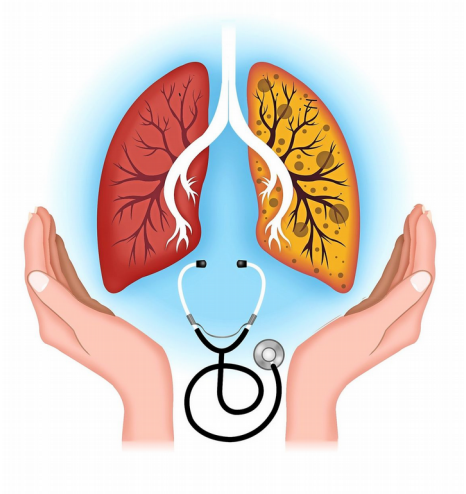
MDR TB Case Presentation



NRITLD
Infectious Diseases Department

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MD , ID
Felowship in infection in immunocompromised host

Case presentation

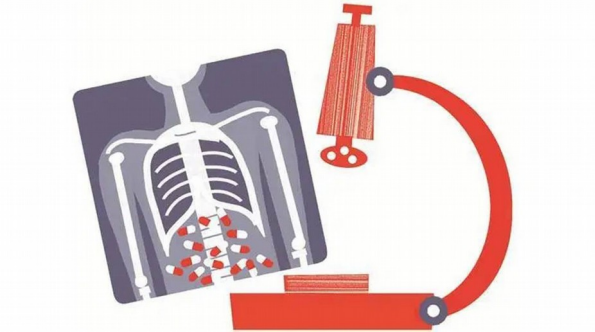
- A 21-year old previously healthy woman **from Azerbaijan** , presented to our department with a **1 months** history of **night sweats**, **weight loss**, **shortness of breath**, and **productive cough**.
- She immigrated to IRAN from Azerbaijan 3 years ago but returns on occasion to visit family.

On physical examination

- V/S:
  OT: 37°C , BP:113/69 mmHg, PR:99 , RR:18
- O2 sat. : 98%
- Auscultation revealed stable rales in the right middle lung.
- The rest of her physical exam were normal.

Laboratory Findings on Admission

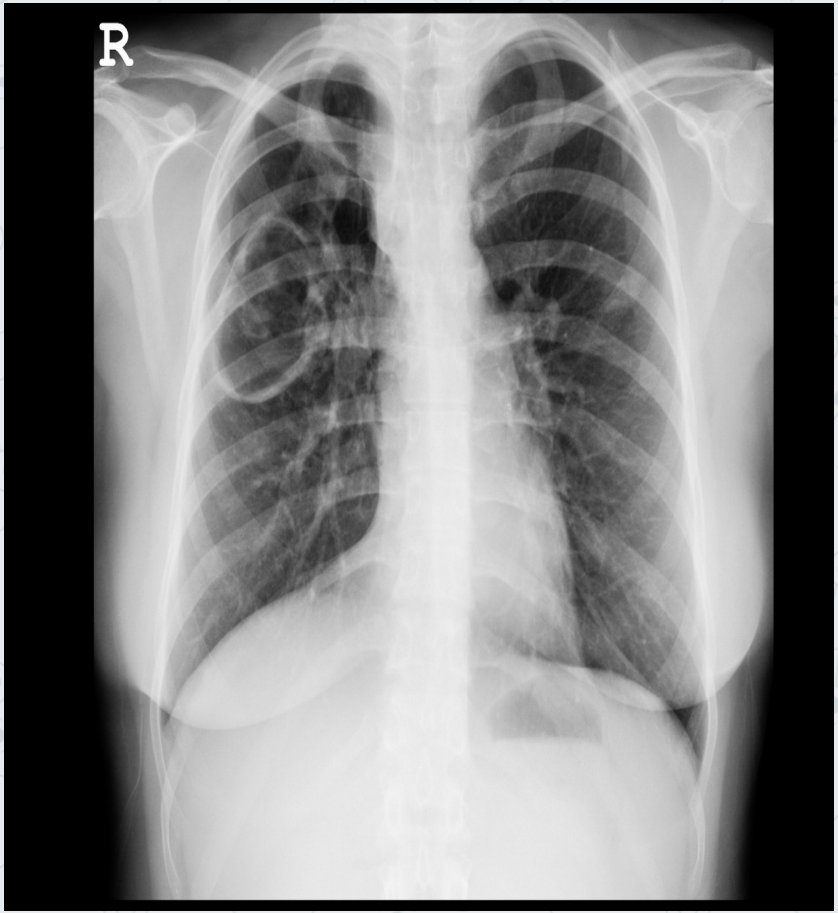
Parameters	Laboratory Findings
WBC, µL	3900
Hb, g/dL	10.3
Platelet, µl	212000
ESR, mm/h	67
CRP, mg/L	27.4
AST, U/L	19
ALT, U/L	17
LDH, U/L	456
Total protein, g/dL	5.7
Albumin, g/dL	2.9
Cr	0.7
Urea, mg/dL	10
HIV Ag-Ab	negative



CXR

A large thick wall cavity in the right mid to upper zone .

