8% of liver transplant recipients *Aspergillus* infections in these patients typically occur in the early posttransplant

period. The median time to onset after transplantation was 17 days in one study and 16 days in

Another. A vast majority of the patients who developed invasive aspergillosis had never left the intensive care unit after liver transplantation surgery. Liver transplant recipients

Are also uniquely predisposed to dissemination of infection beyond the lungs, which occurs in _50 to 60% of cases. Isolation of *Aspergillus* spp. from the respiratory

Tracts of liver transplant recipients is an infrequent event (_1.5%). However, it has a high positive predictive value, ranging from 41 to 72%, for invasive aspergillosis.

Aspergillus species can be detected in airway sample cultures from _25 to 30% of lung transplant recipients Invasive aspergillosis, however, occurs in 3 to 15% (_6% on average) of the patients; 58% of these infections are tracheobronchitis or bronchial anastomotic infections, 32% are invasive pulmonary aspergillosis, and 22%

are disseminated infections with extrapulmonary involvement . *Aspergillus* infection occurs a median of 3.2 months after transplantation, with 51% occurring within 3 months and 72% occurring within 6 months after transplantation. Tracheobronchitis

or anastomotic infections are the most frequently occurring infections within 3 months after transplantation, whereas invasive pulmonary and systemic infections

Tend to occur later. The median times to onset were 2.7 months for tracheobronchitis or bronchial anastomotic infections, 5.5 months for invasive pulmonary, and 10.6 months for systemic infections.

Invasive aspergillosis occurs in 3.3 to 14% (average, 6%) of heart transplant recipients). *Aspergillus* infections are the most commonly occurring mycoses in heart transplant recipients, accounting for 69.8% of all invasive fungal infections after heart transplantation. The usual time of onset of invasive aspergillosis is 36 to

52 days posttransplantation, with nearly 75% of the cases occurring within 90 days of transplantation. At one institution, the onset of invasive aspergillosis was shown to

Have been significantly delayed by the introduction of routine ganciclovir prophylaxis for cytomegalovirus infection.

In renal transplant recipients, invasive aspergillosis has been reported in _0.7% and in up to 4% of patients. Despite a relatively lower overall incidence compared to other organ transplant recipients, invasive aspergillosis is a significant contributor to morbidity in renal transplant recipients.

DIAGNOSIS

Substantial delay in establishing an early diagnosis remains a major impediment to the successful treatment of invasive aspergillosis. Cultures of the respiratory tract secretions lack sensitivity. *Aspergillus* is grown from sputum specimens in only 8 to 34%, and from BAL specimens in 45 to 62%, of patients with invasive aspergillosis. Thus, confirmation of the diagnosis of invasive aspergillosis has typically required histopathologic evaluation.

Characteristic radiographic findings on high-resolution imaging studies e.g., the halo sign, have allowed earlier diagnosis of infection in neutropenic patients.

The halo sign, however, is documented in 33 to 60% of patients and is short-lived . To be useful for the diagnosis of invasive aspergillosis, the computed tomography scan must be performed within 5 days of the onset of infection, since _75% of the initial halo signs disappear within a week. The “air crescent” sign does not appear until the third week of the illness, and its appearance may be too delayed to be helpful in the diagnosis of invasive aspergillosis

Aspergillus galactomannan.

Galactomannan is a polysaccharide cell wall component of *Aspergillus* species that is released into the circulation during fungal growth in the tissues.

The double-sandwich enzyme-linked immunosorbent assay, on the other hand, can detect galactomannan at concentrations of as low as 0.5 ng/ml and has proven to be a potentially promising tool for the early diagnosis of *Aspergillus* infection.

Aspergillus DNA detection by PCR assays. PCR-based molecular diagnostic tests for *Aspergillus* are not commercially available and remain largely unstandardized. Such assays, when performed on blood or BAL samples, have shown a negative predictive value for invasive aspergillosis ranging from 92 to 99%. Thus, a negative test would suggest a low likelihood of invasive aspergillosis.

MANAGEMENT

The following FDA-approved compounds have in vitro, in vivo, and clinical activity against *Aspergillus* species and are licensed for treatment of invasive aspergillosis:

D-AMB and its lipid formulations (AMB lipid complex [ABLC], L-AMB, and AMB colloidal dispersion [ABCD]), itraconazole, voriconazole, posaconazole, and caspofungin.

Invasive pulmonary aspergillosis: Voriconazole (6 mg/kg IV every 12 h for 1 day, followed by 4 mg/kg IV every 12 h; oral dosage is 200 mg every 12 h)

L-AMB (3–5 mg/kg/day IV), ABLC (5 mg/kg/day IV), caspofungin (70 mg day 1 IV

And 50 mg/day IV thereafter), micafungin (IV 100–150 mg/day; dose not establishedc), posaconazole (200 mg QID initially, then 400 mg BID PO after stabilization of diseased), itraconazole (dosage depends upon formulation)

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Review16

BK virus nephropathy in pediatric renal transplantation

Mostafa Sharifian,* *Bijan Hatamian, Abdollah Karimi, Zahra Rahmani, Mahdiyeh Kiahosseini, Reza Dalirani.*

**** Corresponding Author:***

Pediatric Infectious Research Center, Mofid Children's Hospital, Shaheed Beheshti Medical University,Tehran, Iran.

Email: mostafasarifian@yahoo.com

Abstract:

Opportunistic infections are leading causes of morbidity and mortality in transplant patients. Viral infections are a well known complication in immunosuppressed and transplant recipients. Different viral strains have been observed in the allograft, such as CMV, EBV, Herpes Simplex Virus and polyomaviruses of the BK-strain.

BK and JC-Virus belong to the polyomavirus family of double stranded non-enveloped DNA viruses. After a primary infection, which is usually without apparent clinical symptoms, polyomaviruses can remain in a dormant state in the kidneys and ureters of asymptomatic individuals. Under immunocompromised conditions, latent viruses can be reactivated and cause viral nephropathy.

BK nephropathy is an important cause of renal transplant dysfunction, especially in patients with high levels of immunosuppression. BK virus (BKV) is a human polyomavirus associated with a range of clinical syndromes in immunocompromised hosts: viruria and viremia, ureteral ulceration and stenosis, and hemorrhagic cystitis. Up to 85 percent of adults have serologic evidence of exposure to the virus, suggesting the presence of asymptomatic, latent infection. We are investigating its prevalence in our pediatric transplant population.

Active infection of renal allografts has been associated with progressive loss of graft function in some patients.

The diagnosis of BK virus Nephropathy (BKN) can be made histologically in a graft biopsy. The morphological hallmarks are intranuclear viral inclusions seen exclusively in epithelial cells, and focal necrosis of tubular cells

Inclusion bearing cells in the urine can be detected in Papanicolaou stained smears. These cells are named decoy cells. They can be mistaken for tumor cells particularly if nuclei show vesicular changes. Decoy cells are characteristic but not pathognomonic finding in patients with BKN.

Untreated BKV infections can cause kidney allograft dysfunction or loss. Decreased immunosuppression is the principle treatment but predisposes to acute and chronic rejection. Although no approved antiviral drug is available, leflunomide, cidofovir, quinolones, and intravenous immunoglobulin have been used with different success rates. We will present our experience in renal transplant children.

Keywords:
Renal Failure; Renal Transplantation; BK Virus; Nephropathy; Children.

Review17

Mycobacterial infection in the transplant patients

Hamid Emadi.
Department of Infectious Diseases, Imam Khomeini Hospital, Tehran University of Medical Sciences,Tehran , Iran.
Email: dr_emadi@yahoo.com

Tuberculosis and non-tuberculous mycobacterial infections after solid organ transplantation are serious opportunistic infections that may affect transplant recipients and can be associated with significant morbidity and mortality, and diagnosis and treatment are often challenging.

The incidence of tuberculosis among such persons is 20-74 times higher than that for the general population, with a mortality rate of up to 30%. On the basis of the compilation of published reports in the literature, the incidence of Mycobacterium tuberculosis infection in organ transplant recipients worldwide ranged from 0.35% to 15%. Non-renal transplantation, rejection within 6 months before the onset of tuberculosis and type of primary immunosuppressive regimen are predictors of M. tuberculosis infection occurring within 12 months after transplantation.

The most common form of acquisition of tuberculosis after transplantation is the reactivation of latent tuberculosis in patients with previous exposure.

Clinical presentation is frequently atypical and diverse, with unsuspected and elusive sites of affection. Manifestations include fever of unknown origin and allograft dysfunction. Co-infection with other pathogens is not uncommon.

New techniques, such as PCR and quantification of interferon- gamma have been developed to achieve more-rapid and -accurate diagnoses, and are more specific than

the tuberculin skin test to detect latent tuberculosis infection because of lack of cross-reactivity with BCG and most non-tuberculous mycobacterial infections.

Treatment requires control of interactions between antituberculous drugs and immunosuppressive therapy. Treatment with or without rifampicin is possible; the former is associated with a higher risk for allograft rejection.

Prophylaxis against latent tuberculosis is the main approach to treatment, but many issues remain unsolved, because of the difficulty in identifying patients at risk (such as those with non-reactive purified protein derivative test results) and the toxicity of therapy. Isoniazid prophylaxis is recommended for high-risk patients with apparent clinical efficacy. Clinically significant hepatotoxicity due to isoniazid occurred in 2.5%, 4.5%, and 41% of renal, heart and lung, and liver transplant recipients, respectively. The diagnosis and effective management of tuberculosis after transplantation warrant recognition of the unique epidemiological and clinical characteristics of tuberculosis in transplant recipients.

Review18

Fungal infections in the patient with cancer

Hossein Zarrinfar, *Abdolmajid Fata.*
Corresponding Author, Department of Parasitology and Mycology, Tehran University of Medical Sciences,Tehran, Iran.
Email: h.zarrin@gmail.com

Abstract:
Introduction: The use of high-dose cytotoxic chemotherapy and peripheral blood stem cell transplantation (PBSCT) for malignant disorders has contributed to the increased incidence of invasive fungal infections. Cancer patients display unique features as a result of cytotoxic chemotherapy (neutropenia, mucositis) and allogeneic transplantation.

Risk of Fungal infections in cancer patients: It depends on the interaction of several factors: the patient's net state of immunosuppression (type, degree and pace, and duration), the presence of tissue damage, and the patient's degree of exposure to pathogens. Environmental exposure to *Aspergillus* spp. through contaminated heating and cooling systems, *Candida* spp. form health care workers, and *Fusarium* spp. through hospital water systems have been associated with both sporadic cases and outbreaks of invasive fungal infections among cancer patients. The use of antifungal agents may also play an important role in changing the epidemiology of fungal pathogens in cancer patients: fluconazole-resistant *Candida* spp. have been associated with the widespread use of fluconazole prophylaxis.

Fungal infections of particular important: Candidiasis, although *C.albicans* used to be the *Candida* spp. most commonly isolated from blood and deep-tissue sites in cancer patients, the proportion of infections attributed to other members of this genus (*C.krusei, C.glabrata*, and *C.parapsilosis*) is rising. Aspergillosis, from 20%

to 30% of all fungal infections occurring in patients with acute leukemia and in allogenic bone marrow transplant recipients are caused by *Aspergillus* spp. Fusariosis, *Fusarium* is the second most common opportunistic mold after *Aspergillus* spp. in severely immunocompromised patients. The incidence of fusarial infection is around 1.2% among patients undergoing allogeneic PBSCT, but only 0.2% among autologous recipients. Cryptococcosis, meningitis is the most common clinical presentation, with pulmonary and skin manifestations occurring less frequently. Others, *Trichosporon beigelii* and *Blastoschizomyces capitatus, Zygomycetes, Saccharomyces cerevisiae, Rhodotorola* spp. *Malassezia furfur*, and the agents of phaeohyphomycoses and hyalohyphomycoses are increasingly reported among immunosuppressed cancer patients.

Antifungal therapy: L-AmB (AmBisome has a lower incidence of infusion-related adverse effects than CAmB and reduces the risk of emergent fungal infections, Fluconazole seems to be as effective as amphotericin B for the treatment of hematogenous candidiasis, but is not effective against aspergillosis, Flucytosine in combination with other antifungal agents may be useful for the treatment of hematologic candidiasis and cryptococcosis.

Keywords:
Fungal Infections; Cancer.

Review19

Preventing iron take ups by pathogens: a way for confronting medicinal resistance

Iraj Rasooli
Shahed University, Tehran, Iran.
rasooli@shahed.ac.ir

Abstract:
Background & Objectives:
Iron is the only element which prevents growth. Though it is the fourth most frequent element on earth, due to its insolubility under physiologic conditions, it is not accessible by most microorganisms. Hem is the most frequent part of the body with iron. There are, therefore, microorganisms which can utilize hem as a source of iron. These microorganisms possess two superficial receptors for extracting iron from hem. HmbR is a protein of the outer membrane that utilizes iron from both hemoglobin and hem. The bacteria may utilize hem, hemoglobin and hemopoccin as sources of iron. In gram negative bacteria, hem or its complexes are attached to the exterior membrane and then, through the receptor canal they enter an energy related process known as TonB-ExbB-ExbD. They are , therefore similar to the receptors which take up sidrofur, transferrin, and lactoferrin.

