PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML): A DIAGNOSIS TO KEEP IN MIND IN THE ERA OF MONOCLONAL AND IMMUNOSOPPRESSIVE THERAPIES.

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INTRODUCTION: PML is a rare subacute, demyelinating disease of the central nervous system, caused by the reactivation of JC virus in immunocompromised patients [1]. Iatrogenic PML must be taken in mind as possible adverse event in patients assuming immunosuppressive or immunomodulating therapies.

CASE REPORT: A 54 years old Caucasian woman, with a diagnosis of **Multiple Myeloma** (IgG-k IIIA), just treated with **chemotherapeutic drugs** and **stem cells transplantation**, was admitted to neurological unit because of the onset of visual disturbances and bradypsychism since 3 weeks. Chemotherapeutic drugs have been already stopped since 3 months according to hematological judgment. At the admission, the neurological examination revealed left hemianopsia and mild right arm motor deficit. The MMSE was 14,74. CT scan showed hypodense areas in left frontal and right parieto-occipital lobe, interpreted as vascular lesions. These lesions appeared hyperintense on T2 and FLAIR-weighted **MR scans**; they spared the grey matter and did not enhance after Gd administration. The diffusion-weighted images showed diffusion restriction at lesion periphery in contrast to the core. Proton MR spectroscopy showed a reduction of NAA, an increase of choline-compounds and myo-inositol and the presence of the signal of lactate (**Figure 1**). **CSF** showed the presence of 235 copies/ml of JCV DNA. The lymphocyte subset count showed an inversion of CD4+/CD8+ ratio in the peripheral blood. HIV test was negative. **A diagnosis of PML** was made. Patient underwent treatment with **Mirtazapine 30 mg/day**. After one month, in spite of a progressive improvement of clinical status, MRI showed an increase of the size of lesions, which were still unenhancing after Gd administration (**Figure 2**). CD4+/CD8+ ratio in peripheral blood was increased. Three months after onset, a new lumbar puncture was performed. No copy of JCV genome was found in the CSF. **Intrathecal IgG oligoclonal synthesis** was now observed. MRI showed a reduction of the size of the PML related lesions and a reduction of the signal of choline-compounds at 1H-MRS (**Figure 3**). Neurological examination showed only mild left hemianopsia and the MMSE was 27,9.

