Polyradiculopathy in liver transplant patient

ROZITA KHODASHAHI
ID SPECIALIST,FELLOWSHIP IN IC HOST & TRANSPLANT PATIENT
ASSOCIATE PROFESSOR
MASHHAD UNIVERSITY OF MEDICAL SCIENCES

CASE PRESENTATION

- 41-year-old male underwent orthotopic liver retransplantation for chronic allograft failure. His maintenance immunosuppression regimen included Tacrolimus and Mycophenolate Mofetil (MMF).
- CMV D/R status was D-/R+, and he completed standard prophylaxis
- Clinical PresentationAt 12 months post-retransplantation, the patient presented with a two-week history of persistent fever, diffuse arthralgias, and progressive lower extremity weakness that evolved rapidly. Examination revealed severe, asymmetric motor weakness (grade 2/5 in the lower limbs), absent ankle reflexes, and saddle anesthesia, indicating a lumbosacral polyradiculopathy.

DIFFERENTIAL DIAGNOSIS

Differential Diagnosis of Polyradiculopathy After Liver Transplant

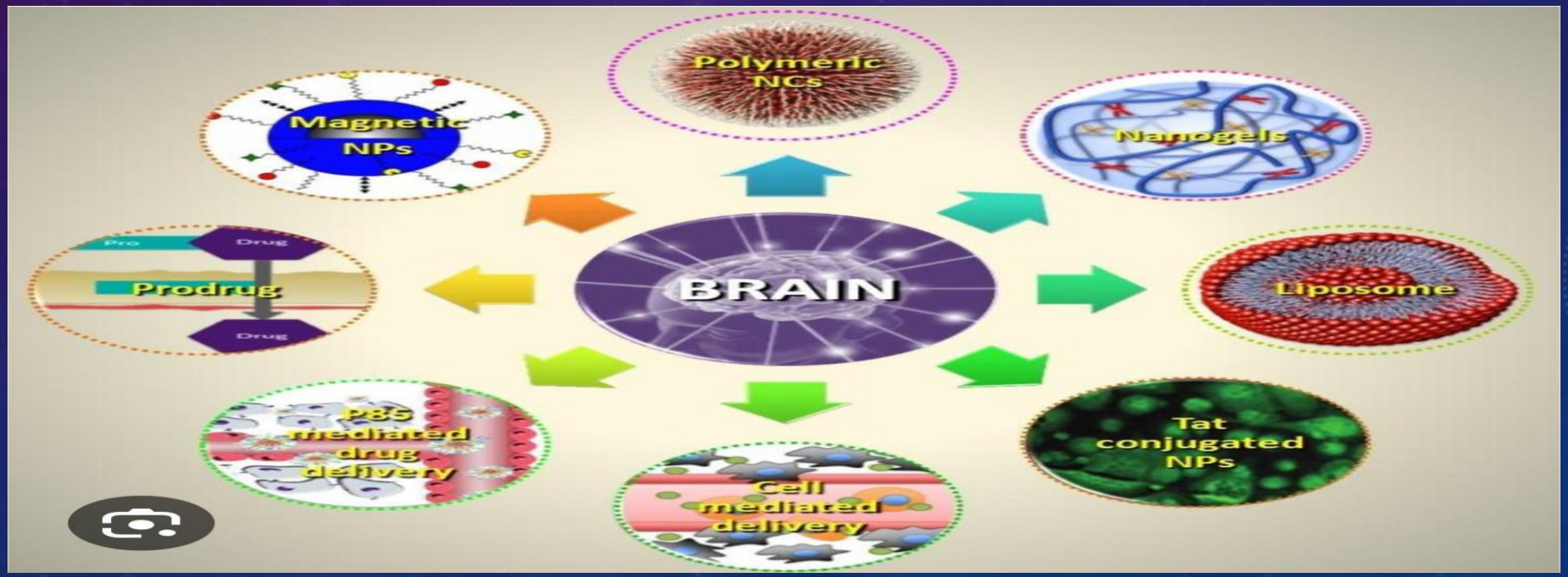
Category	Possible Etiologies	Key Diagnostic Clues / Work–up
Infectious	CMV (most common after transplant); HSV–2; VZV; EBV; HIV; HTLV–1; Listeria; Nocardia	CSF PCR/culture; MRI spine with contrast; serology
Drug–induced / Toxic	Calcineurin inhibitors (Tacrolimus, Cyclosporine); Metronidazole; Linezolid; Isoniazid; Amiodarone	Check drug levels; review medications; clinical improvement after dose reduction or switch
Inflammatory / Autoimmune	GBS (AMAN variant often seen post–transplant); CIDP; Vasculitic neuropathy (Hep B/C, cryoglobulinemia, rheumatologic disorders)	EMG/NCS patterns, CSF albuminocytologic dissociation, autoimmune markers