The remainder of the lungs were normal.



Chest CT scan

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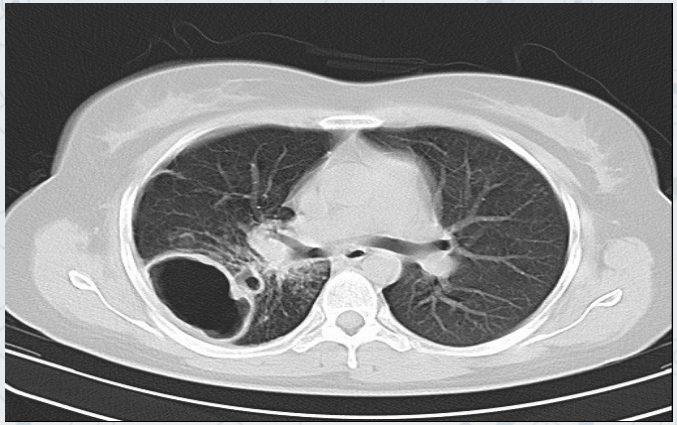
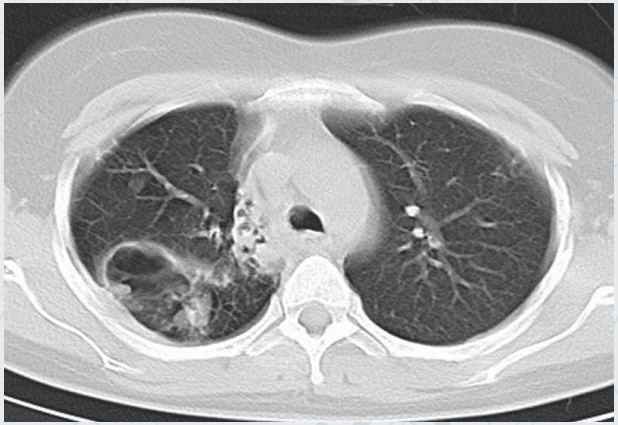
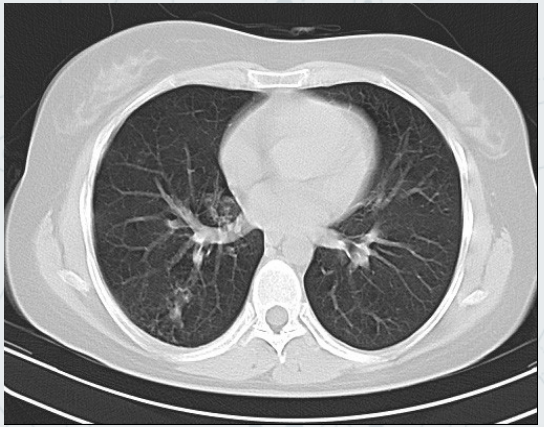


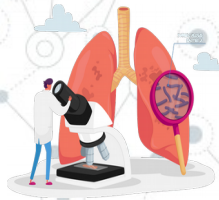




Laboratory tests came back with the following results

- Sputum results were positive AFB smear 3+
- The patient started on standard 4 drug regimen(HREZ) accordingly

Lab results



- 3 days into treatment *Gene-Xpert* MTB/RIF , confirmed the presence of *Mycobacterium tuberculosis* complex (MTBC) along with **detection of RIF resistance** !

- By national guidelines and protocol, molecular analyses were extended **to testing of susceptibility to isoniazid (INH**) and subsequently to **second-line anti-tubercular drugs .**

Following the guidelines of the WHO and national guideline, we started the so-called longer treatment of MDR-TB composed of at least five effective anti-tubercular drugs:

INH + **Linezolid**+ **Bedaquiline** + **Clofazimine** + **Cycloserine**+ **levofloxacin** + **PZA** + **ETM**.