Review20

Screening and prevention of infection in transplantation

Masomeh Alimagham
Shahid Beheshti Medical University
Email: dralimagham@yahoo.com

Increasingly potent immunosuppressive agents have dramatically reduced the risk of rejection of transplanted organs while increasing patients susceptibility to opportunistic infections and cancer.

The risk of infection after transplantation changes over time,particularly with modifications in immunosuppression. Unfortunately, no assays accurately measure a patients risk of infection.

Prophylactic strategies are based on the patients known or likely exposures to infection according to the results of serologic testing and epidemiologic history.

Epidemiologic exposure

Epidemiologic exposure can be divided in to four overlapping categories: donor-derived infections , recipient-derived infections , nosocomial infections , and community infections .

Donor screening

Epidemiologic history

serologic testing for VDRL, HIV, CMV, EBV, HSV, VZV, HBV(HBsAg,Anti-HBsAg), and HCV.

Microbiologic testing of blood and urine

Chest radiography

Known infections (appropriate therapy?)

Possible infections(encephalitis,sepsis)

Special serologic testing,nucleic acid assays,or antigen detection based on epidemiologic factors and recent exposures(toxoplasma,westnile virus,HIV,HCV)

Recipient screening

Epidemiologic history

Vaccination history

Serologic testing for VDRL,HIV,CMV,EBV,HSV,VZV,HBV(HBsAg,anti-HBsAg)and HCV

Tuberculin skin test

Microbiologic testing of blood and urine

Chest radiography

Known infections,past colonization:prophylaxis? , active infection:appropriate therapy?

Possible infections (encephalitis,sepsis)

Special serologic testing, nucleic acid assays, or antigen detection based on epidemiologic factors and recent exposures (strongyloides, histoplasma, coccidioides, HBV or HCV viral load)

Assessment of the risk of infection at the time of transplantation

The risk of infection transmitted from the organ donor or activated in the recipient can be assessed at the time of transplantation.

Donor and the recipient screening are based on the epidemiologic history and serologic testing.

The use of sensitive molecular and protein-based assays may enhance the safety of organ transplantation while expanding the use of potentially infected grafts.

The transplant recipients risk is a function of the technical outcome, epidemiological factors, and the intensity of the immunosuppression.

Prevention of infection

Antimicrobial prophylaxis has dramatically altered the incidence and severity of post-transplantation infections.

Three general preventive strategies are used: vaccination, universal prophylaxis, and preemptive therapy.

The need for immunization against measles, rubella, diphtheria, pertussis, tetanus, HBV infection, poliomyelitis, varicella, influenza, and pneumococcal pneumonia should be evaluated before transplantation.

Vaccination is generally less effective during immunosuppression.

Pneumococcal vaccine is recommended every 3 to 5 years, and influenza vaccine is recommended annually.

Other vaccines are appropriate for patients who travel to regions where certain illnesses are endemic.

Live vaccines are generally contraindicated after transplantation, since they may cause disseminated infection in immunocompromised hosts.

The immunologic protection provided by vaccines may be limited in extent or duration.

Promoting life style changes after transplantation may help limit exposure to some potential pathogens (like hand washing….).

Routine surgical prophylaxis varies, depending on the organ transplanted and local epidemiologic factors.

Anti fungal prophylaxis is based on both risk and epidemiologic factors.

Most transplantation centers use trimethoprim-sulfamethoxasole prophylaxis for as little as 3 months or as long as a life time to prevent PCP as well as infections with toxo,isospora,cyclospora,nocardia,and listeria species, and common urinary, respiratory, and gastrointestinal pathogens.

The prevention of post-transplantation CMV and other herpesvirus infections and the availability of oral antiviral agents have revolutionized post-transplantation care.

The crude risk of specific infections has traditionally been defined by means of serologic testing, the risk is lower in a seropositive host or higher in a seronegative recipient of an organ from a seropositive donor.

A variety of newer techniques (HLA-linked tetramer binding and intracellular cytokine staining) measure pathogen-specific immunity and provide insight into the risk of specific infections and the ability of the host to clear invasive disease.

Changes in immunosuppressive regimens,routine prophylaxis,and improved grft survival have altered the original pattern of infections in transplantation,and new pattern of infections have emerged.

Review21

Screening of infections in transplantation

Shirin Afhami
Shariati Hospital,Tehran University of Medical Sciences,Tehran, iran.
Email: Afhami8@hotmail.com

Abstract:

Infection is the major cause of mortality and morbidity in transplant recipients. Therefore, screening and prevention of common transplant-associated infections have been recommended for accurate management of infectious complications in immunosuppressed patients.

Screening of infections are recommended as follows:

● Donor and recipient should be screened by CMV serology prior to transplant
● Donor and recipient should be screened by EBV serology prior to transplant
● Pre-transplant recipient serology should be obtained for HSV1, HSV2 and VZV
● Screening for HCV should be performed on all patients awaiting liver transplantation
with an EIA ± qualitative PCR
● Screening for HCV can be performed on all patients awaiting nonliver transplantation
with an EIA or a qualitative PCR
● Hepatitis B screening (HbsAg, HBcAb, HbsAb)
● HIV Ab
● Toxoplasma Ab (heart recipients)
● Tuberculin skin test
●Stool for ova and parasites

Screening of infections are not routinely required for :

- Polyomavirus (BK)
- Fungal infections
- Bacterial infections

Since the type, frequency and presentations of infectious complications associated with transplantation will continue to change; these recommendations will continue to evolve undoubtedly.

Review22

Renal transplantation and UTI

Farzaneh Solaimanizadeh,* *Laleh Solaimanizadeh, Roya Ahmad Rajabi.*
**** Corresponding Author:***
College of Nursing, Bam, Iran.
Email: fsolaimanizadeh@yahoo.com

Abstract:
Background & Objectives:
Urinary Tract Infection (UTI) is the most frequent infection after renal transplantation (RT). The literature shows an incidence between 10-98%. The risk of associated bacteraemia is close to 12%. During the first post-transplantation year, 40-80 percent of transplant recipients experience at least 1 infection. Infection of 32% was the most common cause of death. Gram-negative bacteria are the most frequent causal agents (70%), although gram+, mainly enterococcus and staphylococcus, Candida and some other exotic germs such as Corynebacterium are also potential etiological agents.
Theme:
Certain factors present in the receptor during pre-RT, RT itself and post-RT condition the development and evolution of UTIs. Clinical signs and symptoms are multiple ranging from asymptomatic bacteriuria to graft's abscess or septic shock. Incidence in females (54%) is higher than in males (29%). Immunosuppressive regimes based on Cyclosporine (35%) show lower incidence of UTI than those based in Azathioprine (50%).

Conclusion:

Antibiotic prophylaxis with Co-trimoxazol reduces incidence of UTIs at post-RT and delays the time of appearance of the first UTI episode. These infections are decreasing as more transplant recipients receive preoperative immunizations and take post transplantation anti biotic prophylaxis.

Keywords:

Infection; Renal Transplant; Urinary Tract.

Review23

The Role of granulocyte growth factor in fever and neutropenia

Nematollah Rostami,
Department of Oncology, Moddarres Hospital, Shahid Beheshti Medical Universit, Tehran, Iran.
Email: ne_rostami@sbmu.ac.ir

Abstract:

Introduction:

This group of glycoproteins which are known as growth factor of blood producing cells have important roles in reproduction and differentiation of blood cell… .

In the 1960 the role of granulocyte growth factor in the reproduction of blood cells was recognized, and 20 years later, its structure was begun to be made after its gene was determined. In animal studies, its role in neutrophil proliferation, especially after bone marrow suppression became known.

Physiology:

G-CSF or Granulocyte Colony Stimulating under natural conditions is primarily secreted from monocytes, macrophages, and endothelial cells under other factors such as $IL_1$and TNF. These factors will have their influence through the receptors of immature ……granulocyte cell walls. These factors are necessary in responses to infection.

Usages:

The usages of G-CSF are vast and numerous as follows:

The usage in chemotherapy: granulocytopenia is one of the common complications in chemotherapy. G-CSF is used under the following conditions:

1) Primary Prophylaxis: In most chemotherapy treatments attention is not paid to prophylactic functions. However, studies have shown that the hospitalization period and nutropenia will reduce under G-CSF usage.

2) Secondary Prophylaxis: In patients with fever and nutropenia it is better to use G-CSF for one course which is recommended in tumors such as lymphoma, and leukemia, in orde not to reduce the recommended dosage.

3) Fever and Nutropenia: Probability of infection onset in patients with cancer following chemotherapy is dependent upon the severity and length of nutropenia. It does not mean that all patients with fever and nutropenia will die. These patients may be divided into two groups of low risk and high risk groups.

Low Risk Group:Patients with nutropenia period of 7-10 days have controllable tumors such as breast cancers, while patients with a nutropenia period of more than 10 days, such as patients with blood cancers, or bone marrow transplantations, the risk of infection and complications increase. These are in the high risk group. Therefore, the following recommendations are suggested by oncology authorities such as ASCO:

1)In low-risk patients, G-CSF is not recommended.

2) In patients in the high risk group, G-CSF is recommended to be used to reduce pneumonia, organ dysfunctions, hypertension, fungi infection, and nutropenia for for than 10 days. However, G-CSF can reduce nutropenia, yet it can not reduce mortality.

G-CSF in Bone Marrow Transplantation Patients: This patients will require G-CSF due to the severity of their underlying diseases.

Complications: The most common complications in G-CSF usage is muscular pain seen in 20-30 % of the patients. The pain may be due to myeloid proliferation in bone marrow.

Review24

The prevention and treatment of infections disease in transplanted patients:

Mohammad Reza Ganji,
Shariati Hospital. Tehran University of Medical Sciences, Tehran, Iran.
Email: mrezaganji@yahoo.com

One of the most successful goals in last decade in medicine is transplantation with > 90% survival in first year compare to 70% in previous era. This success build up or understanding of tissue typing and level of sensitization, better donor selection and surgical techniques, improving new immunosuppressive protocol to prevent and treat rejection and prophylactic antimicrobial managements. But with introduction of new drugs, still there is a lag for proper clinical trial, for prevention and treatments of infectors, so optimizing screening and diagnostic laboratory tests with light sensitivity and specificity needed for proper diagnosis and aggressive treatment of microbial invasion when prevention fails. Following observation should be accounted in immunosuppressed patients that due to anti-inflammatory effects of drugs, the infection presentation is occult with delayed diagnosis and greater microbial load. Low antibody titer due to interaction of immunosuppressive drugs will add to the problem for diagnosis by serology. Followings are brief discussion of the most prevalent infections in post transplant period with emphasis on UTI.

Cytomegalovirus (CMV):

CMV is one of the most common opportunistic pathogen in the first several months following solid organ transplantation. Without preventive therapy, infection occurs in 60-70% of recipients at risk and disease in up to 20%. Consequences of infection are often characterized as 'direct' versus 'indirect' effects. Direct effects are

symptomatic CMV syndrome and tissue invasive disease; these entities are well-defined and clearly related to viral replication. Indirect effects are postulated to be causally related to increases in rejection, graft dysfunction, graft loss, patient mortality and other infections. Two approaches to prevention of CMV disease are used widely, prophylaxis and preemptive therapy. Using prophylaxis, patients at risk (R-/D+ and R+) receive anti-viral treatment, typically for 90-100 days post-transplant. Using preemptive therapy, patients are monitored with pp65 antigenemia or PCR to identify viremia before the onset of symptoms or tissue invasion. Patients with viral replication receive therapeutic doses of anti-viral treatment. By definition, preemptive therapy does not aim to prevent infection but rather to prevent disease. Recent data showed that prophylaxis, compared to no prevention, significantly reduces the risk of CMV disease, CMV infection, overall mortality and other infections caused by herpes viruses and bacteria. Data on direct comparisons between prophylaxis and preemptive therapy are sparse. But the incidence of CMV infection during the first year post-transplant was significantly lower in the prophylaxis groups versus the preemptive therapy groups [29% vs. 59%, p = 0.004 and 41 % vs. 75%, p = 0.007] in the last trials. Thus, even with 'late' CMV infections following the end of prophylaxis, the overall incidence of CMV infections during the first year was lower with prophylaxis versus preemptive therapy.

Screening:

Donor and recipient should be screened by CMV serology prior to transplant.

Monitoring:

-All risk groups except D-/R- should be monitored by using quantative viral load assays.

-Monitoring once a mouth for the first year, CMV most commonly occur in the 1st-4th mouth

Post-transplant, but if you use prophylaxis it can delay the onset of CMV.

Epstein-Barr Virus (EBV):

EBV infects human with 40-90% by adolescence. The oncogenic potential of EBV relates to its ability to transform and immortalize B-lymphocyte leading to post transplant lymphoproliferative disease (PTLD).

The risk present especially in D+/R- , and it is infrequent in soropositive recipient.

Monitoring:

Serology in both donor and recipient, EBV VCA IgG and EBNA Abs recommended, and followed by PCR (nucleic acid based) post transplant in seronegative recipient monthly in the first year and in seropoitive patient when there is high viral load or change in immunosuppression after first year.