Metabolic / Nutritional	Diabetic neuropathy; Deficiencies of B1, B6, B12; **Copper deficiency**; Severe electrolyte abnormalities	Vitamin and copper levels; glucose and HbA1c; correct metabolic derangements
Structural / Mechanical	Spinal root compression due to positioning during surgery; postoperative epidural hematoma; degenerative spondylotic radiculopathy; spinal ischemia	MRI lumbar/cervical spine to rule out compressive lesions
Renal / Hepatic Dysfunction–related	Uremic neuropathy; Persistent neuropathy from pre–transplant hepatic failure	Evaluate renal function; chronic course predating transplant
Graft–versus–host disease (rare in liver transplant)	Immune–mediated radiculoneuropathy	Histology/biopsy if suspected; systemic GVHD signs

- **Immediate Workup Priority**
- Given the patient's status (post-transplant, immunosuppressed) and the **rapid, severe, asymmetric motor deficit with fever and saddle anesthesia**, **CMV Polyradiculomyelitis** is the leading and most critical diagnosis to rule in/out, followed closely by **GBS** and **Spinal Abscess/PTLD**.
- **Urgent: Spinal MRI** (to rule out compressive lesions like abscess or PTLD)
- **Urgent: Lumbar Puncture (LP)** and **CSF Analysis** (Protein, WBC count/diff, Glucose, **CMV PCR**, VZV PCR, Culture/Gram stain, Cytology).
- **Urgent:** Blood work (CMV PCR/Antigenemia, Tacrolimus level, ESR/CRP)'HIV test.
- **Early: NCS/EMG** (to confirm the localization and assess for demyelination/axonal loss).

LUMBAR PUNCTURE

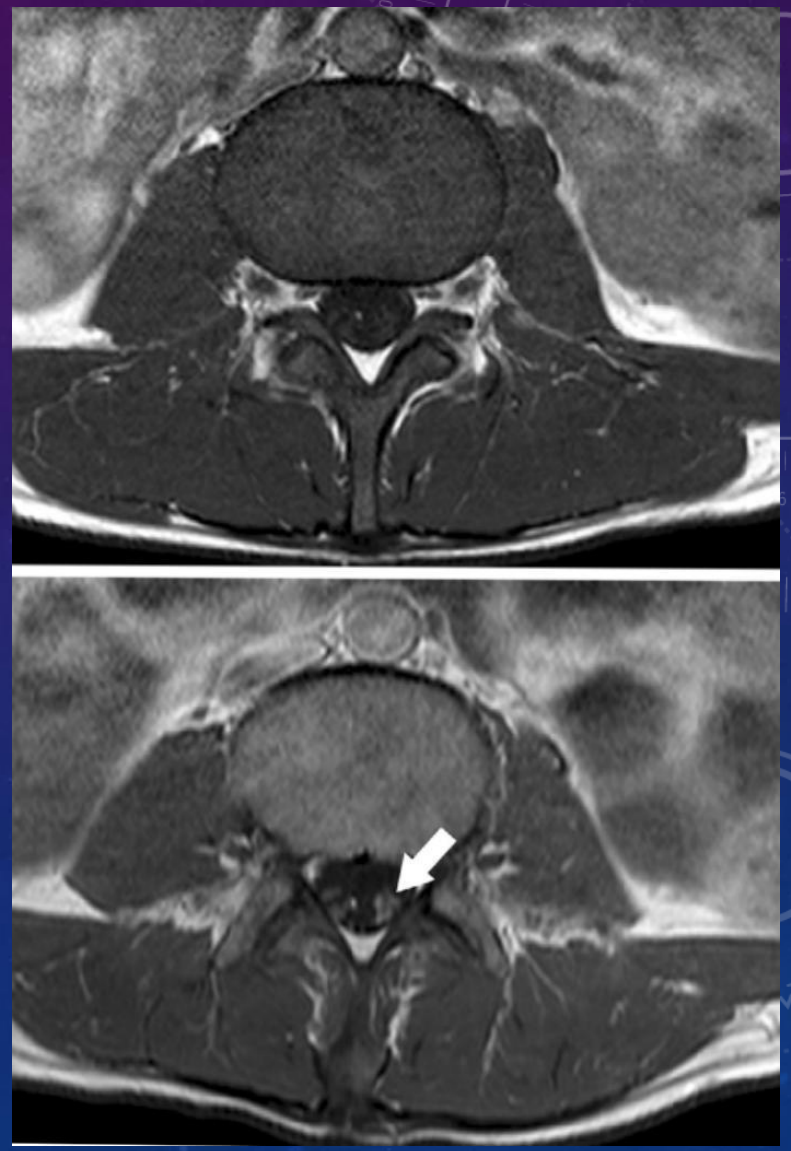
- Pleocytosis with polymorphonuclear leucocyte predominance
- Hypoglycorrhachia
- Increased protein levels