- 2 weeks into treatment preliminary susceptibilities reported her isolate was **resistant to INH and RIF**

Grouping of medicines recommended for use in longer MDR-TB regimens

Group A:
Include all three **medicines**

1- Levofloxacin or Moxifloxacin
2- Bedaquiline
3- Linezolid

Group B:
Add one or both medicines

1-Clofazimine
2-Cycloserine *OR* Terizidone

Group C:
Add to complete the regimen and when medicines from Groups A and B cannot be used:

1-Ethambutol

2-Delamanid

3-Pyrazinamide

4-Imipenem–cilastatin or meropenem

5-Amikacin (*OR* streptomycin)

6-Ethionamide *OR* Prothionamide

7-P-aminosalicylic acid(PAS)

Longer regimens for MDR/RR-TB

- In multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) patients on longer regimens, **all three Group A agents** and **at least one Group B agent** should be included to ensure that treatment starts with at least four TB agents likely to be effective, and that at least three agents are included for the rest of the treatment if bedaquiline is stopped.

- **If only one or two Group A agents are used**, **both Group B agents are to be included**.

- If the regimen cannot be composed with agents from Groups A and B alone, Group C agents are added to complete it.

Longer regimens for MDR/RR-TB

- In MDR/RR-TB patients **on longer regimens**, **a total treatment duration** of **18–20 months** is suggested for most patients; the duration may be modified according to the patient's response to therapy.

- In MDR/RR-TB patients on longer regimens, **a treatment duration** of **15–17 months after culture conversion** is suggested for most patients; the duration may be modified according to the patient's response to therapy.

- In MDR/RR-TB patients on longer regimens **containing Amikacin or Streptomycin**, an **intensive phase of 6–7 months** is suggested for most patients; the duration may be modified according to the patient's response to therapy.

The 6-month Bedaquiline, Pretomanid, Linezolid and Moxifloxacin (BPaLM) regimen for MDR/RR-TB (NEW)

WHO suggests the use of **a 6-month treatment regimen** composed of
1-Bedaquiline,
2-Pretomanid,
3-Linezolid (600 mg) and
4-Moxifloxacin

rather than the 9-month or longer (18-month) regimens in MDR/RR-TB patients.

The 6-month Bedaquiline, Pretomanid, Linezolid and Moxifloxacin (BPaLM) regimen for MDR/RR-TB (NEW)

This recommendation applies to the following:
a. People with **MDR/RR-TB** or **with MDR/RR-TB and resistance to FQs (pre-XDR-TB).**

b. People with confirmed pul-TB and all forms of extrapulmonary TB **except for** TB involving the **CNS, Osteoarticular and Disseminated (miliary) TB**.

c. Adults and adolescents **≥14 years** .

d. All people **regardless of HIV status**.

e. Patients with **<1-month previous exposure** to **Bedaquiline, Linezolid, Pretomanid or Delamanid**. When exposure is **>1 month**, these patients may **still receive these regimens if resistance** to the specific medicines with such exposure **has been ruled out**.

3. This recommendation **does not apply to pregnant and breastfeeding women** owing to **limited evidence on the safety of pretomanid**.

The 9-month all-oral regimen for MDR/RR-TB (NEW)

WHO suggests the use of the 9-month all-oral regimen rather than longer (18-m) regimens in patients with MDR/RR-TB and **in whom resistance to FQs has been excluded**

