"Progressive Multifocal Leukoencephalopathy with JC Virus reactivation in the setting of Rituximab- A Case Report."

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Introduction

Rituximab targets the surface receptor CD20 on immature and mature B-lymphocytes. Immunosuppressive agents and monoclonal antibodies like Rituximab are potential risk factors for progressive multifocal leukoencephalopathy (PML), a rare but fatal neurological demyelinating condition. Programmed cell death protein 1 (PD-1) is a negative regulator of the immune response that impairs clearance of the John Cunningham virus (JC virus).

Case Presentation

A 68-year-old male with a past medical history of Mantle Cell Lymphoma on Rituximab and Bendamustine presented to the emergency department for worsening left-sided weakness and ataxia for the last two weeks.

- **Vitals:** Temperature 96.3 Fahrenheit, heart rate 50 beats/minute, blood pressure 128/56 mmHg, respiratory rate 18 breaths/minute, and oxygen saturation 98% on room air.
  The patient was alert and oriented to person, place, and time on examination. Generalized weakness with a power of 3/5 on the left extremities was noted, and the cranial nerves were grossly intact.
- **Significant labs:** Sodium of 132 mmol/L, Anion Gap of 18 mmol/L, Blood Glucose of 350 mg/dL, and Platelets of 102 B/L, with remaining chemistry labs unremarkable.
  - He tested negative for Human Immunodeficiency Virus.
- **CT head** (non-contrast) unveiled a low-density lesion in the right frontoparietal region with increasing edema.
- **MRI of the brain** unmasked an increased signal within the splenium of the corpus callosum, enhancement of right parietal focus, and left-sided lesions with enhancement (Figure 1).
- Stereotactic **brain needle biopsy** revealed Progressive Multifocal Leukoencephalopathy (PML)
  - Microscopic pathology unveiled oligodendrocytes containing JC virus, strong positive staining for SV40 and Ki67 immunohistochemical.

Treatment: He received levetiracetam for seizure prophylaxis and dexamethasone for edema. This hospitalization was complicated by acute deep vein thrombosis of the upper extremities, which was treated with therapeutic Enoxaparin.

- The **National Institutes of Health Clinical Center** accepted the patient. He underwent a lumbar puncture, which revealed 2.5 Million JC virus copies, and received one infusion of Pembrolizumab.
- The weakness persisted for three months; the patient opted for home hospice and passed away seven months after diagnosis.

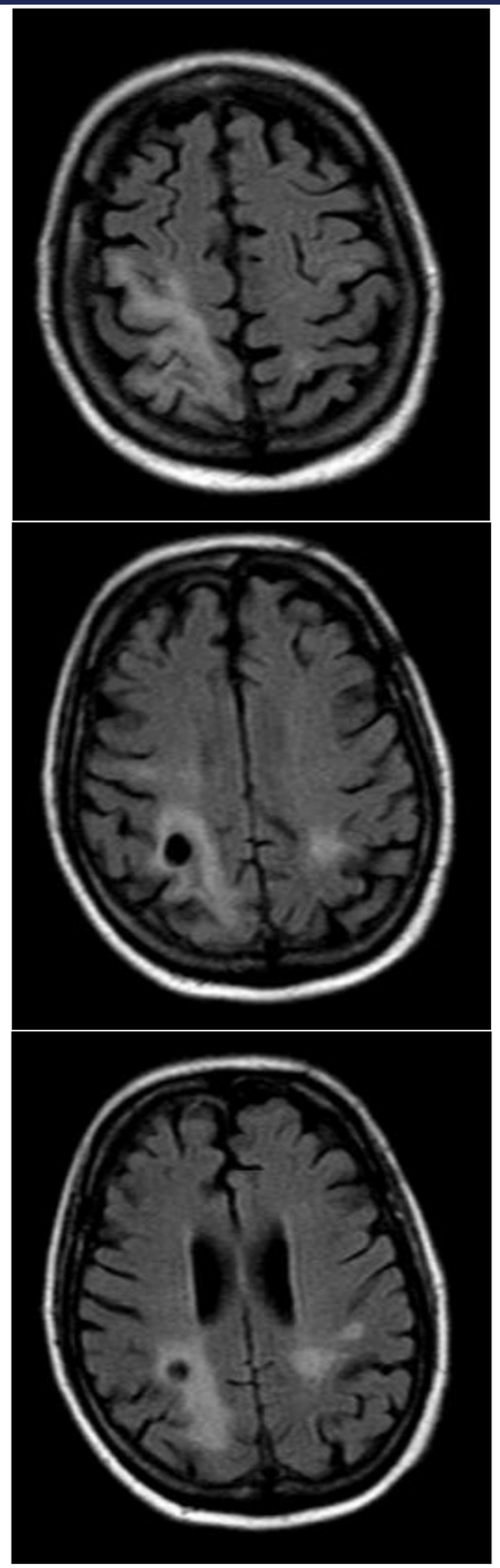

Figure. 1: MRI Brain- right parietal focus and enhancement

Discussion

In patients with HIV, Antiretroviral therapy (ART) is used to preserve immune function and reverse HIV-associated immunosuppression.

In adults with HIV-negative, therapeutic monoclonal antibodies, including natalizumab, efalizumab, rituximab, and alemtuzumab, are associated with increased incidence of PML.

Conclusion

Our case aims to raise awareness regarding the following points:

- ***CSF JC virus DNA isolation with PCR confirms the diagnosis of PML.***
- ***Importance of excluding and timely diagnosis of PML in any patient displaying neurological deficits while being treated with an immunosuppressive biological agent.***
- ***Furthermore, pembrolizumab increases CD4+ and CD8+ activity against the JC virus to reduce viral load; however, further study of immune checkpoint inhibitors for the cure for PML is warranted.***

References

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