Other herpes viruses: HZV, HSV and Human Herpes virus (HHV)-6,-7,-8

Screening:

-Pre transplant recipient serology should be obtained for HSV1, HSV2 and VZV.

-Monitoring:

Not recommended routinely

HHV-8 monitoring in high risk patient (HIV).

BK Virus:

BK infection clinically defined on viruria or viremia. When decoy cell in urine is suggestive for infection confirmation needed by PCR or renal biopsy. Proven nephropathy is defined by the presence of a) ATN-like picture b) Interstitial nephritis mimicking acute rejection or c) chronic allograft nephropathy + prescience of BK virus in biopsy.

Screening for BK virus:

-Not recommended pre transplant.

Monitoring:

-For trials, monitoring blood, serum or urine monthly for 6 month, then as 9,

and mouth 12,
then every 3 mouth for 2 years.

HCV:
Screening: in all patients with Enzyme immunoasay (EIA) or a qualitative PCR.
Monitoring: every 3 month in the first year by RNA-PCR and pre transplant liver biopsy.

Fungal infection:
There is no recommendation for screening and monitoring of fungal infections.

Urinary tract infections:
UTI is the most reported infections. Due to direct effect of infection on graft survival prompt
diagnostic and treatment of UTI is mandatory.
Bacterial infections: At least 10^5 bacteria per ml of fresh unspun midstream urine. In a
symptomatic transplant recipient, a pure culture of at least 10^2 bacteria per ml with
pyuria is diagnostic.
Asymptomatic bacteriuria should be defined as at least 10^5 bacteria per ml of urine, no
evidence of pyuria >3/ hpf of unspan urine (> 10 WBC/hpf) or positive leukocyte esterase
(ideally from two separate samples).
Acute uncomplicated cystitis: positive urine culture +pyuria , +/- dysuria, frequency and
urgency.
Acute pyelonephritis or graft pyelonephritis: positive culture + pyuria and graft tenderness, with fever and or positive blood culture.

- 72% occurred after the first 6 months

- 13% occurred in the first months.

Early UTI: (4-6 months after Transplantation), treated for 10-14 days with antimicrobials

If ureteric stent is present, it should be removed and sent for culture.

Cystitis with sepsis or pyelonephritis

Requires 10-14 days of antimicrobial therapy

Two empirical intravenous antibiotics

Uncomplicated late UTIs: treated for 5-7 days.

Relapsing or recurrent UTI

Treated for six week or more

Prophylactic antimicrobials

- A single dose of second or third generation cephalosporin before induction of anesthesia
- A single dose of second or third generation cephalosporin before removal of urethral catheters
- 3-6 months of antimicrobial prophylaxis(Co-Trimaxazole)
- Risk of UTI 98% without prophylaxis

Graft outcome after UTI

- Inflammatory cytokine response
- Free radical production
- CMV reactvation
- Precipitation of rejection
- Pyelonephritis-induced renal scaring
- Urinary level of granzyme B messenger RNA to be raised during rejection but

undetectable during UTI Can differentiate Rejection wih pyelonephritis

Screening of UTI:

- Interleukin 8

- Gram negative endotoxin
- Limulus amebocyte lysate test

UTI outcome:

- Graft dysfuction
- Sepsis
- Death

Management of infective episodes

- Antibiotic to cover both gram-negative and gram-positive bacteria
- Cystitis without signs of sepsis can be managed on an outpatient basis.
- Pyelonephritis requires admission to hospital, parenteral antibiotic and hydration.
- Follow up culture for eradication of organisms

Effect of interactions between antimicrobials and immunosuppressants:

Aminoglicosides :

Increase risk of nephrotoxicity when administered with cyclosporin or tacrolimus

Trimethoprin :

Reversibly inhibits tubular secretion of creatinine

Increases risk of nephrotoxic effects when administered with cyclosporin

Reduced plasma concentration of cyclosporin when administered intravenously

Erythromycin

Increase plasma concentration of ciclosporin and tacrolimus via inhibition of cytochrome P450 synthetase

Rifampin

Reduced plasma concentration of ciclosporin and tacrolimus via inhibition of cytochrome P450 synthetase

Amphotericin

Increase risk of nephrotoxicity when administered with cyclosporin or tacrolimus

Increased risk of hypokalemia when administered with steroid

Conazoles
Increase plasma concentration of ciclosporin and tacrolimus via inhibition of cytochrome P450 synthetase

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Review25

Diagnostic virology in transplant recipients

Seyed Alireza Nadji, Ph.D
National Research Institute of Tuberculosis and Lung Disease, Shaheed Beheshti Medical University, Tehran, Iran.
Email: sarnadji@nritld.ac.ir

Abstract:
Perturbations of immunity can influence the pathogenesis of viral infections in several ways. In all profoundly compromised- immune system situations, patients predispose to unusually severe or prolonged infections with a wide range of viruses. Prominent among these is increased frequency or severity of disease, exemplified par excellence by the debilitating manifestations of many herpesvirus infections in immunocompromised hosts.

Diagnosis of viral infections in immunocompromised patients can be difficult. Total and differential leukocyte counts tend to be unhelpful, clinical signs and symptoms of infection are often atypical, and symptoms produced by the host's immune response may be absent.

Serology has little role in diagnosis because patients with dysfunctional immunity do not usually mount appropriate immune responses rapidly enough to influence decisions about management.

The mainstay of diagnosis is detection of virus in appropriate clinical specimens: rapid procedures, such as direct antigen detection, nucleic acid detection and culture amplified enzyme immunoassays, have increased the usefulness of laboratory diagnosis enormously.

In post-transplantation, regular surveillance may be helpful; virus shedding may precede the onset of symptoms, and initiation of therapy as soon as virus is detected may prevent extensive tissue damage.

Herpesviruses, Adenoviruses, Respiratory viruses and BKV and JCV are the important opportunistic pathogens in transplant recipients.

Oral1

A Comparative study of saprophyte fungi in Oncology and bone marrow transplantation at Shariati Hospital inTehran

Mitra Amooqoli-Tabari,* *Seyed Jamal Hashemi*
Corresponding Author :
Microbiology Department,Beheshti Hospital, Babol, Iran.
Email:mitratabari@yahoo.com

Abstract:
Background & Objectives:
Bone marrow transplantation is one of the most important traputhic methods in many malignant and non malignant diseases. Recipients of bone marrow transplantation suffer immunity systems due to radiotherapy and chemotherapy followed by neoutropenia and Graft Versus Host Disease (GVHD). These patients are usually polluted through air and instruments in wards of hospital pre- and post-transplantation. Therefore, evaluation of the fungal flore in air and instruments in patients' rooms and clinical sample for comparison and probably estimatied pullution becomes necessary.
Materials & Methods:
This 8-month survey was done in space, instruments and ventilators of Blood and Oncology Center wards and clinical samples in patients with transplantation. Methods of this survey was based on sampling from space around patients to used plates containing saboro dextrose agar with choloramphnicol(SC) and sampling from instruments. Sampling from vantilators in wards was used by soap strile, and they were cultured on (SC). Rotine clinical samples such as (sputum,urine, nasal

discharges)and doubtful clinical samples such as (CSF fluid, Pricard fluid ,…)were cultured on (SC) and direct examination to bludo metylen.

Results:

In this survey, from 4838 plates , 985 postive fungal cases were isolated, including Penicillum(33.6%), Cladosporium(33.4%), Aspergillus flavus(11.6%). From rotine clinical samples we did not isolate postive fungi cases. But from 50 doubtful patieants who were isolated, 3 postive cases from whom 2 cases showed aspergillus flavus and 1 case Trichoderma from nasal sinus discharge was seen.

Conclusion:

Considering the results found in the present study, it seems that proper ventilation plays a major role in decreasing fungal infections. It is necessary to perform direct examinations and cultures on SC.

Keywords:
Saprophyte fungi;Bone Marrow Transplantation

Oral2

Pulmonary infiltrates in cancer patients. A comparison between solid and oncohematologic tumors

Marcelo Zylberman, Fernando Diaz Couselo, Jose Moereo, Flavio Sanchez, ***Mostafa Alavi-Moghaddam*** *

* ***Corresponding auther:***
Shaheed Beheshti University, Tehran ,Iran
Email: mosalavi@yahoo.com

Abstract:

Background & Objectives:

We compared the etiology, diagnostic methods utilization, ICU admission and in hospital mortality between patients with solid and oncohematologic tumors with pulmonary infiltrates (PI).

Materials & Methods:

Between August 2003 and March 2006 all patients with cancer and new PI admitted to the IAF, and they were prospectively included in the study. Diagnostic methods were applied according to a pre- specified protocol in sequential steps of complexity (The first step: radiological pattern of the PI, blood and sputum cultures, serological tests and empirical treatment response; (The second step: BAL, non bronchoscopic treatment aspirate and mini- BAL; (The third step: pulmonary or estrapulmonary biopsies). PI aetiology was classified as: infection, treatment complications, disease progression, cardiovascular or mixed. Diagnosis was classified as proven (histopathologic, microbiologic and / or serologic confirmation) or probable (cases not categorized as proven diagnosis with treatment response to a presumptive

diagnosis). Patients not categorized as proven nor probable diagnosis were classified as non- diagnostic. Descriptive statistics, x^2 and Fisher exact test were used.

Results:

106 cases out of 103 patients were included: 63 male and 43 female. Median age: 58 years (18-83). Seventy seven cases had solid and 29 had oncohematilogic tumors. Etiology in the solid tumor group (STG) was: infection in 41 cases (38 bacterial, 2 mycotic and 1 mycobacterial), disease progression in 4, and treatment complications in 1, cardiovascular in 6 and mixed in 6. Nineteen cases classified as non- diagnostic. In the oncohematilogic group (OHG), 20 cases were infection (11 bacterial, 8 mycotic and 1 viral), 5 treatment complications, 1 mixed. Three cases were classified as non- diagnostic. Mycoses were more frequent in the OHG ($p<0.001$). Bacterial infection was more frequent in the STG ($p<0.01$). In the STG, 76.6% cases were diagnosed at the first step, while 23.4% of the cases stopped at the second step. In the OHG, 37.9% cases were diagnosed at the first step, 48.3% at the second and 13.8% of the cases reached the highest stage. Proven diagnosis was obtained in 24.7% cases in the STG and 27.6% cases in the OHG. Probable diagnosis was obtained in 51.9% and in 58.6% cases, respectively. No diagnosis was achieved in 23.4% and 13.8% cases, respectively. BAL was done in 14.3% cases in the STG and 37.9% cases in the OHG ($p<0.01$). Thirty nine percent in the STG and 41.4% in the OHG, were admitted to the ICU. Mortality was 33.8% in the STG and 20.7% in the OHG (Pns). In neutopenic cases in hospital, mortality was 37.5% as compared to 28.9% in non neutropenic (Pns).

Conclusions:

In our study, infection was the most frequent etiology of the PI in both groups. Mycoses were more frequent in the OHG and bacterial infections in the STG. BAL were used more frequently in the OHG. ICU admission and mortality were similar in both groups. There was no difference in mortality between neutropenic and non neutropenic patients.

Keywords:
Tumors; Pulmonary Infiltrates; Cancer Patients; Oncohematology.

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Oral3

A Study on fever and its causes among in-patients at the radiotherapy ward in Imam Hussein Hospital,Tehran in 2006

Simindokht Shoaie,* *Morteza Tabatabaiefar, Melodi Omrani Nava.*
Corresponding Author
Department of Infectious Disease, Imam Hossein Hospital, Shahid Beheshti Mdical University, Tehran, Iran.
Email: drsimin2@yahoo.com

Abstract:
Background & Objectives:
The goal of this study is to determine the incidence and etiology of fever, after radiotherapy in admitted patients with malignancy in Radiotherapy Unit in Imam Hussein Hospital, Tehran.
Materials & Methods :
In this survey, febrile patients with secondary to radiotherapy in the unit without age, sex and kind of malignant disease limitations were studied, from March 2006 to March 2007. Forty four cases from 320 admitted patients had fever (oral temperature >38^0c, more than one hour). An exact history, repeated examination and routine para-clinic tests on the basis of involved system in primary findings were done. Numeric parameters including age, sex, neutropenia, steroid therapy, chemotherapy, oral mucositis and field of radiotherapy were studied.
Results:
From 320 patients with radiotherapy in Radiotherapy Unit, 44 persons (14%) had fever (55% F + 45% M), 9% were under age of 30, 68% between 30-70 and 23% over 70 years old. Forty four percent had radiotherapy to abdomen and pelvis,

32% to thorax, 20% to head and neck and 4% in other sites, 77% with concurrent chemotherapy and 28% with concurrent steroid therapy. In 22%, oral mucositis and 50% neutropenia were seen. Infectious etiologies include: pneumonia(18%) , UTI(18%) , oral mucositis(14%) , dysentery(11%) , sepsis syndrome(5%) , PID(2%) , peritonitis(2%) , mediastinitis(2%) , wound infection(2%) and noninfectious etiologies include: DVT(2%) , after transfusion(2%) , after hemodialysis (2%) and idiopathic(18%). Detailed data of etiology due to site of radiotherapy are presented in full text.

