NEGATIVE CSF JCV-DNA AND PUNCTATE GADOLINIUM ENHANCEMENT IN NATALIZUMAB TREATED MS PATIENTS: A TRICKY SITUATION

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Introduction:

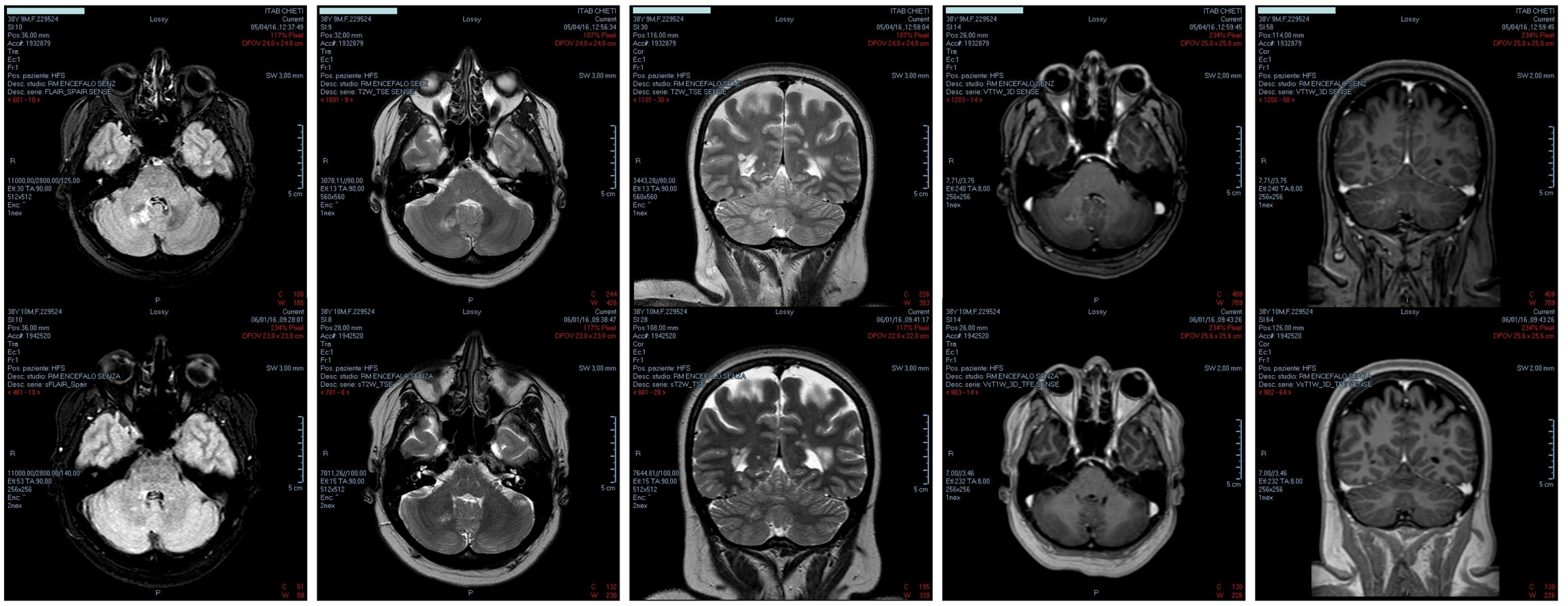
Ten years after approval, Natalizumab (NTZ) remains one of the most efficacious drugs for Relapsing Remitting Multiple Sclerosis (RR-MS). Progressive Multifocal Leukoencephalopathy (PML) continues to represent its most worrisome adverse event, although the better understanding of its characteristics in MS has lead to an increasing rate of preclinical diagnoses, mainly due to identification of early Magnetic Resonance Imaging (MRI) signs of PML. In particular, the punctate pattern (PP) is considered highly accurate in differentiating a PML from a MS lesion. [1]

Objective:

To highlight the difficulties in the differential diagnosis between MS relapse and PML when diagnostic tools are discordant.

Materials and methods:

A 37-year-old female MS patient, seropositive to JC virus (index=3.22), previously treated with azathioprine and mitoxantrone, suddenly developed dysphagia, diplopia, truncal and left arm ataxia 24 hours after her seventy-third NTZ infusion, administered 73 days after the previous one, due to cholecystectomy. MRI showed a new hyperintense on T2 lesion extending from the right dentate nucleus to the ipsilateral superior cerebellar peduncle, with punctate contrast enhancement. PML was deemed the most probable diagnosis. PCR did not detect JC virus DNA in the CSF (local lab and Unilabs, Copenhagen). The patient was treated with i.v. methylprednisolone, showing a full and stable recovery within two weeks. A 4 weeks follow-up MRI demonstrated a substantial reduction of the size and the contrast enhancement of the lesion. The patient has not restarted NTZ.



Discussion:

The differential diagnosis between MS relapse, facilitated by the long interval between the last two NTZ infusions, and PML is challenging. The good response to steroid therapy and the lack of further progression despite the recent NTZ infusion, not followed by plasma exchange or immunoadsorption, would strengthen the hypothesis of a relapse, although it is not possible to definitively rule-out a PML. Since a negative CSF JCV-DNA cannot exclude PML, progression of symptoms and new punctate MRI lesion(s), characteristic for PML, suggest a watchful monitoring and avoiding drugs associated with PML.

Conclusions:

After a reported 100% specificity of PP for PML-MS lesions differentiation [1], we believe that this case does not represent the first and unique false positive result. PML cases with initially undetectable JCV-DNA have been reported. Further experience is needed to improve MRI accuracy in distinguishing PML from MS lesions (84,7% specificity in a recent analysis [2]). Thorough evaluation of MRI findings by an experienced neuroradiologist is mandatory to ensure prompt NTZ discontinuation.

References

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