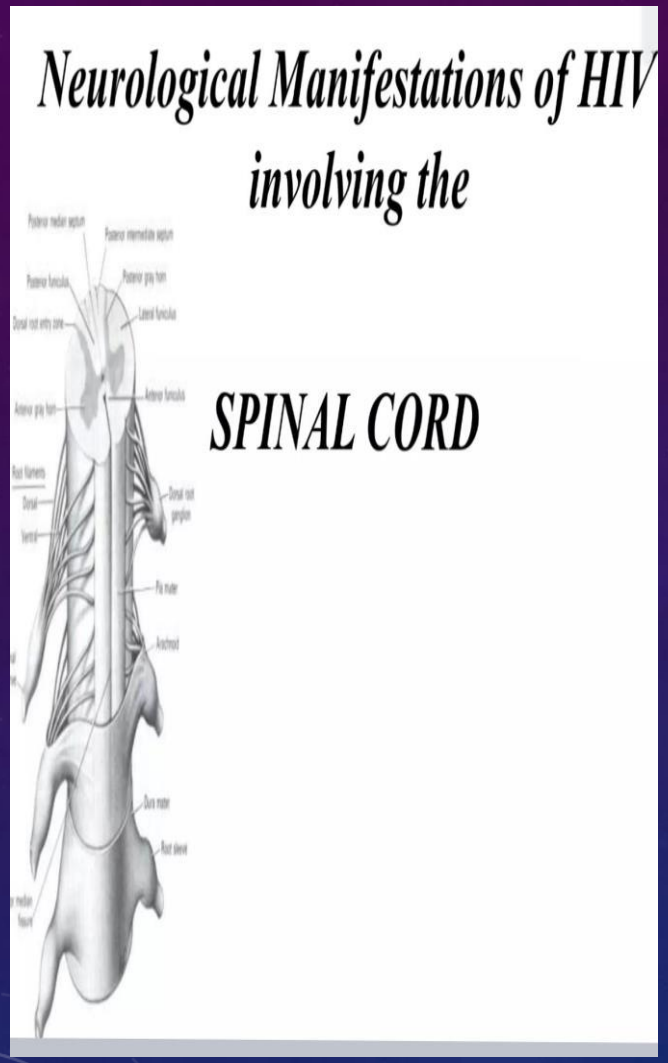


CASE PRESENTATION

- CSF analysis showed a WBC count of 291/µL, with 62% of Polymorphonuclear leukocytes, as well as a protein level of 269 mg/dL and glucose level of 31 mg/dL.
- Cryptococcus antigen assay and cultures for bacteria,mycobacteria and fungi were negative

- Lumbar spine MRI performed without contrast showed no abnormalities
- Lumbar spine CE-MRI showed contrast enhancement in the cauda equina predominantly on the left side





On day 2, the CSF CMV DNA level was 2.0×109 copies/mL.

ophthalmologic examination were done

CASE PRESENTATION

- HIV screening test was positive, with an HIV-1 RNA level of 4.6×104copies/mL and CD4+ cell count of 80/μL.

CASE PRESENTATION

- **Critical Considerations:**
- **Rule out CMV First:** Given the high morbidity, **CMV Polyradiculopathy** must be assumed until proven otherwise, and empirical antiviral therapy should often be initiated promptly pending CSF results.
- **Imaging Urgency: Spinal MRI** is mandatory to immediately exclude compressive structural emergencies like an abscess, hematoma, or PTLD mass.

