Progressive Multifocal Leukoencephalopathy in an HIV Patient with Negative JC Virus PCR

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Introduction

- The HIV/AIDS epidemic initially posed significant challenges for physicians, particularly in rural areas with limited resources. Early efforts prioritized education and managing opportunistic infections due to limited HIV therapies [2].
- Antiretroviral therapy (ART) revolutionized HIV care, transforming it into a manageable chronic condition [2].
- Severe immunosuppression still predisposes patients to Progressive Multifocal Leukoencephalopathy (PML), a rare disease caused by JC virus reactivation [3].
- PML presents with progressive neurological deficits and characteristic MRI findings, but false-negative JC virus PCR in CSF may require brain biopsy for diagnosis [4].
- With no effective prophylaxis or treatment for PML, management focuses on immune restoration via ART [6].
- Adjunctive therapies such as mirtazapine and intravenous immunoglobulin (IVIG) are sometimes utilized, though their efficacy remains uncertain [7].
- Prognosis is poor, primarily dependent on the degree of immune reconstitution [8].

Objectives

- Highlight the diagnostic and therapeutic challenges of Progressive Multifocal Leukoencephalopathy (PML) in immunosuppressed individuals, particularly in those with HIV/AIDS
- Emphasize the importance of clinical suspicion in patients with progressive neurological deficits and negative JC virus in cerebrospinal fluid (CSF)
- Reinforce the role of brain biopsy as the definitive diagnostic tool for PML
- Explore the potential efficacy of adjunctive therapies in the management of PML
- Propose the integration of osteopathic manipulative treatment (OMT) to enhance immune restoration in immunosuppressed patients

Case Description

A 47-year-old African American female with long-standing but **poorly controlled HIV diagnosed in 2007**, was brought in by her daughter due to two months of **progressive confusion, disorientation, and weight loss**. Previously independent, she became increasingly withdrawn, only recognizing her daughter, and struggled with conversations. She had been unemployed for over a year and had a **history of incarceration in 2013-2015**, during which she received ART, but **discontinued it after release**. On evaluation, she was alert, but significantly disoriented, incorrectly identifying the year as 2004 and unable to recall the month or day and did not know why she was hospitalized. Laboratory workup revealed **pancytopenia**, a **CD4 count of 53**, and an HIV RNA viral load of **485,648 copies/mL**. Brain MRI demonstrated **nonspecific T2/FLAIR hyperintensities**, and initial CSF studies were negative for JC virus PCR. Bone marrow biopsy was unremarkable. Given persistent cognitive decline, **brain biopsy confirmed PML**, later supported by a positive JC virus PCR. Treatment included **ART, mirtazapine, IVIG, and seizure prophylaxis**. Despite immune improvement, the patient's **cognitive deficits and incontinence persisted**, highlighting the guarded prognosis of PML.

Discussion

- **Progressive multifocal leukoencephalopathy (PML)** is caused by **JC virus reactivation** and can mimic **HIV encephalitis** or **CNS lymphoma** [3].
- **Diagnostic work-up** includes:
  - **MRI** for characteristic findings.
  - **JC virus PCR in CSF**, though results may be negative.
  - **Brain biopsy** remains the **gold standard** for definitive diagnosis [1].
- **Mirtazapine**:
  - Targets **5HT2A receptors**, potentially blocking **JC virus entry** into the CNS [5].
  - Originally an **antidepressant**, but its clinical impact on PML remains **uncertain** [6].
- **Intravenous immunoglobulin (IVIG)**:
  - Modulates immune responses, aiding in **immune reconstitution**.
  - Its efficacy in **altering PML progression** remains **unclear** [7].
- **Osteopathic Manipulative Treatment (OMT)**:
  - **Lymphatic pump treatment (LPT)** may enhance **lymphatic circulation** and **redistribute immune mediators**.
  - May contribute to **reducing inflammation** and improving **immune surveillance**.
  - Offers a **promising osteopathic approach** to **complement immune restoration strategies** [2].
- Barriers such as housing instability and unemployment likely contributed to poor ART adherence, exacerbated by challenges faced by formerly incarcerated individuals in re-engaging with healthcare.

Conclusion

- Maintain high suspicion for **progressive multifocal leukoencephalopathy (PML)** in advanced **HIV/AIDS** patients with progressive neurological symptoms.
- **Brain biopsy** may be necessary for definitive diagnosis when **JC virus PCR in CSF is repeatedly negative**.
- Treatment focuses on **immune reconstitution** through **antiretroviral therapy (ART)**.
- **Adjunctive therapies** such as **mirtazapine** and **intravenous immunoglobulin (IVIG)** may provide additional support.
- Prognosis remains **guarded**, largely dependent on the extent of **immune system recovery**.
- **Osteopathic approaches** to immune modulation offer a **promising avenue** for adjunctive PML management.

Reference

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