Discussion:

The most important factors in causing fever are chemotherapy accompanied with radiotherapy, and fever isn't prevalent in radiotherapy alone. Neutropenia is obvious in chemotherapy accompanied with radiotherapy and radiation place is very important because of its effects on bone marrow stem cells in adults, especially in gastrointestinal tract and pulmonary system malignancies.

More prevalent factors in causing fever in common radiotherapy (Particularly accompanied with chemotherapy) are infectious.

Keywords:
Radiotherapy; Fever; Infectious Etiology; Noninfectious Etiology.

Oral4

Efficient therapy for mucormycosios

Alirezad Fahimzad
Pediatric Infectious Research Center(PIRC) ,Faculty of Medicine, Shahid Beheshti Medical University, Tehran, Iran.
Email: safahimzad@yahoo.com

Case Presentation:

Mucormycosis, an infection that is associated with significant morbidity and mortality, after aspergillosis is the second most common mycosis caused by filamentous fungi. A delayed diagnosis means that appropriate doses of antifungal treatment and efficient surgical debridement are started late, which can have the consequence of increasing the number of failures. We report a case of rhinocerebral mucormycosis in a neutropenic child with underlying hematologic malignancy. He was cured with antifungal therapy including amphotericin B followed by oral posaconazole, surgery, and medical management of the nertopenia.

Keywords:
Mucormycosis, Neutropenia, Posaconazole, Children

Case report:

An 4 years old boy known case of acute lymphoblastic leukemia (type L_1) who became neutropenic after one month chemotherapy.He lived in khash city from south east of Iran. He had necrotic ulcer between right eye medial canthus and nasal bridge following neutropenia.(figure1) This progressive ulcer was associated with black nasal discharge. CT scan of sinuses was shown right maxillary and etmoidal involvement with necrotic nasal septum. Right globe and orbital area was intact. Ulcer biopsy was illustrated skin, subcutaneous and muscle fibers necrosis with neutrophils infiltration. Numerous fungal wide hyphae with right angle branching were seen that invading the vessel walls compatible with mucormycosis.

Antifungal therapy with parentral Amphotericin B was started after disruption of chemotherapy. The patient became afebrile after wide surgical debridement and antifungal therapy. Amphotericin B was substituted with oral posaconazole after one month. The lesion was repaired completely with oral antifungal drug after two months. Chemotherapy was restarted after three months disruption.

Discussion:

Mucormycosis is an invasive fungal infection caused by various members of the class Phycomycetes,especially Mucoraceae, subdivided into the genera Absidia, Rhizopus and Mucor. This rare filamentous fungal infection occurs most frequently in neutropenic patients with acute leukemia.Among patients with hematologic disorders, mucormycosis most commonly occurs in those with acute leukemia or lymphoma who have developed neutropenia due to malignancy or to chemotherapy, and in transplanted patients receiving immunosuppressive treatment.(2) The infection is characterized by a high rate of mortality (~70%).(3) Extensive and aggressive diagnostic and therapeutic procedures are essential in order to improve the prognosis in these patients. Introduction of new antifungal drugs in the routine treatment of fungal infections led us to make a new reappraise of the characteristics and outcome of mucormycosis in patients with a hematologic malignancy.

Amphotericin B is the first-line drug of choice for mucormycosis.(4) The therapeutic activity of Amphotericin B is limited by its potentially severe side effects. The majority of zygomycetes demonstrate resistance to fluconazole, itraconazole and 5-fluorocytosine.(5) Posaconazole is a new extended spectrum azole antifungal that has demonstrated in vitro and in vivo activity against zygomycetes.(6) This report showed that Amphotericin B following by posaconazole was effective choice against mucormycosis.

The most frequent form of mucormycosis presentation is rhinocerebral, followed by pulmonary, skin and soft-tissue, disseminated, and gastrointestinal forms. Rhinocerebral form initially develops in the nasal sinuses and extends to the paranasal sinuses and the ethmoidal and sphenoidal cells.(7) Late symptoms that indicate invasion of the orbital nerves and vessels include diplopia and visual loss.

These late symptoms indicate a poor prognosis and are usually followed by reduced consciousness.[8] Fortunately, our case due to early diagnosis and treatment was not involved his orbital area.

Zygomycosis are ubiquitous in the environment, and infection can result from inhalation, direct contact, or ingestion of spores. They are not usually commensals, but nosocomial exposure can lead to colonization and invasive disease.[9] Place patients with severe prolonged neutropenia in rooms equipped with High-Efficiency Particulate Air (HEPA) filters is practicable and efficient.[10]

Early tissue diagnosis and the consequent surgical excision of the necrotic tissue and aggressive antifungal therapy might salvage life in this fatal condition. The use of growth factors reconstituting altered host defenses and reducing the duration of neutropenia might increase the recovery from mucormycosis.

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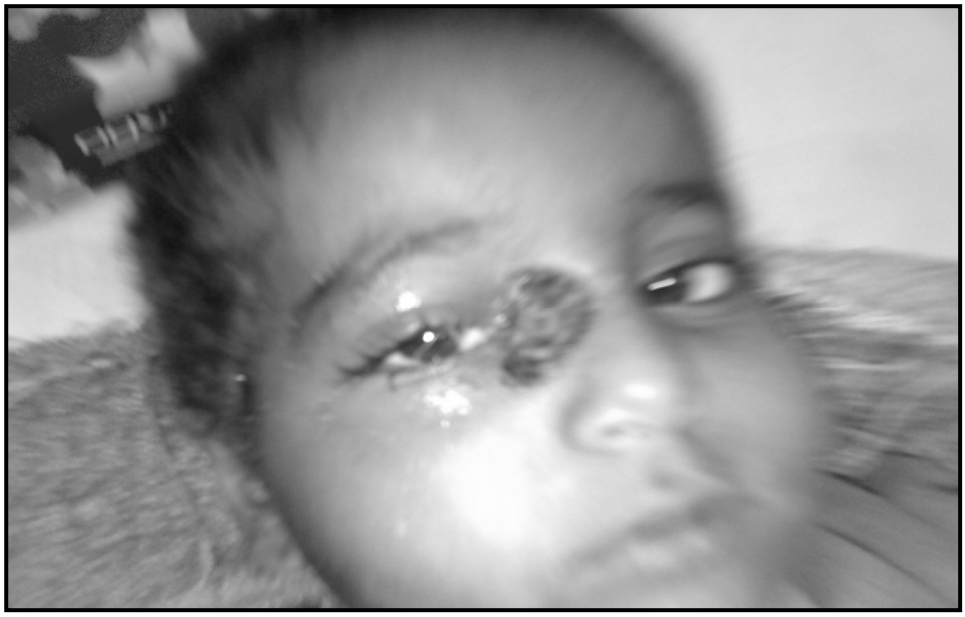

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Oral5

Outcomes of risk factors of viral hepatitis in clinical conditions of Non-Hodgkin Lymphoma patients

Mehdi Roshan Nia Jahromi [1*], *Ramin Yaghobi, Mani Ramzi, Farzan Mahmoodi Nezhad, Nader Kohan.*

***Corresponding auther:**
Hematology research center, Shiraz University of Medical Sciences, Shiraz, Iran
Email: Roshan_2000_2005@yahoo.com:

Abstract:

Background & Objectives:

Different and multiple risk factors can threaten the clinical outcomes of Non – Hodgkin lymphoma (NHL). Environmental, genetic, microbial, and personal characteristics are some of these risk factors which may influence the pattern of clinical pathogenesis of multiple types of NHL. Between microbial indexes viral infections and especially hepatitis type B (HBV) and hepatitis type C (HCV) viruses may have a critical role in clinical outcomes of this type of lymphoproliferative cancers. In this research the possible correlations which may occur between the pattern of pathogenesis of HBV and HCV infections with personal and environmental characteristics of NHL patients were evaluated.

Materials & Methods:

In this investigation the 70 and 100 EDTA treated blood samples were collected from March 2006 to September 2007 from NHL patients and normal controls, respectively. The possible correlations were analyzed between HBV and HCV serological and molecular markers considering gender, marriage, occupation, chemical detergents, social class, smoking, alcohol, chemical war exposure, HIV,

glucortieoid, surgery, chronic unknown disease, bone marrow transplantation, endoscopy, dialysis, chemotherapy, organ transplantation, radiotherapy, rheumatoid autoimmune disease.

Results:

In lymphoma disordered patients the prevalence of different serological markers of HBV and HCV infections are as follows : HBs Ag = 3%, HBs Ab = 8.6%, HBe Ag = 4.3%, HBe Ab = 11%, HBc IgG = 25.7%, HBc IgM = 0 and HCV Ab = 1.4%. The molecular prevalence of HBV and HCV genoms are as follow in NHL patients : HBV PCR = 11.57%, HCV RT- PCR = 15.71%. Significant correlations were found between smoking with HBs Ag presentation ($p = 0.02$) and with HCV viremia ($p = 0.01$). Detection of HBs Ab was correlated with bone marrow transplantation ($p = 0.05$). Also, we did not find any correlations between other risk factors with outcomes of HBV and HCV infections in NHL patients.

Conclusion:

Assaying of significant correlations between HBV and HCV serological and molecular markers with personal and clinical risk factors announced the need of complicated study for accurate determination of the role of these risk factors in pathogenicity of these viral infections in NHL patients.

Keywords:
Risk Factors; Viral Hepatitis; Non-Hodgkin Lymphoma

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Oral6

Determining the prevalence of *Cryptosporidium* in hemodialysis patients and subjects in chemotherapy process in Hajar Hospital, Shahrekord, Iran

Bahman Khalili [*], *Esmaeel Tahmasebian*
[*]***Corresponding Auther:***
Department of Parasitology and Mycology, Faculty of medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
Email:bahman_khalili@yahoo.com

Abstract:
Background & Objectives:
*Cryptosporidiosis i*s a cosmopolitan protozoan disease that is recently known as one of the main causes of diarrhea in immunocompromised subjects. The majority of studies about this parasite in the last 3 decades has mainly focused on immunocompromised cases and was reported from developed countries and there have been no ample studies investigating the prevalence of the parasite in Iran. This study has investigated the prevalence of *Cryptosporidium* infection in hemodialysis and patients in chemotropy process in Hajar Hospital, Shahrekord, Iran.
Materials & Methods:
137 stool sample were examined by Ziehl- Neelsen staining method to detect *Cryptosporidium* oocyst in the stools from April to September 2006. Data were obtained by standard questionnaire including socio-economic background, family characteristics and medical history of patients. All patients agreed to attend in this survey. Then using statistical test (Fisher test…), data were analyzed by Epiifo2002 software.

Result:

Out of 137 stool samples, 9(7%) cases were positive for cryptosporidiosis.

Meanwhile, the frequency of infection with the parasite in hemodiahysis group was 8 %(5 / 67) cases, it was 6% (4/ 70) cases in patients undergoing chemotherapy process. The frequency of infection was not statistically significant between the two groups. In the study, no relation was found between infection with the parasite and gender. Also no trend was seen between frequency of infection and age. There was a positive relation between previous diarrhea in all patients and *Cryptosporidiosis*.

Discussion:

These results indicates that prevalence of cryptosporidiosis in these subjects is similar to studies which have reported the prevalence of cryptosporidiosis in other studies in Iran and elsewhere.

Keywords:

Cryptosporidium; Hemodialysis; Chemotherapy; Stool.

Oral7

Human cytomegalovirus micro infection levels in glioblastoma multiforme are of high predictive value for patient survival

Afsar Rahbar,* *Orrago Abiel, Stragliotto Giusoppe, Peredo Inti, Wolmer- Solberg Nina, Straat Klas, Soderberg- Naucler Cecilia.*

Corresponding Auther:

Department of Medicine,Center for Molecular Medicine,Karolinska Institute and the Cancer and Department of Neurosurgery,Karolinska University Hospital,Stockholm, Sweden.

Email: Afsar.rahbar@ki.se

Abstract:

Background & Objectives:

Patients with glioblastoma multiforme (GBM) generally live less that 1 year after diagnosis, despite maximal surgical resection, adjuvant radiotherapy, and chemotherapy. No clear clinical or histopathological markers can predict the prognosis for individual patients. Human cytomegalovirus (HCMV) has recently been detected in 90 to 100 percent of GBMs. In this study, we sought to define the predictive value of the HCMV load in GBMs.

Patients & Methods :

Paraffin- embedded sections of GBMs Irom, 52 patients were examined for expression of HCMV, human herpesvirus 6, and Epstein- Barr virus. Tumor sections were scored negative or grade 1 to grade 4 depending on the percentage of infected cells. Survival data were analyzed Cox regression models.

Results:

Active HCMV infection was detected in tumor samples from 61 patients (98%). Patients with low- grade infection (0% to <25% infected tumor cells) lived a median

of 19.4 months longer (P=0.0022) than patients with high- grade infections (>25% infected cells). GBMs with high- grade infections also had p53 mutations (P=0.05).

Conclusion:

Patients with low- grade HCMV infections in their tumors lived more than twice as long as patients with high- grade infection (median survival, 34 versus 14.6 months). Thus, the HCMV micro infection level in GBMs is of high prognostic values, suggesting that HCMV has a pathogenic role in this disease. This may give now hope for alternative treatment strategies for this group of patients.

