Monofocal Posterior Fossa Natalizumab-Associated PML-IRIS

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BACKGROUND

Progressive multifocal leucoencephalopathy [PML] has emerged as a potentially fatal opportunistic infection with limited, if any treatment options, complicating natalizumab [NTZ] treatment for people with multiple sclerosis [MS][1]. Mainstream management is to restore immune competence by suspending NTZ. Plasmapheresis [PLEX] can also be used to speed drug elimination[1]. However, this can be further complicated by immune reconstitution inflammatory syndrome [IRIS][2].

OBJECTIVES

We report a rare case of cerebellar PML-IRIS**.**

CASE-REPORT

A 36 year old woman responded to NTZ every 4 weeks for relapsing MS since 2007 after failing interferon-beta, with no prior immunosuppression. Serum JC virus antibody was known positive since 2011 but she continued treatment due to sustained NTZ high efficacy, monitored clinically and on MRI every 4 to 6 months. In September 2016 she noticed subtle worsening of speech and balance, and emotional lability; physical examination confirmed a cerebellar syndrome and MRI revealed an ill-defined area of increased T2 signal within the right cerebellum and brachium pontis, T1 hypointensity in the pons with patchy and nodular gadolinium enhancement (figure 1). Ultra-sensitive cerebrospinal fluid tested positive for JCV DNA, with a low but inconclusive viral count. She underwent 5 courses of PLEX uneventfully and initiated Mefloquine+Mirtazapine but a week later she worsened again. MRI showed patchy enhancing white matter lesions in the bilateral pons, cerebellar hemispheres and peduncles suggestive of IRIS (figure 2). After 14 days of IV 1g/d steroids, she gradually showed sustained improvement both clinically and on MRI (figure 3).

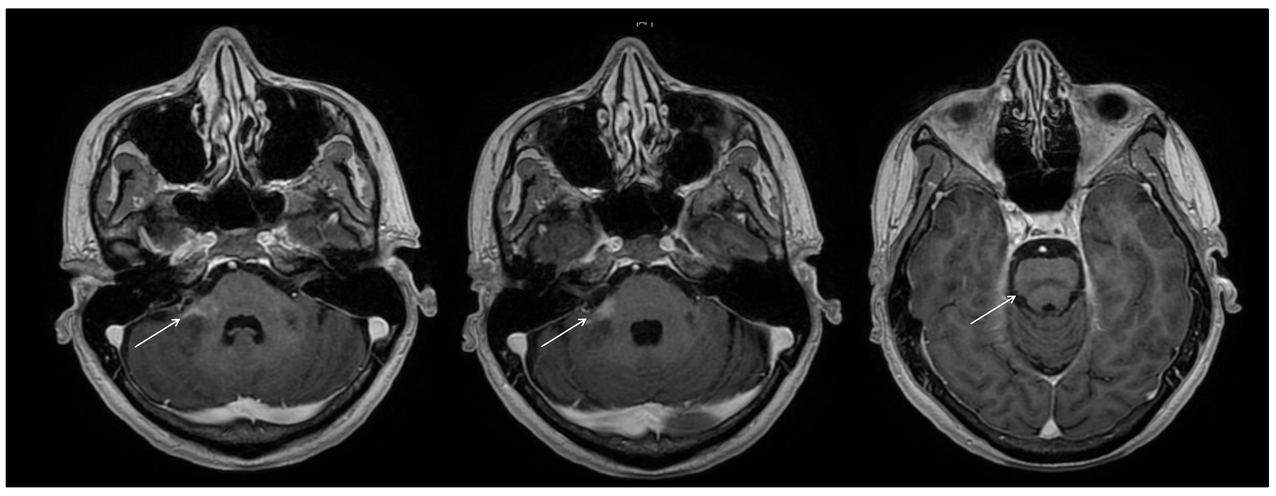

Figure 1. Head MRI. Axial T1 post-gadolinium. **A** and **B** PML lesion. **C** Hot-cross bun sign.