CASE PRESENTATION

- A CSF sample obtained on day 22 revealed and, the CMV treatment regimen was stopped.
- The patient's left lower extremity strength subsequently improved, such that he was able to walk by himself with the help of a cane, and he was discharged on day 33.

- *Preferred Therapy*
- Ganciclovir[a] 5 mg/kg IV every 12 hours plus foscarnet[a] (60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours) (BIII)
- The role of oral valganciclovir has not been established.
- *Duration of Anti-CMV Therapy*
- ≥21 days based on clinical response (AIII)
- Note: After resolution of acute disease, maintenance therapy is not routinely recommended for CMV CNS disease unless there is concurrent retinitis, there have already been recurrent infections, or severe disease was present initially.

1. Immediate Anti-CMV Treatment

This is the top priority due to the rapid, potentially irreversible neurological deficits.

Detail	Rationale
IV Ganciclovir (Full dose: 5 mg/kg IV q12h).	Ganciclovir is the standard agent for CNS CMV disease. IV formulation ensures adequate CNS penetration.
Induction for 3-6 weeks, followed by maintenance therapy with Valganciclovir.	Prevents relapse, which is common with CNS involvement.

2. Timing and Initiation of ART

The timing of ART is crucial to prevent **Immune Reconstitution Inflammatory Syndrome (IRIS)**, which could worsen the neurological status.

Rationale	Timing
To restore immune function (CD4 count) to help clear the CMV infection, which is necessary for long-term control.	**Delayed.** ART should be **deferred for 2 to 4 weeks** after the start of anti-CMV therapy.
Early ART initiation risks severe **CMV-associated IRIS** in the CNS, leading to increased inflammation and potentially irreversible neurological deterioration.	ART should be initiated once clinical stabilization is observed and the CMV viral load is trending down.
ART regimen selection must consider potential **drug-drug interactions** with Tacrolimus (a potent CYP3A4 substrate).	**Avoid boosted PIs** (e.g., Ritonavir, Cobicistat) unless absolutely necessary, as they dramatically increase Tacrolimus levels, requiring substantial dose reduction and frequent monitoring. **Integrase inhibitors (INSTIs)** are often preferred for their cleaner interaction profile.

3. Transplant Immunosuppression Adjustment

Immunosuppression must be reduced to allow the host immune system to fight the infection, without triggering allograft rejection.

Drug	Adjustment	Rationale
Mycophenolate Mofetil (MMF)	Reduce or Discontinue.	It is a potent myelosuppressive agent the first drug to be reduced or stopp severe opportunistic infections.
Tacrolimus	Lower dose, monitor closely.	A lower trough level may be targeted drug should **not be stopped** complet the high risk of liver graft rejection.

Summary of Action: Start Ganciclovir immediately, reduce MMF, closely monitor and potentially reduce Tacrolimus, and **delay ART initiation for 2-4 weeks.**

- **If the patient gives a history of previous monotherapy for similar or different CMV manifestations or if the serial CSF reading shows persistent pleocytosis and hypoglycorrhachia after induction of ganciclovir therapy, the likelihood of treatment failure is high, and treatment with alternative drug.**

- Although early progression of CMV disease (within 2 months) in patients who recently started anti-CMV drug treatment is typically not a result of drug resistance, late CMV reactivation after many months of treatment may be due to resistance.
- By themselves, peripheral blood CMV viral load measurements have poor positive predictive value for treatment failure.
- Maribavir has recently been approved by the U.S. Food and Drug Administration for treatment of posttransplant refractory CMV but has not been studied extensively in people with HIV.

- CMV neurologic disease is diagnosed on the basis of a compatible clinical syndrome and the presence of CMV in CSF or brain tissue, most often evaluated with PCR.
- Blood tests to detect CMV by antigen detection, culture, or PCR are not recommended for diagnosis of CMV end-organ disease because of their poor positive predictive value in people with advanced AIDS.

. A negative serum or plasma PCR assay does not rule out CMV end-organ.

Monitoring for CMV viremia is not recommended.

- **CMV-associated polyradiculopathy, a devastating necrotizing radiculomyelitis, is typically seen in patients with advanced acquired immunodeficiency syndrome (AIDS) or in solid organ transplant (SOT) recipients under intense IS.**

Thank You!