1-Bedaquiline (used for 6 months)+

2-levofloxacin/moxifloxacin +

3-Ethionamide+

4-INH(high-dose) +

5-PZA+

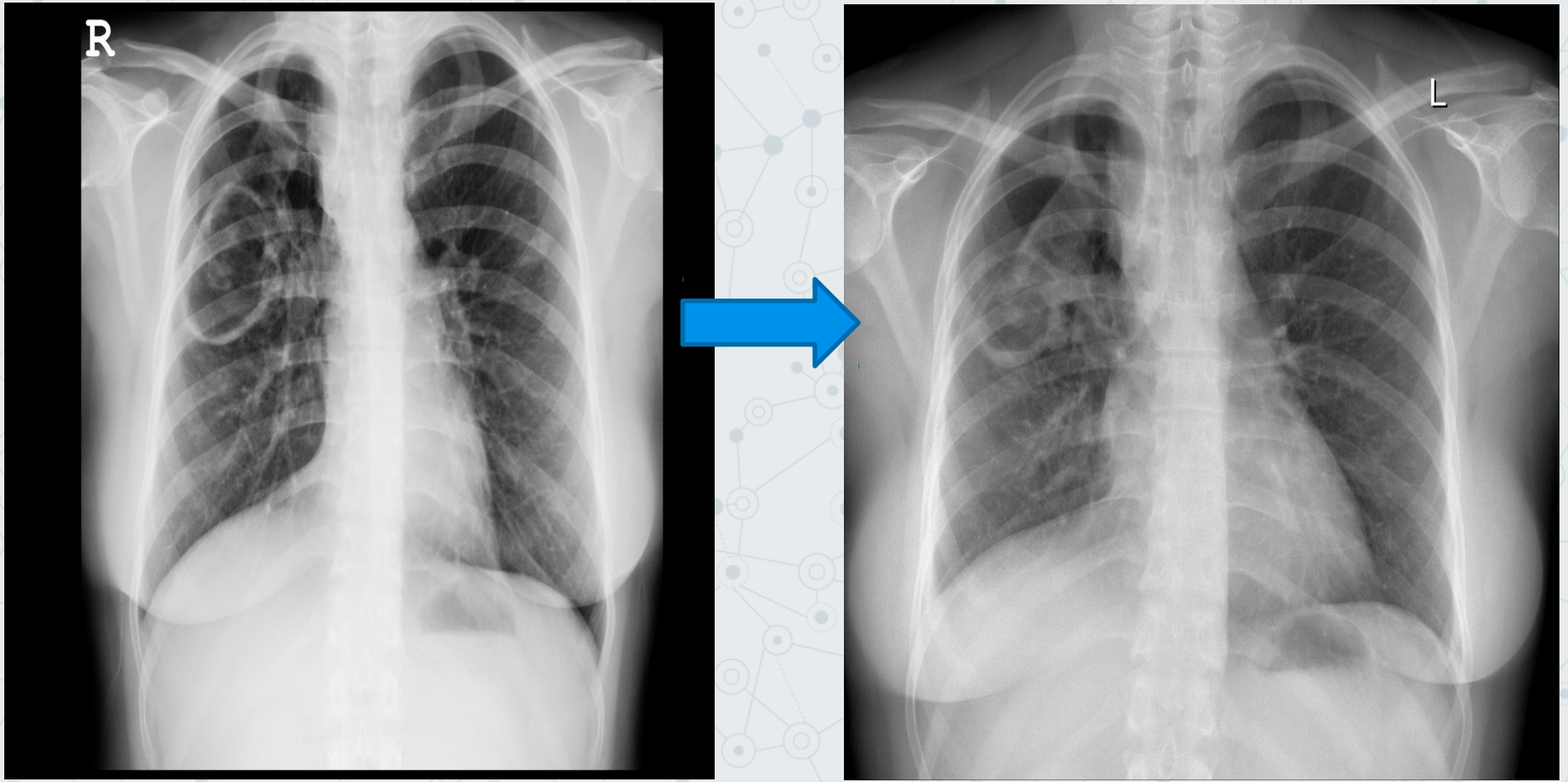
6-ETM +

7-Clofazimine (for 4 months),
(with the possibility of extending to 6 months if the patient remains sputum smear positive at the end of 4 months),

followed by treatment with:
levofloxacin/ moxifloxacin, **clofazimine**, **ETM and PZA** (for 5 months).
Ethionamide can be replaced by 2 months of linezolid (600 mg daily)

Hospital course

After about 50 days of treatment, the patient's sputum smear was reported negative two weeks apart and the clinical condition of the patient improved a lot.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How do you continue to treat the patient from now on?

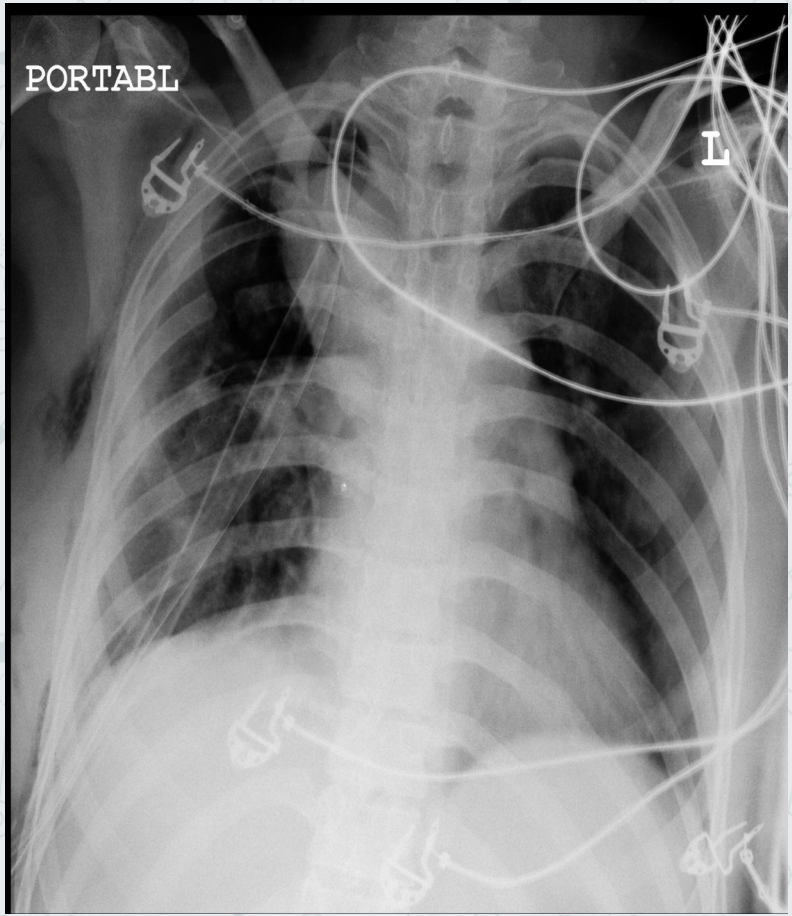
- Cavitary TB carries a poor prognosis. There is a **higher risk of treatment failure and relapse** if cavities are radiographically **present during the first two months of therapy.**