Keywords:

Cytomegalovirus; Micro Infection; Predictive Value; Patient Survival; Glioblastoma Multiforme

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Oral8

The Role of different risk factors in HBV and HCV prevalence in leukemia patients

Ramin Yaghoobi*, *Mitra Mirzaee, Mani Ramzi,Nader Kohan, Narges Rezaee, Vida Moayed*
***Corresponding Auther:**
Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
Email:Rayaviro@yahoo.com

Abstract:
Background& Objectives:
Different types of acute and chronic hematological malignancies threaten the human population all around the world. Multiple risk factors have roles in clinical presentations of different types of hematological malignancies. Definition of the correlations occurring between environmental and microbial risk factors may have a role in clinical outcomes of this type of cancers. In this research the possible correlations which may occur between HBV and HCV infections with different environmental risk factors were studied in leukemia patients.
Material & Methods:
In this study, 100 EDTA treated blood samples were collected for 2 years from different types of leukemia patients and healthy control group, respectively. In this research the possible correlations between the prevalence of HBV and HCV serological and molecular markers including HBs Ag, HBs Ab, HBe Ag, HBe Ab, HBc Ab (IgG&IgM), HCV Ab, HBV-DNA and HCV-RNA with gender, marriage, and history of smoking, surgery, transplantation, transfusion and HIV infection were analyzed.

Results:
Significant differences were diagnosed between positive results of serological and molecular markers of HBV and HCV in leukemia patients and control group as follows: HCV-RNA (P=0.005), HBs Ag (P=0.02) and HBe Ab (P=0.009). Significant correlations were detected between positive results of HBV and HCV markers and risk factors as follows: HBs Ag and gender (P=0.02), HBs Ab and marriage (P=0.05) and HBe Ag and smoking (P=0.02).
Conclusion:
Detection of significant correlations between some serological and molecular markers of HBV and HCV infections with gender, marriage and smoking announced the need of complete studies for determination of the accurate role of these risk factors in clinical presentation of HBV and HCV infection in leukemia patients.

Keywords:
HBV ; HCV; Leukemia; Risk Factors

Oral9

Role of pre-transplant donor and recipient HCMV molecular relationships in post-kidney transplant HCMV clinical conditions

Ramin Yaghoobi***,** *Zahra Joekar, Bita Geramizadeh*
***Corresponding Auther:**
Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
Email :Rayaviro@yahoo.com

Abstract:
Background & Objectives:
Use of immunosuppressive drugs can increase the potential of viral infections in solid organ transplant patients. Human cytomegalovirus (HCMV) infection is an important risk factor that threatens the surveillance of kidney transplant patients. In this research, the prevalence and the pattern of HCMV transmission was monitored pre and post-renal transplantation.
Materials & Methods:
In this cohort and retrospective study, EDTA treated blood (plasma and leukocyte) and urine samples were collected pre- and post-transplantation from 40 kidney donors (D) and recipients (R). The prevalence of HCMV infection was analyzed in these samples by an in-house semi-nested PCR method. Also the pattern of HCMV transmission between D/R different relationships was studied pre- and post-transplantation.
Results:
The positive results of HCMV-PCR were diagnosed in donor samples including: leukocyte (52.5%), plasma (27.5%) and urine (7.5%) samples. The human

cytomegalovirus genome was detected in leukocyte (45%), plasma (17.5%) and urine (15%) samples of recipients pre-transplantation. Also HCMV-PCR positive results were detected in leukocyte (50%), plasma (52.3%) and urine (16%) samples of kidney recipients' post-transplantations. From 40 donors and recipients different patterns of D/R relationships were detected pre- and post-kidney transplant as follows: D^+/R^+ leading to R^+ (13/18, 32.5%), D^+/R^+ leading to R^- (5/18,12.5%), and D^+/R^- leading to R^+ (9/10,22.5%), D^+/R^- leading to R^- (1/10,2.5%), and D^-/R^- leading to R^+ (5/6,12.5%), D^-/R^- leading to R^- (1/6,2.5%), and also D^-/R^+ leading to R^+ (3/6,7.5%), D^-/R^+ leading to R^- (3/6,7.5%), respectively.

Conclusion:

The differences were detected in spreading of HCMV infection in different clinical samples of donors and recipient pre- and post- renal transplant. Also the pattern of HCMV transmission from pre to post-transplant periods was different between multiple types of D/R relationships, especially in D^+/R^- leading to R^+ post-kidney transplant condition.

Keywords:
HCMV; Donor; Recipient; RT; Pre- & Post Transplant.

Oral10

Post-renal transplant tuberculosis:a case-control,country-wide study

Abbas Basiri [*], *Seyed Mehdi Hosseini-Moghaddam, Naser Simforoosh, Behzad Einollahi, Mohammad Hosseini, Ahmad Firouzan, Fatemeh Pourrezagholi, Mohsen Nafar, Mohammad Ali Zargar, Gholam Reza Pourmand, Ahmad Tara, Hayat Mombeni, Mohammad Reza Moradi, Afshar Ali Taghizadeh, Hamid Reza Gholamrezaee, Abolfazl Bohlouli, Hamid Nezhadgashti, Abazar Akbarzadehpasha, Eejaz Ahmad, Mahdi Salehipour, Mohammad Yazdani, Aliraza Nasrollahi, Narges Oghbaee, Ramak Esmaeeli Azad, Zahra Mohammadi, Zahra Razzaghi*

[*]***Corresponding auther:***
Urology/ Nephrology Research Center, Shaheed Beheshti Medical University, Tehran, Iran.
Email: basiri@unrc.ir

Background & Objectives:

Tuberculosis (TB) plays an important role in morbidity and mortality of kidney recipients and is often misdiagnosed. We performed this study to determine the frequency of multiple risk factors for post-renal transplantation TB.

Materials & Methods:

Out of 12,820 patients who referred to 12 kidney transplantation centers in Iran between 1984 and 2003, a total of 44 subjects (0.3%) were compared with 184 healthy kidney recipients who were operated by the same surgical team.

Results:

The mean age of cases and controls was 37.7 (13–63) and 35.6 (8–67) years, respectively (P=0.3). The mean duration of pre-transplantation hemodialysis in cases and controls was 30.3 (3–168) and 18.2 (1–180) months, respectively (P=0.03). A positive past history of TB was reported in 2 cases and 1 control (P=0.3). No significant difference was seen in the mean doses of initial and maintenance

immunosuppressive drugs between cases and controls. A total of 25 cases (56.8%) and 60 controls (32.6%) rejected the graft before TB was diagnosed (P=0.004; OR=2.7, $CI_{95\%}$: 1.3–5.6).

Conclusions:

To our knowledge, this is the first study demonstrated that increase in the duration of pre-transplant hemodialysis and number of post-transplant rejection episodes lead to an increase in the risk of post-transplant TB. Obviously, further investigation must be done to clarify our new findings.

Keywords:
Tuberculosis; Post-Renal Transplant; Iran.

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Oral11

Leishmaniasis in renal transplant recipient: aspects and diagnosis

***Shahram Khademvatan**,** *Jasem Saki Hormozd Oormazdi, Lame Akhlaghi, Mohammad Javad Gharavi*

****Corresponding Auther:***
Department of Parasitology Faculty of Medicine, Iran medical University,.Tehran, Iran.
Email: khademvatan@yahoo.com

Abstract:

Leishmaniasis in renal transplant recipient: aspects and diagnosis Introduction: Leishmaniasis is a parasitic disease caused by a trypanosomatid protozoan belonging to the genus Leishmania. The disease transmitted by a sandfly, which bites a vertebrate host. There are four clinical syndromes of disease: visceral, cutaneous, mucocutaneous and diffuse cutaneous caused mainly by Leishmania infantum, L. tropica, L. brasiliensis, and L. mexicana, respectively. Visceral leishmaniasis is an unusual disease reported in kidney transplant recipients. In the last 25 years, the increasing frequency of renal transplantations and improvement of the associated immunosuppressive treatments have led to the leishmaniasis complicating renal transplantations. Because leishmania is endemic in Iran, insight about manifestation and diagnosis of leishmaniasis in renal transplant recipient is very important. Material and methods: In this retrospective study, we were review new studies about manifestation and different diagnostic methods in recipient suffer from leishmaniasis until end of 2007. Result: The clinical signs observed in patients were predominantly irregular fever, splenomegaly, hepatomegaly, and weight loss. In addition, leucopoenia, anaemia, thrombocytopenia and pancytopoenia were present. The diagnosis of leishmaniasis in transplantation is not easy, due to inconsistency of

the symptoms and clinical signs. PCR for blood and for bone marrow has high sensitivity. Unlike HIV co-infection, serology (IFA or ELISA and Western blot) has good results in leishmaniasis occurring after transplantation. Diagnosis by urine is a new and simple method that need more development. Conclusion: Renal transplantation is the most frequent transplantation complicated by leishmaniasis.It is recommended that transplant patients living or travelling in endemic areas should be tested regularly for leishmaniasis and clinician should be aware in suspect cases. Prospective studies would be useful for a better understanding of interactions between outcome of the Leishmaniasis and graft tolerance.

Keywords:
Renal transplant; leishmaniasis

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Oral12

Molecular study of HCMV infection by two new nested-PCR Protocols in HSCT patients and donors

Amir Abbas Banan [*]***,*** *Yaghobi Ramin, Ramzi Mani, Rasooli Manoochehr, Mehrabani Davood, Amirzadeh Saeed, Rezaee Narges, Moayed Vida*

[*]***Corresponding Author:***
Department of Microbiology ,Jahrom Azad University, Jahrom, Iran .
Email: amirabbasbanan_2005@yahoo.com

Background & Objectives:

Human Cytomegalovirus (HCMV) infection is the most important complications in hematopoietic stem cell transplant (HSCT) recipients. Accurate detection of HCMV infection in pre and post transplant period can be useful in presentation of clinical disorders and increasing the HSCT patient's surveillance. For this purpose, the prevalence of HCMV infection was analyzed in HSCT donors and recipients by in-house UL4 and UL55 nested-PCR protocols, pre and post transplantation.

Materials & Methods:

In this cohort and prospective study, the prevalence of HCMV infection was evaluated in plasma, Buffy coat and urine samples of 110 HSCT donors and recipients pre-transplantation and followed for one-hundred days post transplantation. The determination of this viral infection was evaluated by two different nested-PCR protocols including: UL4 nested-PCR and also UL55 nested-PCR techniques.

Results:

The UL4 nested-PCR positive results were documented in 64%, 61.5% and 61% of plasma, Buffy coat and urine samples respectively. The amplification of UL-55

sequence of HCMV was the detection of 71.5%, 73.4%, and 66.5% of plasma, Buffy coat and urine samples of HCMV patients post transplantation. Also HCMV genome was diagnosed in 25% of donor blood samples.

Conclusion:

Detection of HCMV genome in more than 60% of HSCT blood and urine samples of transplant recipients announced that the need of molecular monitoring of HCMV infection for prevention of HSCT viral complications and graft rejection is essential.

Keywords:
HSCT; HCMV Infection; Nested-PCR; UL55; UL4

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Oral13

Serological study of toxoplasma gondii infection in renal transplant recipients and donors

Saeed Haghighi, ***Parviz Kavakeb,**** *Mojdeh Hakemivala*, *Mohammad Javad Taghvai.*
Corresponding Author:
Clinical Laboratory Department, Sina Hospital, Imam Khomeini Street, Tehran, Iran.
E-mail: pkavakeb@gmail.com

Abstract:
Background & Objectives:
Toxoplasmosis is a wide distributed opportunistic infection caused by a protozoan parasite *Toxoplasma gondii*. The aim of this study was determination of antibodies against *Toxoplasma* in renal transplant recipients and donors.
Materials & Methods:
This study was carried out on 31 kidney transplant recipients and 39 donors subjects referred to Sina Hospital in Tehran during August 2007 to April 2008. Immunoglobulin G (IgG) antibodies against *Toxoplasma* was assessed by Enzyme-Linked Immunosorbent Assay (ELISA) technique on serum samples.
Results:
23 cases (58.9%) of 39 donors' samples and 17 cases from totally 31 recipients' samples were positive for IgG anti-Toxoplasma antibody.
Conclusion:
According to the relatively high prevalence of positive cases in either recipients or donors, clinical awareness of the potential risks of reactivation of latent infection or occurring of primary infection due to regular administration of suppressive drugs

is necessary and Toxoplasmosis should be considered in the differential diagnosis of complications in renal transplant recipients.

Keywords:
Toxoplasmosis; Renal Transplant Recipients; Serology; ELISA

Oral14

Antibody Response to Influenza Immunization in Kidney Transplant Recipients Receiving either Azathioprine or Mycophenolate: A Controlled Trial

Maryam Keshkar- Jahromi *, Hassan Argani , Mohammad Rahnavardi Elham Mirchi , Shahnaz Atabak , Seied Ahmad Tara , Latif Gachkar , Azam Noori- Froothghe , Talat Mokhtari- Azad , Sara Rahmati Rodsari*
Corresponding Author:
Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti Medical University (M.C.), Tehran,Iran.
Email: maryam_keshtkar@yahoo.com

Abstract:

Aims: we aimed to assess humoral immune response to the influenza vaccine in adult kidney transplant recipients (KTRs) subjected to two immunosuppressive regimens containing either mycophenolate mofetil (MMF) or azathioprine (Aza).