FIGURE 1

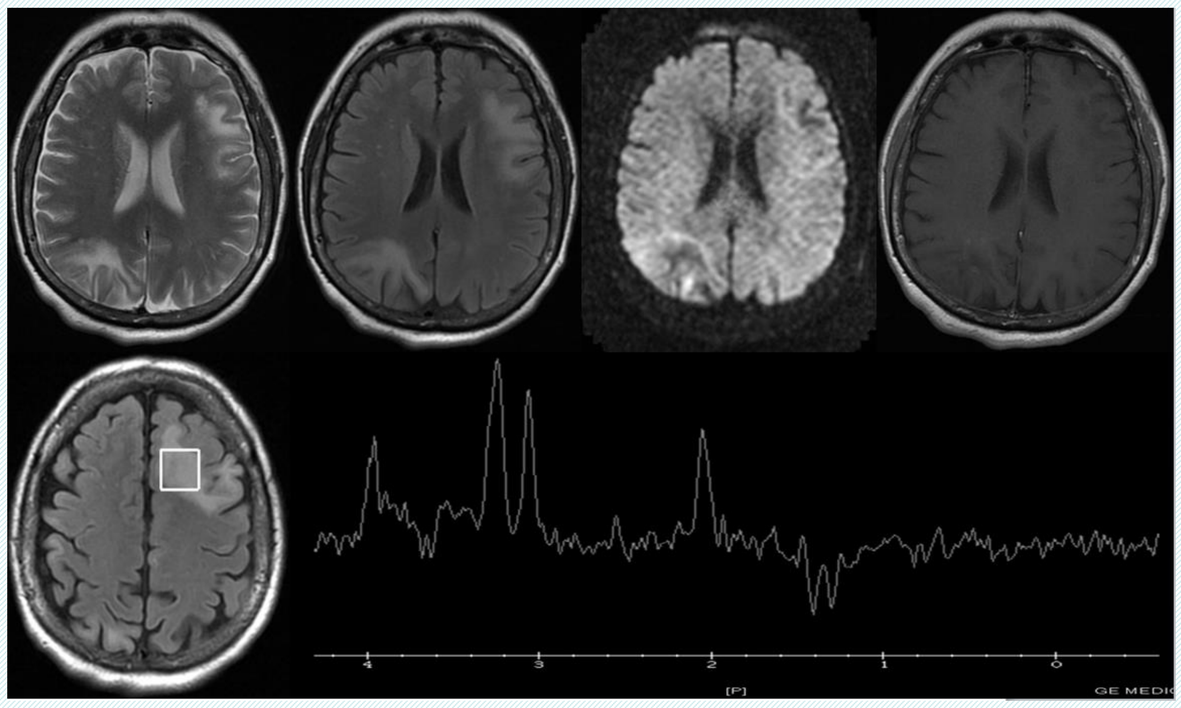


FIGURE 2

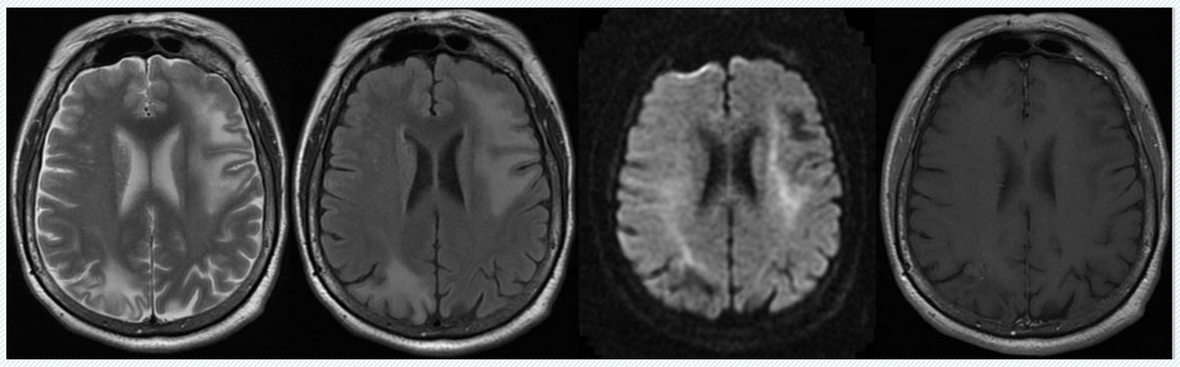
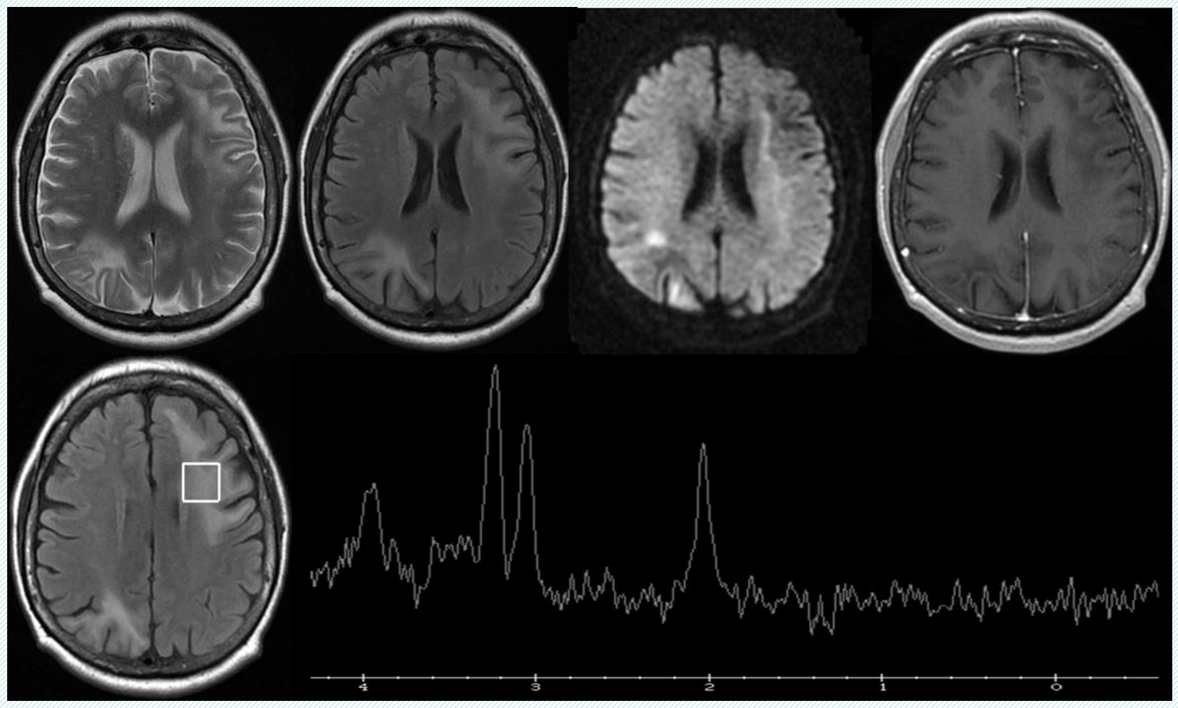


FIGURE 3



CONCLUSIONS: **Early diagnosis** is the only therapeutic chance in iatrogenic PML because of the lack of therapeutic options except for stopping the causative drug [2]. Few cases of PML in patients with Multiple Myeloma have been described [3]. Favorable outcome in our patient is probably related to the timing of JCV infection (after the discontinuation of immunosuppressive drugs). Clinicians need to remind that **MRI allows recognizing PML lesions far before clinical symptoms**. Nevertheless, our observation supports that the **improving of MR features may be slower than clinical benefit and JCV DNA disappearance**.

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