- Then, if cavities **persist after six months of treatment**, **the risk of relapse doubles** compared to those whose cavities close by treatment completion.

- The association between cavitation and relapse could be attributable to **poor drug penetration into the poorly vascularized cavity**. Alternatively, **cavitation could be a marker for high bacillary burden** from extensive disease.

- MDR-TB patients with **pulmonary cavity greatly lowered the cure rate**

- In some cases, surgery such as lobectomy and pneumonectomy were performed as adjuvant treatment for cure, but concern of the overall surgical efficacy and eligibility remains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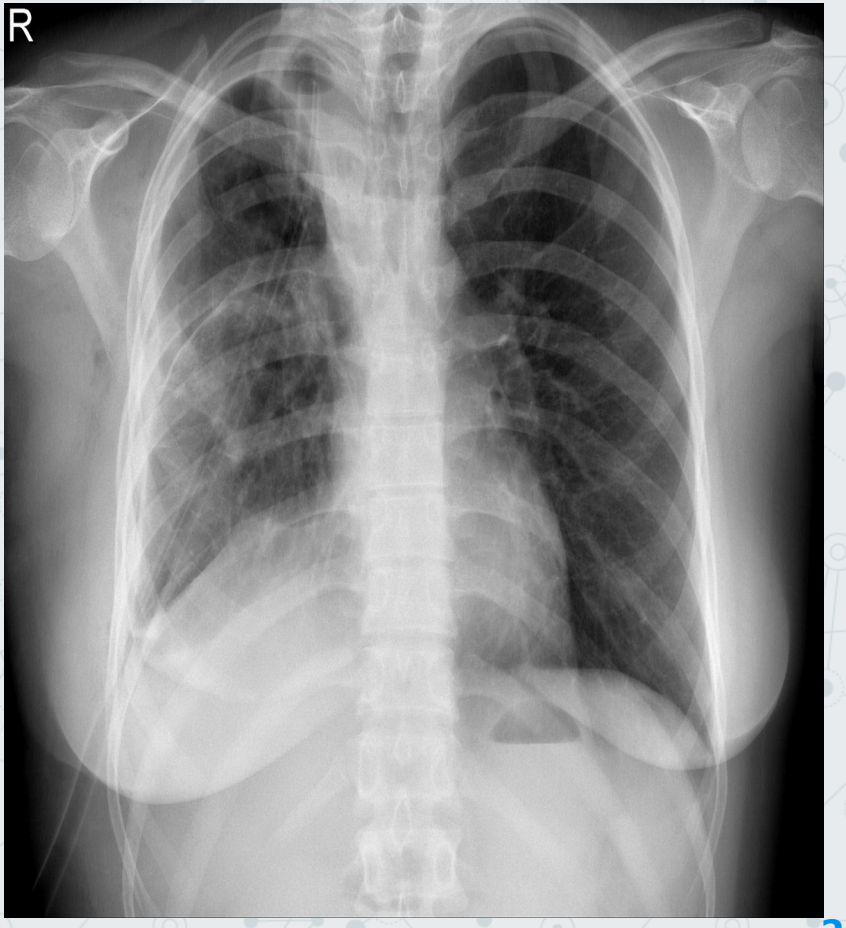
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Pathology report

- Chronic granulomatous inflammation with contains **high concentrations of extracellular mycobacteria** and **Intracellular mycobacteria sporadically within macrophages**

Thanks for your kind attention!