Methods: 40 eligible KTRs (24 treated with Aza [KTRs- Aza] and 16 treated with MMF [KTRs- MMF] and 40 matched healthy controls (HCs) were administered trivalent 2006 – 2007 anti- influenza vaccine. Antibody (Ab) titers were measured before (pre- vacc) and 1 month after (post- vacc) vaccination. The proportion of protective Ab titers (i.e.≥ 1: 40), the serological response (i.e. ≥4 - fold in titers) rates, and the magnitudes of change in titers were evaluated.

Results: KTRs and HCs were similar in serologic responses, magnitudes of change in Ab titers, and proportions of acquired protective titers against all antigens. Whereas KTRs- MMF and KTRs- Aza were identical in magnitude of rise in titers as well as in serologic responses, KTRs- MMF did poorer in developing post- vacc-

protective titers against A/H1N1 ($p < 0.05$). The function of the transplanted kidney has not deteriorated after vaccination.

Conclusions: Anti- influenza vaccination was safe in KTRs and evoked Ab responses comparable to those of HCs. KTRs- MMF and KTRs- Aza responded almost equally to the vaccine. Annual anti- influenza vaccination can be recommended to all stable KTRs.

Keyword:
Influenza. Vaccination. Immunization. Kidney transplant recipient. Antibody response. Azathioprine. Mycophenolate mofetil.

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Poster1

Cloning and molecular characterization of aspf1 gene, coding antigen-allergen *Aspergillus fumigatus* in pTZ57R

Sara Mardani, Shahla Roudbar Mohamadi, ***Fatemeh Ghaffarifar *.***
**Corresponding Author:*
Parasitology Dept., School of Medical science, Tarbiat Modarres University, P.O.Box: 14115-331. Tehran, Iran.
Email: ghaffarifar@yahoo.com

Abstract:

Background & Objectives:

Aspergillosis is a lethal infection in immunocopromised individuals such as bone marrow recipients. Aspf1 is a major antigen\ allergen in aspergillus fumigatus that produces on conidial and mycelial from of aspergillus . Aspergillus fumigatus is the most important etiologic agent of invasive Aspergillosis.

Materials & Methods:

Aspergillus cultured on sabouro decxtrose agar and then spores were collected and disrupted with lysing buffer and liquid nitrogen. DNA extraction was prepared by phenol / chloroform method. Then, PCR product was purified and cloned in pTZ57R and finally transformed into E.coli .

Results:

The DNA of *Aspergillus fumigatus* was extracted and Aspf1 gene was amplified. The PCR product was seen as 678 bp in 1% agarose gel. After cloning and transformation, to recognize the E.coli recombinant plasmid, the bacteria were cultured in LB with ampicilin, X-gal and IPTG. To confirm the data, the plasmid were extracted and the DNA of Aspf1 was amplified by PCR method. The cloned plasmid was confirmed by sequencing and the results showed 100% homology with Aspf1 gene in gene bank.

Conclusion:

It was noticed that as for transformation of plasmid with the DNA of Aspf1 gene was transformed in E.coli successfully . This cloned plasmid can be used as a positive control for diagnosis of the patients with *Aspergillus fumigatus infection*.

Keywords:
Aspergillus fumigatus, Aspf1 gene, E.coli , PTZ57R.

Poster2

Diagnostic value of Galactomannan measurement in diagnosis of invasive pulmonary aspergillus among immunocompromised patients

Shokouh Azam Sarrafzadeh, ***Zahra Pourpak*** [*]***,*** *Fatemeh Fattahi, Seyed Davood Mansoori.*
[*]***Corresponding Author:***
Immunology, Asthma and Alley research institute,Tehran University of Medical Sciences,Tehran, Iran.
Email: zpourpak@yahoo.com

Background & Objectives:

The incidence of invasive aspergillosis has risen due to increased number of patients undergoing heamatopoietic stem cell, allograft transplantation, and receiving prolonged courses of corticosteroid therapy. Galactomannan antigen is an aspergillus specific antigen that is released during the growth phase of invasive aspergillosis. A rapid and important method for invasive aspergillus diagnostic could be the circulating galactomannan aspergillus measurement in the serum samples of the patients.

Materials & Methods:

Patients suspected to aspergillosis in the base of a lung HRCT (high-resolution computed tomography) referred to Immunology, Asthma and Allergy Research Institute from 2006 to 2008 were entered this study. Aspergillus cultures (sputum and BAL) were done for all of the patients. Also IgG anti-aspergillus and measuring of Galactomannan level with ELISA method were done for all of them.

Results:

One hundred-four cases of immunocompromised patients were found and they were divided into 4 groups in the base of EROTC/MSG that were 8 proven, 25

probable, 26 possible and 45 didn't have invasive pulmonary aspergillus. Thirty-two had bone marrow transplants, 28 had solid transplant, 25 had leukemia, and 19 had other oncology diseases. Galactomannan was detected in 100% of proven and 92% of probable cases. The overall sensitivity, specificity, positive and negative predictive value and efficiency of this assay using a 1 index cut-off value were 68%, 95%, 94%, 75% and 82% respectively. Twenty one percent of cases showed anti-aspergillus antibody (IgG) by serological methods. Decreasing of the Galactomannan cut-off value from 1 to 0.7 seemed to be more relevant for immunocompromised patients with sensitivity 95%, specificity 90%, positive and negative predictive value 90% and 95% and efficiency 93%.

Conclusion:

We found that Galactomannan Elisa cut-off was 7% for immunocompromised patients that can help us for better detection of aspergillus in them. In our study, the sensitivity of Galactomannan Elisa was clearly higher in patients without anti-aspergillus antibody. In immunocompromised patients suspected to invasive aspergillus, anti-aspergillus antibody (IgG) test should always be done in conjunction with the Galactomannan test, as these can be used to explain false-negative Galactomannan Elisa test.

Keywords:
Galactomannan; Pulmonary Aspergillus; Immunocompromised Patients.

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Poster3

Human Cytomegalovirus Infects Stem Cell-Like Cells of the Central Nervous System - Implications for Stem Cell Transplantation

Nina Wolmer*, *Cecilia Soderberg-Naucler, Jenny Odeberg*
**** Corresponding Author:***
Department of Medicine, Center for Molecular Medicine., Karolinska Institutet, Karolinska University Hospital, 17176 Stockholm, Sweden.
E-Mail:Nina.Wolmer@ki.se

Abstract:
Background & objectives:
Human cytomegalovirus is a large threat to transplant patients due to its opportunistic and manipulative nature. The last decade antiviral treatments have come available, but still this virus is a big problem for immunocompromised individuals. Transplantation of neural stem cells has emerged as a possibility to treat patients with neurodegenerative diseases or trauma to the nervous system. It is not yet a routine treatment, but the results are promising.
Materials & Methods:
We have investigated the impact of cytomegalovirus on early progenitor cells of the brain and tried to mimic the event of cytomegalovirus entering the brain.
Results:
Our results show that early neural precursors and stem cell-like cells are highly susceptible to cytomegalovirus infection *in vitro*. We have also shown that there is a difference in the response in immature cells and their differentiating progenies.

Early astrocytes and neurons induce apoptosis, reduce proliferation and stop differentiating upon infection while progenitor cells lower the expression of some stem cell markers but their proliferation is only marginally affected and apoptosis does not seem to be induced at all. Further more, since cytomegalovirus suppress migration of stem cell-like cells in the brain, transplanted cells would not be able to home to the site of injury, which would severely lower therapeutic response.

Conclusions:

These data suggest that cytomegalovirus is an important factor to take into consideration when further developing neural stem cell transplantation protocols and that if infected, the cells of the brain and possibly also the peripheral nervous system will be severely targeted.

In general, it is clear that although a low grade infection may not cause any acute symptoms, the infected cells may be at risk for more subtle changes in their phenotype or function. We may be forced in the future to be more aware of so called un-symptomatic infections and their impact on immunocompromised patients or evolving diseases such as cancer, autoimmunity or opportunistic infections.

Keywords:
Cytomegalovirus; Stem Cell Transplantation; CNS.

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Poster4

Molecular presentation of HBV infection in hematopoietic stem cell transplant recipient

Ramin Yaghoobi***,***Fatemeh Karimi, Maryam Zakerinia,Ma*
*** *Corresponding auther:***
Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
E mail:Rayaviro@yahoo.com

Abstract:
Background& Objectives:
Hematopoietic stem cell transplantation (HSCT) has been threatened by different and multiple genetic, environmental, and microbial risk factors including viral infections. Hepatitis type B (HBV) is one of the clinical complications inducing agent which may play a role in GVHD presentation and graft rejection in these patients.
Material & Methods:
In this study EDTA-treated blood samples were collected from all HSCT recipients and donors for 3 years. The molecular prevalence of HBV infection was analyzed by a qualitative PCR protocol in HSCT donors and patients pre-transplantation and for three months separately post-transplantation.
Results:
Between 53 HSCT donors and recipients HBV infection was detected in 1 HSCT donor. Also, the positive results of HBV-PCR were detected in 4 and 5 HSCT recipients pre and post-transplantation, respectively. Only 1 patient was infected with HBV-DNA both pre and post-transplantation. HBV-DNA was mostly diagnosed in HSCT patients in the first month post-transplantation.

Conclusion:

Results of this investigation proposed the potential role of HBV infection in HSCT clinical complications. Also most of HBV infections were presented in the first month post-transplantation, but we need further and completed study for determination of the origin of HBV transmission to these transplant recipients.

Keywords:
HBV Infection; Hematopoietic; Stem Cell; Transplant; Recipient.

Poster5

Urinary tract infections in renal transplantation patient

Habib Zeighami *, *Ali Mota, Morteza Sattari.*
****Corresponding Author:***
Department of Bacteriology,Tarbiat Modarres University,Tehran, Iran.
Email:habib.59@gmail.com

Abstract:
Background & Objectives:
Urinary tract infection (UTI) can be associated with significant morbidity after renal transplantation. While the use of postoperative antibiotic prophylaxis has dramatically reduced the incidence of UTI after renal transplantation over the past decades, rates of serious complications associated with UTI, such as bacterial septicemia, remain high for post transplantation patients even in the modern era. However, late post transplantation UTI has been widely considered as benign based on relatively small studies. The majority of transplant centers administers prophylactic antibiotics post transplantation, but most generally stop antibiotic prophylaxis 6 months after transplantation. However, emerging concepts from recent studies suggest that UTI, even if late after renal transplantation, has definite risks, suggesting that this clinical entity may not be as "benign" as was previously supposed.
Material & Methods:
A total of 185 midstream urine samples were collected in sterile containers from patient with kidney transplantation. With standard calibrated loop delivery method, 0.01 ml of urine was inoculated on Blood agar and EMB agar and incubated aerobically at 37°C for 24-48 h. Urinary tract infection was diagnosed by growth of at least 100000 colony-forming units of a urinary tract pathogen per milliliter in a

culture of a midstream urine sample. Any specimen containing high colony counts with more than one species of bacteria in asymptomatic patient was considered contamination. Identification of bacterial pathogens was made on the basis of gram reactions, morphology and biochemical characteristics.

Results:

185 kidney transplantation patients were studied, of whom 52 (28.10%) were identified to have asymptomatic bacteriuria. In the present study, the most common isolate was E.coli 33 (56.89%), followed by Klebsiella pneumoniae 13 (22.41%), Pseudomonas aeruginosa 5 (8.62%), Proteus mirabilis 3 (5.17%), Citrobacter freundii 3 (5.17%) and Staphylococcus aureus 1(1.72%).

Discussion:

UTIs are frequent problems after kidney transplantation. In the long-term, UTIs should be considered as potential risks for poorer graft outcomes. In this study, the incidence of UTIs was 31.35% among renal transplant recipients, with E coli as the most common cause. While ureteral double-J catheter and female gender were the risk factors for UTI, female gender was the only independent risk factor.

Keywords:
Urinary Tract Infections; Renal Transplantation.

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Poster6

CMV pneumonia in a CLL patient

Davood Yadegarynia,* *Farhad Abbasi, Mehrdad Haghighi, Soolmaz Korooni Fardkhani, Sina Yadegarynia. Reza Rafi zadeh*

Corresponding auther:

Infectious Disease and Tropical Medical Research Center, Shahid Besheshti Medical University, Tehran, Iran

Email: yadegarynia@yahoo.com

Abstract:

Background & Objectives:

CMV pneumonia is one of the most important infections in immunocompromised host. Immunosuppressive therapy plays a major role in reactivation of CMV.

Patients & Methods:

The patient was a 56- year-old lady , a known case of CLL, had been taking prednisolone and chlombucil , who presented with dyspnea and productive cough.

After BAL, TBLB and CT-guided biopsy, CMV pneumonia was diagnosed.

Conclusion:

CMV should be suspected as a cause of pneumonia in immunocompromised patient and diagnosis may require invasive procedures.