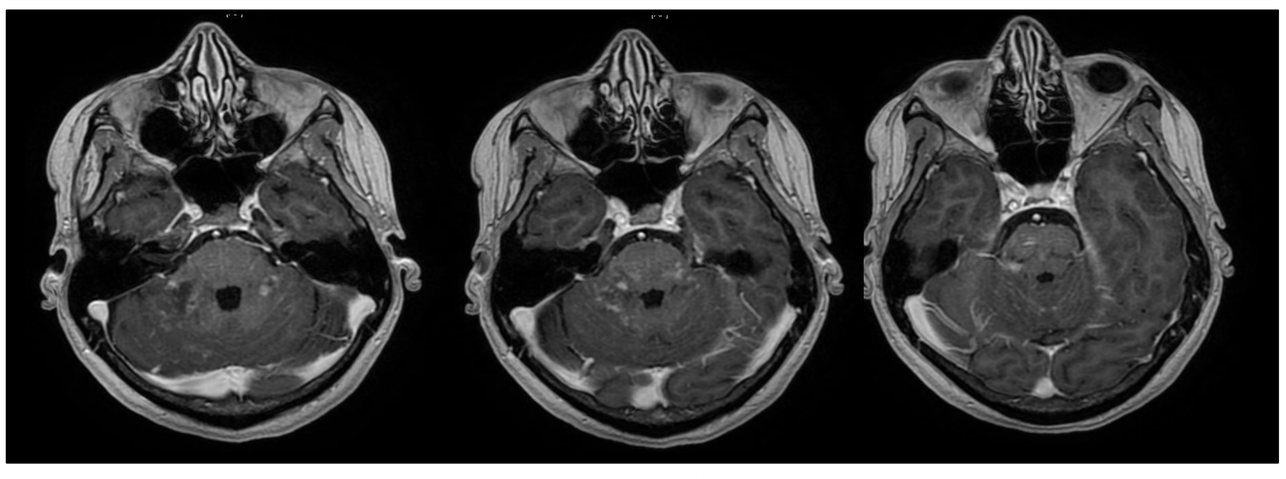

Figure 2. Head MRI. Axial T1 post-gadolinium demosntrating PML-IRIS.

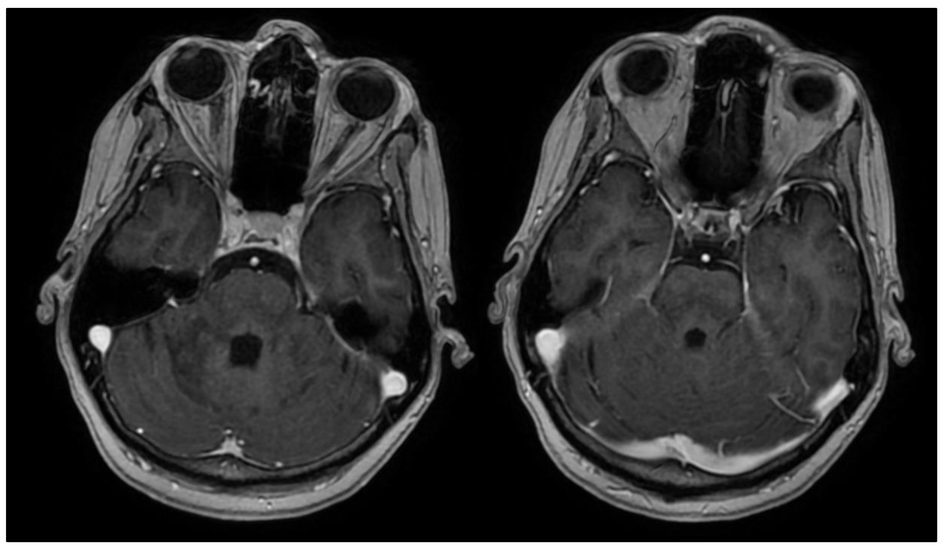

Figure 3. Head MRI. Axial T1 post-gadolinium after high-dosis steroids treatment.

DISCUSSION

NTZ-associated progressive multifocal leucoencephalopathy (PML) has emerged as a potentially fatal oportunistic infection for which there is no known effective therapy[1]. Mainstream management is to restore immune competence by suspending NTZ. PLEX can speed drug elimination[1]. However, this can be further complicated by IRIS[2]. Early PML diagnosis, mainly in a pre-symptomatic monofocal phase, associates with better outcomes[3]. Routine MRI vigilance is reasonable. Howbeit, diagnosing PML, mainly early, is challenging[4,5]. Cerebral hemispheres are the most common locations[6], but our patient presented with isolated cerebellar lesions, a less common topography, 10% of known cases[4]. Though JCV classically infects oligodendrocytes, it is proven that the virus can also affect the cerebellar granular cells causing cerebellar atrophy, without evidence of cerebral hemispheres affection[7]. Remarkably her MRI showed T1 hypointensity in the pons that has been previously described in HIV-PML but never in MS[8,9,10].

CONCLUSION

Clinical and MRI vigilance in NTZ treatment for MS is paramount. Early PML diagnosis and aggressive IRIS management increase the odds for a better outcome. Remarkably this case showed T1 hypointensity “across” the pons on MRI, rarely described in HIV-PML but never published yet in MS[8,9,10].

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