When Immunotherapy backfires: A case report of Progressive Multifocal Leukoencephalopathy in a patient with NMOSD on Rituximab & review of literature

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Background:

Progressive multifocal leukoencephalopathy (PML) is usually a fatal demyelinating disorder often associated with HIV positive patients.[1] The most common drug associated with PML is Natalizumab.[2] We present a rare case of drug associated PML secondary to Rituximab in a patient with Neuromyelitis optica spectrum disorder (NMOSD).

Case Summary:

A 45 year old known case of aquaporin-4 antibody positive Longitudinally Extensive Transverse Myelitis on inj. Rituximab 1000mg at 6monthly intervals for 3 years, presented with bilateral painless vision loss and rapidly progressive dementia of 25 days duration. She had impaired attention, comprehension, memory, naming and calculation with apraxia. She was evaluated and her contrast enhanced MRI Brain showed T2/FLAIR hyperintensity without contrast enhancement in bilateral parietal and right frontal lobe. Her cerebrospinal fluid analysis revealed normal cytology and biochemistry with positive polymerase chain reaction (PCR) for John Cunningham (JC) Virus. Her HIV ELISA was negative. Her CD 19 & CD 20 counts were 0/uL. Absolute CD4 count was 160/uL. In view of Progressive Multifocal Leukoencephalopathy patient was treated with IVIG 2gm/kg over 5 days, but her condition did not improve and her cognition further worsened. She was readmitted 3 months after diagnosis with status epilepticus which was managed with anti-epileptics & was discharged in mRS-5 state. Currently she is in same clinical state with seizures controlled.

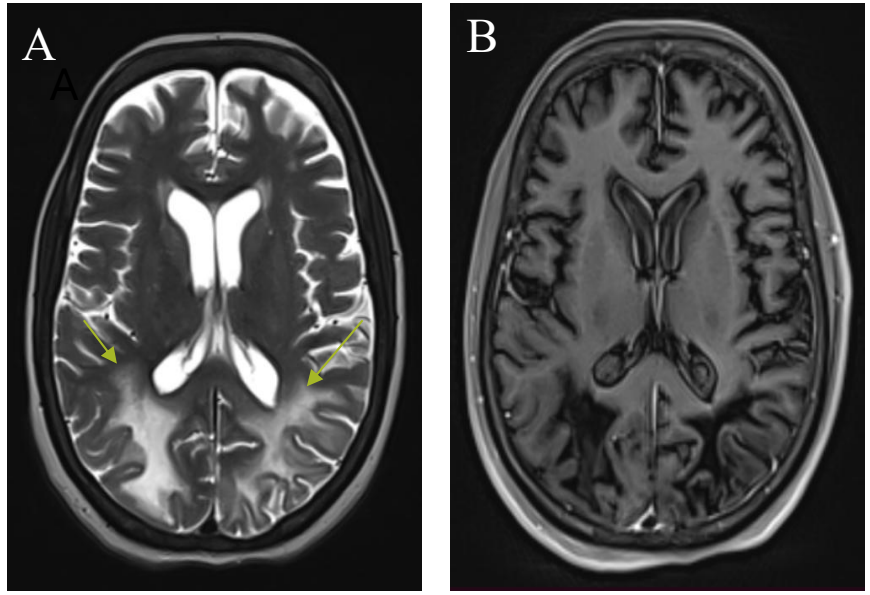

Figure 1. MRI Brain (at the time of presentation) axial T2 weighted sequence (A) showing hyperintensity in the periventricular deep white matter of bilateral parietal & right frontal lobes. No enhancement seen on axial postcontrast T1-weighted sequence (B).

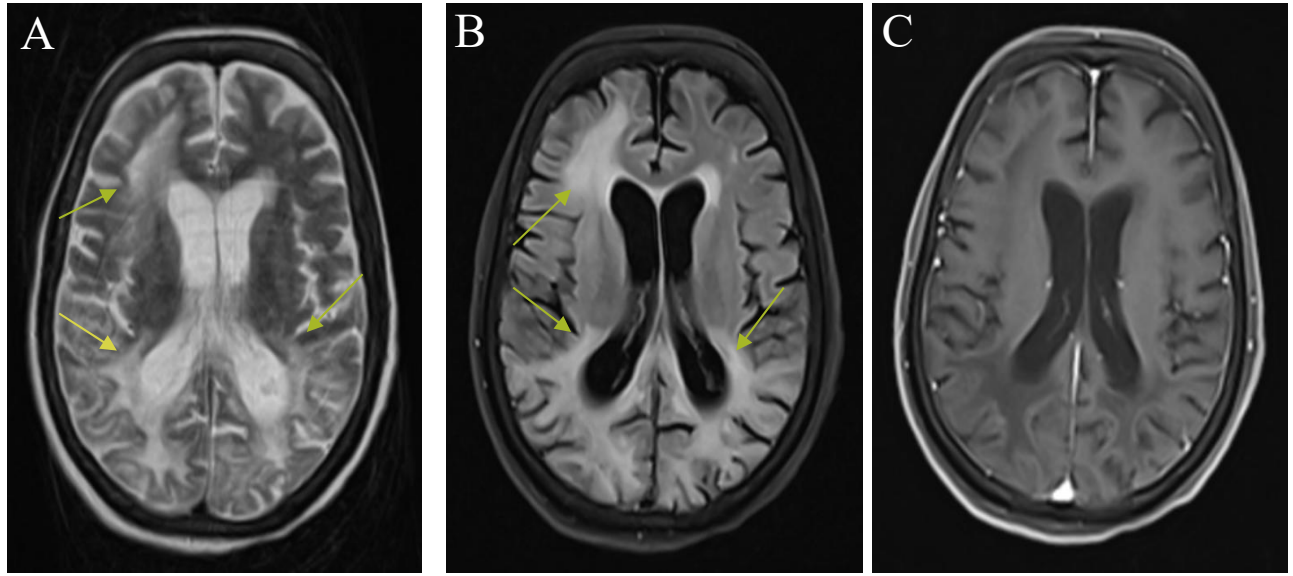

Figure 2. MRI Brain (3 months after diagnosis) axial T2 weighted (A) & fluid-attenuated inversion recovery (FLAIR) sequence (B) showing hyperintensity in bilateral parieto-occipital & right frontal region. No enhancement seen on axial postcontrast T1-weighted sequence (C).

Discussion:

PML is a rare critical demyelinating disease caused by reactivation of JC virus in immunosuppressed patients. Rituximab, a CD 20 monoclonal antibody, used in NMOSD increases the risk of PML by disproportionate increment in immature B lymphocytes, along with an immunocompromised state. Our patient, though immunocompetent at baseline, developed PML following Rituximab therapy- a rare complication proven by MRI & CSF findings. We gave our patient IVIG based on favorable anecdotal reports. Although drugs such as cidofovir, cytarabine, and mefloquine have been investigated, they have not shown to be clinically beneficial in the treatment of PML. Recently Pembrolizumab has been the drug of interest in PML & there have been case reports where Pembrolizumab has proven beneficial in PML. Currently, clinical trials are ongoing for Pembrolizumab in PML (results awaited). In our patient Pembrolizumab could not be given because of financial constraints.

Conclusion:

Rituximab therapy may lead to serious adverse effect of PML. Patients with NMOSD on Rituximab must be regularly followed by clinical and radiological investigations to detect PML. It may be prudent to consider JC virus serology in the patients started on Rituximab.

References:

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