Keywords:

CMV; Pneumonia; CLL;

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Poster7

Chickenpox in a young man with kidney transplantation

Davood Yadegarynia *, *Farhad Abbasi, Soolmaz Korooni Fardkhani, Sina Yadegarynia. Reza Rafi zadeh, Zohreh Mirheydari*

****Corresponding auther:***

Infectious Diseases and Tropical Medicine Research Center, Shahid Beheshti Medical University, Tehran, Iran

Email: yadegarynia@yahoo.com

Abstract:

Background & Objectives:

Chickenpox in immunocomprmised patients is a cause of significant mortality and morbidity. Progressive visceral organ involvement is an important problem.

Patients & Methods:

The patient was a 19-year-old man, a case of kidney transplantation, who presented with generalized vesicular rash. He had been taking immunosuppressive drugs. He had positive IgM-Ab of varicella zoster. IV acyclovir strated with a good clinical response.

Conculsion:

Prompt diagnosis and treatment with IV acyclovir can be life saving and decreases mortality and morbidity in immunocompmised patients .

Keywords:

Chickenpox, Varicella Zoter, Kidney Transplantation.

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Poster8

High dose itraconazole as maintenance therapy for CNS aspergillosis in a immunocompetent patient

Davood Yadegarynia, [*] *Mehrdad Haghighi, Farhad Abbasi, Mohammad Moshfegh. Reza Rafi zadeh, Sara Rahmati Roodsari*

[*]***Corresponding auther:***
Infectious Diseases and Tropical Medicine Research Center, Tehran, Iran.
Email: yadegarynia@yahoo.com

Abstract:

Background & Objectives:

Cerebral aspergillosis is associated with the highest mortality of invasive aspergillosis. Voriconazole is recommended as the primary systemic antifungal therapy of CNS aspergillosis. Prophylactic strategies may be useful in patients who are at high risk for invasive aspergillosis.

Patient & Methods:

We describe a 63- year- old woman presented with headache and ptosis beginning a few weeks before diagnosis. Imaging study was done and a mass measuring about 4 cm was detected in pituitary gland. By trans sphenoidal surgery the mass excised and pathological study revealed invasive aspergillosis. She was treated with amphotericin B and after 10 days the treatment was changed to PO itraconazole as maintenance therapy.

Conclusion: Itraconazole can be used as maintenance therapy for invasive aspergillosis .

Keywords:
Aspergillosis; Itraconazole; Voriconazole.

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Poster9

Severe facial herpes zoster in a young woman with kidney transplantation

Fatemeh Pourrezagholi,*Davood Yadegarynia, Farhad Abbasi, Minoosh Sha'bani, Sina Yadegarynia.*
Corresponding auther:
Labbafeenejad Medical Center, Shaheed Beheshti Medical University, Tehran, Iran.
Email :poorreza@hotmail.com

Abstract:
Background:
Solid organ transplant recipients are at high risk for developing herpes zoster. Immune-o-suppression may be a predisposing factor for herpes zoster.
Patients& Methods:
The patient was a 25-year-old woman, a case of kidney transplantation on immunosuppressant drugs who developed vesicular rashes on her face and scalp. With diagnosis of herpes zoster IV acyclovir started for her and after several days the lesions recovered.
Conclusion:
Herpes zoster is a frequent and severe complication of organ transplantation. Prompt diagnosis and treatment reduces the mortality and morbidity associated with herpes zoster.

Keywords:
Herpes Zoster; Transplantation; Acyclovir

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Poster10

Kaposi sarcoma and mucormycosis infection in a patient after renal transplantation

Mohammad Mehdi Adib Sereshki *, *Zahra Chitsasian, Mohammad Ali Asadi.*
****Corresponding auther:***
Hematologist & Oncologist,Kashan University of Medical Sciences;Kashan, Iran.
Email: dr_adibs@yahoo.com

Abstract:
Background & Objectives:
Solid organs and Bone marrow transplantations are used increasingly in the treatment of end stage diseases. Successful transplantation of these organs is threatened by occurrence of infections and secondary malignancies due to chronic usage of immunosuppressive drugs that are used to prevent immune system from rejecting the newly transplanted organs. Early diagnosis and treatment of these complications help us to decrease mortality and morbidity after transplantation dramatically.
Materials and Methods:
The patient is a 55-year-old man that has received renal transplantation for renal failure due to diabetic nephropathy 4 years ago and then received cyclosporine and mycofenolate mofetil. He developed plaque-like lesions in right lower extremity. Biopsy of skin lesions was done and the diagnosis was Kaposi sarcoma. The dosage of immunosuppressive drugs was reduced . Chemotherapy was intiated because of the continual skin lesions. The patient developed fever & swelling of left maxillary sinus following chemotherapy . Biopsy of mucous layer of Maxillary sinus and culture of sinus discharge confirmed mucormycosis infection.

Discussion &Conclusion:

Transplant – related (acquired) Kaposi sarcoma develops in people who receive immunosuppressive drugs after an organ transplant. Kaposi sarcoma is 150 to 200 times more likely to develop in transplant patients than in the general population. This disease is due to infection with human herpes virus type 8 (HMV – 8). Often transplant related Kaposi sarcoma affects only the skin. The treatment includes stopping or reducing immunosuppressive drugs and then local therapies such as surgery and radiotherapy or systemic therapies such as chemotherapy. Due to drug induced immunosuppressant and neutropenia after transplantation we must pay attention to opportunistic infections specially serious fungal infections . In this patient with the history of diabetes mellitus and previous immune defects, after fever & face swelling , radiography & ct scanning of face sinuses were done. After detection of left maxillary sinus mucosal involvement, mucosal biopsy and culture of sinus discharge was done. Mucormycosis grew in the culture media, so, mucormycosis infection was confirmed . Following treatment with amphotricine B, sinusal infection was improved.

Keywords:
Kaposi Sarcoma; Mucormycosis; Renal Transplant

Poster11

Fever, Hepatosplenomegaly and pancytopenia in a renal transplant recipient

Negin Esmailpour
Infectious Diseases Specialist Tehran University of Medical Science, Tehran, Iran.
Email: esmailnegin@yahoo.com

Case Presentation:

A 50-year-old man was admitted to the hospital because of fever of 3 week's duration, fatigue, and anorexia and weight loss. He had been diagnosed with end stage renal failure due to diabetes mellitus. Three months before admission, he received a renal transplant and started an immunosuppressive regimen.

His postoperative course was uncomplicated and he was discharged on the 11th post-transplant day with good renal function.

He remained well until 3 weeks before admission. The patient was living in Ghazvin.

On examination the patient appeared pale and ill. He reported loss of 7 Kg of body weight within the last month.

His vital signs were: T^{oral}: 38.5 C, PR: 95/min, RR: 16/min, BP: 130/80 mmhg.

No lymph node, normal head and neck, normal heart sounds and normal lung exam were reported. The edge of the liver was palpable 4 cm below the right costal margin. The spleen was also palpable 6 cm below the left costal margin and was tender.

There was no tenderness over the renal allograft. Rectal exam was normal.

Lab data: PPD: negative- U/A and U/C and B/C were normal.

Hct 29

WBC 2100/mm^3(neut %38-lymph %45- mono %12- eos %1- baso %4)

PLT	89000/mm^3
Creat	1.5 mg/dl
CRP	89mg/l
ESR	62mm/h
RF	4+

A radiograph of the chest and a renal ultra sound were both normal. A CT scan of the abdomen and pelvis, performed after oral and intravenous contrast, disclosed hepatosplenomegaly without focal lesions; there was no evidence of free fluid within the abdomen or a focal fluid collection suggestive an abscess.

What is your diagnosis?

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Poster12

Diatoms application in medical nanotechnology and large scale production in photo bio reactors

Reza Ranjbar *, Habibollah Peyrovi
*** Corresponding Author:**
Department of Nanotechnology, Taleqani Hospital, Shahid Beheshti Medical University, Tehran, Iran.
Email:

Abstract:

Diatoms are groups of single cell microscopic beings galore in lakes, seas, and oceans. Their unique cell wall membrane is made of silicate, which differentiates them from other species. These cell walls are like very organized networks with pores in nanometer dimensions. This characteristic has presented them as powerful tools in making biosensors. Monitoring different compounds such as specific glucose and proteins in blood are among such applications. Moreover, the cell walls may have various applications in immunoisolation of transplanted cells to support these cells not to follow body system rejection and provide oxygen and the necessary materials for cell growth, as well as applications as nanocapsules in drug delivery. The best advantage of these species is their potential for large scale production with inexpensive material and uniform products. In this presentation the application of these species in medical nanotechnology is elaborated and their large scale production in photo bio reactors are explained.

Keywords:
Nanotechnology; Diatoms; Medicine; Photo Bio Reactors.

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Poster13

Increased frequency of the multi drug resistance mycobacterium tuberculosis strains & necessitate for correctly Determining of the MTB strains to pyrazinamide

Mohammad Najafimosleh [*]***,*** *Kiyoomars Ghazisaeedi, Parisa Farnia.*
[*]***Corresponding author:***
Department of Microbiology, Faculty of medicine,Hamedan University of Medical Sciences.Hamedan, Iran.
E-mail: n_mosleh@yahoo.com

Background & Objectives:

Pyrazinamide is an important front-line anti-tuberculosis agent. This drug plays a unique role in shortening the therapy, while being metabolically active and replicating bacilli; it kills a population of semi-dormant organisms that are not killed by other first-line anti tuberculosis drugs. The activity of pyrazinamide correlates with the acidity of the medium, being most active at pH 5.5 less active at pH 6 and inactive at neutral pH. The problem is that such an acidic environment is quite unfavorable for Mycobacterium tuberculosis growth. Therefore, the pyrazinamide susceptibility testing is difficult and often unreliable because of the acid pH requirement for drug activity. For this reason, many clinical microbiology laboratories do not perform pyrazinamide susceptibility testing and most drug-resistance surveys do not have pyrazinamide resistance data. For this reason, a special condition that could be to support the optimal growth of organisms & allow to performing pyrazinamide susceptibility testing at favorable pH has been developed.

Material & Methods:

The continuously buffered Middlebrook 7H10 agar base with an acidic pH of 6.0 was used to provide optimal conditions for pyrazinamide acidity; it also differs from conventional 7H10 medium in that it is supplemented with animal serum instead of oleic acid to support optimal growth of organism at low pH of 6.0. Individual critical concentrations of pyrazinamide were used according to the Hassle- Bausch´s enzyme- substrate activity correlation in this medium made it possible to differentiate between PZA-susceptible and pyrazinamide -resistant clinical isolates. Indeed, the drugs susceptibility of the test strains against rifampin , isoniazid , etambotul and streptomycin were examined that would have been presented thoroughly in the text of this paper

Results:

During two years survey the following results were obtained; approximately 6٪ of isolated were identified as pyrazinamide -resistance together with other drugs resistance, with about 1٪ only pyrazinamide -resistance.

Conclusion:

As controls were shown with pyrazinamide positive & pyrazinamide negative standard strains, the method that was used in this study obtains reliable results. Compared to a liquid medium this agar medium also has the following advantages: it allows determination of the actual proportion of pyrazinamide -resistant bacteria in the isolates and it is simple and inexpensive. In addition, it has the potential of being used for a direct susceptibility test with pyrazinamide..

Keywords:
Mycobacterium; Tuberculosis; Pyrazinamide; 7H10 agar.

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Poster14

In Vitro activity of tigecycline against strains of methicillin resistant staphylococcus isolated from wound and soft tissue in an Iranian 1000 bed tertiary hospital

Mohammad Rahbar,* *Mohammad Kabeh –Monnavar, Fatemeh Savaheli Moghadam, Mahmood Yaghoobi*

Corresponding Author:
Iranian Reference Health Laboratory, Tehran, Iran.
Email: mhhfrz@yahoo.com

Background &Objectives:

The aim of this study was to evaluate the in vitro activity of tigecycline and other comparator agents against Staphylococcus aureus isolated from surgical wound and soft tissue infections in an Iranian 1000-bedtertiary hospital.

Materials & Methods:

In vitro activity of tigecycline against 67 Strains of Staphylococcus aureus isolated from different patients hospitalized at Milad Hospital, Tehran, during last six month of 2007. All strains were identified according the routine bacteriological methods. Susceptibility testing were performed by disk diffusion methods as recommended by Clinical laboratory standards institute. Cefoxitin (30µg) disk was used for detection of methicillin resistant strains of S.aureus.

Results:

In total, during this study 67 strain of S.aureus were isolated from patients .The majority of patients were from surgical wards including open heart, orthopedic ward and had post operation wound infections. Of 67 strains (38.29%) were MRSA. All isolates including MRSA strains were susceptible to tigecyline , Linozolide and vancmycin. 100% of the strains were penicillin resistant. Resistance of S .aureus to other antibiotics including teicoplanine, ciprofloxacin, clindamycin, erythromycin,

cotri-moxazole and rifampin were 6.4%, 38.29%,40.42%, 27.6% and 19.4% respectively. All isolates were also susceptible to vancomycin and linozold.

Conclusion:

It is concluded that all strains of S.aureus, isolated from wound and soft tissue in our hospital were susceptible to tigecyline, linozolide and vancomycin

Keywords:

In Vitro; Tigecycline; Methicillin Resistant Staphylococcus; Wound; Hospital

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Poster15

The Effect of essential oil of an endemic savory (*Satureja intermedia* C. A. Mey.) on some bacteria

Shahnazi Sahar,* *Farahnaz Khalighi-Sigaroodi, Yousef Ajani, Darab Yazdani, Maryam Ahvazi.*
**** Corresponding Author:***
Institute of Medicinal Plants, ACECR, Kavosh Ave., Supa Blvd., km 55th , Tehran-Qazvin Freeway,Karaj, Iran.
E-mail: Shahnazi@imp.ac.ir

Background & Objectives:
The genus *Satureja* belongs to Lamiaceae family. *Satureja* species are present in mountainous areas in Iran, mainly in western and northern parts. 12 species exist in Iran of which 8 are endemic. *Satureja intermedia* C. A. Mey. is a rare species endemic of Iran and Talish. This genus has antiseptic effect. In this research, antibacterial activity of essential oil of *Satureja intermedia* was identified for the first time.

Materials & Methods:
Satureja intermedia were collected from the elevation of Ardabil province, northwestern Iran, in August 2006. Then, air-dried aerial parts of the plant were submitted to hydro-distillation using a Clevenger apparatus to produce the essential oil. Antibacterial activity was conducted by disc-diffusion and broth dilution technique, using standard (ATCC and PTCC) Gram-positive and Gram-negative bacteria in order to determine MIC (Minimum Inhibitory Concentration) and MBC (Minimum Bactericidal Concentration).

Results:
The antibacterial test results showed that essential oil of this plant had a great potential antibacterial activity against Gram-positive and Gram-negative bacteria.

Conclusion:

Results presented here may suggest that the essential oil of *Satureja intermedia* possesses antibacterial properties and is; therefore, a potential source of antibacterial ingredients for the food and pharmaceutical industry.

Keywords:
Satureja, Essential Oil; Antimicrobial Activity, Savory

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Poster16

Antibacterial activity of essential oil of *Thymus trautvetteri* Klokov & Desj – Shost.

Sahar Shahnazi,* *Farahnaz Khalighi-Sigaroodi, Yousef Ajani, Darab Yazdani, Maryam Ahvazi.*
Corresponding Author:
Institute of Medicinal Plants, ACECR, Kavosh Ave., Supa Blvd., km 55th ; Tehran-Qazvin Freeway, Karaj, Iran.
E-mail: Shahnazi@imp.ac.ir

Abstract:

Background & Objectives:

Lamiaceae is one of the big plant families in flora of Iran. The family comprises some aromatic and medicinal species. In the flora Iranica, 14 species have been introduced for *Thymus*. Of these, four species are endemic to Iran. One of them is *Thymus trautvetteri* Klokov & Desj – Shost. In this study, antibacterial activity of essential oil of *Thymus trautvetteri* was identified for the first time.

Materials & Methods:

Thymus trautvetteri was collected from Ardabil province, northwestern Iran, in June 2006. Then, air-dried aerial parts of the plant were submitted to hydro-distillation using Clevenger apparatus to produce the essential oil. Investigation of antimicrobial activity was conducted by Disc-diffusion technique, MIC and MBC of the essential oil were determined using different antibiotics as positive control.

Results:

In this study, the antibacterial activity of essential oil of this plant was assayed against seven bacteria and *Staphylococcus aureus* resulted to be the most sensitive microorganism with a MIC value of 125 µg /ml. Also this study showed essential oil of this plant has strong inhibitory and bactricidal effects against gram-positive and gram-negative bacteria.

Conclusion:

The results of this research showed that essential oil of *Thymus trautvetteri* can be used an alternative remedy of the infections caused by these bacteria.

Keywords:
Thymus; Essential Oil; Antimicrobial Activity; Thyme.

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Poster17

Environment Specifications in Hematopoietic Stem Cell Transplantation (HSCT) Ward

Abbas Hajifathali, ***Afshin Mohammad-Alizadeh*,*** *Reyhaneh Kabiri-Movahed, Mahshid Mehdizadeh Mehdi, Tabarraie.*

**** Corresponding Author:***
Department of Hematology,Taleqani Hospital,Shaheed Beheshti Medical University,Tehran, Iran.
Email: rayhanehkabiri@yahoo.com

Due to their specific disease conditions and treatments, HSCT patients have to avoid certain environments and materials. In case of any contact, the risk of infective agents especially fungi will increase. For these patients there has to be protective environments prepared, the conditions of which are outlined below:

Allogenic HSCT patient environments have to have the fewest number of fungus spores in the air. Aspergillus is one example. In searches on aspergillus epidemics, building processes have been attributed to them. The American association of Civil Engineering defines the environmental infection control guidelines as follows:

1- HEPA filteration;
2- Direct air-flow to the room;
3- Positive room air pressure compared to the corridor;
4- Appropriate room coverage(including
Walls, floor, ceiling, Windows, and electric plugs);
5- 12 times/hr air-ventilation

Renovations and building buildings is accompanied with the outbreaks of hospital fungus infections, especially aspergillus in patients with deficient immune systems.

Therefore, it is suggested to use high quality masks such as N95, especially when the patient is leaving the ward.

Among other important factors, water hygiene (differential water routine culture to find any infections); equipment (such as controlling the nursing materials used in transplantation department and taking measures to destroy any out-of-date ones); plants (preventing entrance of any fresh or artificial flowers to the transplantation department as they may make breathing problems for transplant patients due to aspergillus-related respiratory problems); play areas & toys (weekly cleaning of the child- playing equipment); and surfaces (dusting with only wet towels, and using vacuum cleaners).

Keywords:
Aspergillus; Transplant Patients; HSCT; Environment

Poster18

Breast-feeding lasting longer than 6 months protects against childhood acute leukemia and lymphomas

Azam Fazel, ***Mahmood Asqari *,*** *Abdollah Bani Hashem, Habibollah Esmaieli.*
**** Corresponding Author:***
College of Nursing, Zahedan University of Medical Sciences; Zahedan, Iran.
Email: mahmoud_asqarie@yahoo.com

Abstract:

Background & Objectives:

The role of breast-feeding in protecting against childhood acute leukemia and lymphomas is uncertain.

Patients & Methods:

We investigated this issue in a case-control study comprising 57 patients, aged 1-15 years, with acute lymphocytic leukemia (ALL), acute myeloblastic leukemia (AML) , Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL), as well as 57 controls matched for age, sex and ethnicity. Information was collected via a face to face interview with the mothers.

Results:

The median duration of breast-feeding among patients was significantly shorter than among controls , 14.76 and 21.61 months , respectively (P=0.001).

Discussion &Conclusion:

Breast-feeding of 0-6 months duration, when compared with feeding of longer than 6 months, was associated with increased odds ratios for leukemia and lymphoma (OR = 7.34 ; 95 % , CI= 1.68 – 32.06) . In the patient group, there were a significantly higher number of children, and patients were of a lower income and number of bedroom per family than controls. In multivariate analysis, breast-feeding

duration continues to be an independent predictor of lymphoid malignancies (P=0.008). Breast-feeding lasting longer than 6 months may protect against childhood acute leukemia and lymphomas.

Keywords:
Breast-Feeding ; Childhood Leukemia & Lymphoma

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Poster19

Experimental bone defect healing with bovine fetal growth plate as a new xenograft transplantation and xenogenic demineralized bone matrix: Radiological, histo-pathological and biomechanical evaluation

Zahra Shafiei*, *Dehghani, S.N.; Bigham, A.S.; Torabi Nezhad, S.*
****Corresponding Author:***
Department of Surgery, School of Veterinary Medicine, Shiraz University, Shiraz, Iran.

Abstract:

Background & Objectives :

The following study was designed to evaluate xenogenic bovine demineralized bone matrix (DBM) and new xenograft (Bovine fetal growth plate) effects on bone healing process.

Materials & methods:

wenty male White New Zealand rabbits were used in this study. In group I (n=10) the defect was filled by xenogenic DBM and in xenograft group the defect was filled by a segment of bovine fetal growth plate and was fixed by cercelage wire. Radiological, histopathological and biomechanical evaluations were performed blindly and results scored and analyzed statistically.

Results:

Statistical tests did not support significant differences between two groups radiographically (P> 0.05). There was a significant difference for union at the 28nd post operative radiologically (P<0.05). Xenograft was superior to DBM group at the 28th postoperative day for radiological union (P<0.03). Histopathological and biomechanical evaluation revealed no significant differences between two groups.

Conclusion:

In conclusion the results of this study indicate that satisfactory healing occurred in rabbit radius defect filled with xenogenic bovine DBM and xenogenic bovine fetal growth plate. Complications were not identified and healing was faster in two grafting groups.

Keywords:

Bovine Fetal Growth Plate; Xenograft; Bone Healing; Rabbit.

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Poster20

Stem cell collection contamination:clinical impact, and review

Mehdi Tabarraee***,** *Mahshid.Mahdizadeh , Abbas Hajifathali, Mojtaba Ghadiani, Afshin Alizadeh*
****Coressponding auther:***
Bone Marrow transplantation ward, Taleghani hospital, Shahid Bebeshti medical University.
Email: mehditabarraee@yahoo.com

Abstract:
Case Presentation:
A 42-year-old man, known case of Hodgkin disease in the 5th remission admitted for autologous HSCT. The patient was mobilized with cyclophosphamid 2.5gr/m^2 + GCSF.
A total of 4.9×10^8/kg mononuclear cells with 2% CD_{34} + cells were separated during 2 consecutive days.

He received conditioning regime as protocol CCNU + Etoposide cytosar + melphalan after administration of conditioning regime culture of stem cell collection reported staff epidermis.
What are you doing?

We infused stem cell collection without antibiotic coverage. On the 4th day popular lesion appeared in the skin (like folliculatise); on the 5th day, he was febrile and WBC was 50.

We administered Imipenem + Vancomycin + Clindamycin.
48 hours after the beginning of treatment he was afebrile. Culture from skin lesion was staff coagulase+.

WBC engraftment was done on the 11th day and plt. engraftment on the 12th day.

We administered IV antibiotic for one week and then changed it to oral cloxacillin for one additional week.

The American association of blood banks requires routine culture of hematopoietic stem cells prior to bone marrow transplantation. What action should be taken in case of positive culture? We try to answer this question by reviewing previous articles.

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Poster21

Case Presentation : gram negative sepsis

Mahshid Mehdizadeh***,** *Hamid Attarian*
****Coressponding auther:***
Bone Marrow transplantation ward, Taleghani hospital, Shahid Bebeshti medical uviversity, Tehran, Iran.
Email: mahshid_mehdizadeh@yahoo.com

Abstract:
Case Presentation:

A 26-year- old male patient with Hodgkin lymphoma on the 3rd remission was admitted for autologous Hematopoietic stem cell transplantation. After catheter insertion mobilization and stem cell harvesting, conditioning was performed. Before HSCT he was treated with cefixim which continued until day + 5 for a suspicious sinusitis. Patient's culture at the time of admission was negative. On day +5 he complained of nausea and dizziness and a mild erythema in inguinal area [WBC =100], no fever.

What should we do?

On day +8 a sudden rise in temperature up to 39.5° c with nausea, with vomiting and diarrhea occurred

WBC = 0

Hb = 7.5 g/dl

Plt = 8000

In physical examination a few folliculitis were observed.

What is the next therapeutic step?

The next day he had abdominal pain and epigastric tenseness. The blood culture was reported gram negative bacilli cutaneous lesions which progressed and he had

pain on both auxiliary areas and edema even around the catheter insertion site, and sub icter.

WBC = 100

Plt = 2000

What do you recommend?

His fever decreased gradually until day + 12 and then stopped. Abscesses in both auxiliary areas were formed and on day + 18 (WBC = 1380) fistulized. secretion on culture was positive .

Poster22

Case presentation: Central vein catheter infection

Mahshid Mehdizadeh [*] ***,****Hamid Attarian*
[*]***Coressponding auther:***
Bone MarrowTtransplantation Ward Taleghani Hospital, Shahid Bebeshti MedicalUviversity.
Email: mahshid_mehdizadeh@yahoo.com

Abstract:
Case Presentation:
A 45-year- old male patient with Non Hodgkin lymphoma since 04/2007 referred to us. His disease relapsed 2 months after completion of chemotherapy and was then admitted in the second remission for autologus bone marrow transplantation. After mobilization, stem cell separation and conditioning, BMT was performed. After BMT, he had diarrhea from day + 5 to + 11 (WBC = 70) .

Pain in the anal area due to a hemorrhoid from day + 7 and fever (WBC = 100 , Plt = 10000)

What treatment do you recommend?

Fever stopped but his hemorrhoid pain continued he had another episode of fever and neutropenia on day + 20 (WBC=70) that stopped after antibiotic therapy. On day =40 (WBC=2100,Plt =8000) he had fever and vomiting.

What treatment do you recommend?

4 days later, fever continued and he suffered from severe headache. His blood culture reported staphylococcus coagulase negative. Sinus CT scan showed ethmoidal sinusitis, Brain CT scan was normal.

What treatment do you recommend?

Fever and headache continued. His subsequent blood cultures were positive and the catheter was removed and was sent for culture. Its culture was negative but patient's fever stopped 24 hours later and his general condition improved.