

Background

Neuromyelitis optica (NMO) is an inflammatory demyelinating disease of the central nervous system that generally involves the optic nerve and the spinal cord. The discovery of a biomarker that has high specificity for NMO led us to consider Devic's disease a "spectrum of disorders" (NMOsd) rather than a single nosologic entity. NMOsd includes Devic's disease and other limited forms such as recurrent transverse myelitis (LETM) and recurrent optic neuritis. A brain involvement in NMO has been described in more than 30-40% of cases and different brain lesion patterns have been reported. Moreover, the fact that this biomarker is an autoantibody (NMO IgG) that recognizes aquaporin 4 (AQP4), a water channel expressed on astrocyte podocytes, has substantially contributed to the hypothesis that NMO is a humorally mediated autoimmune disease. Baló's concentric sclerosis (BCS) is an inflammatory demyelinating disease considered a rare variant of Multiple Sclerosis. It is characterized by the presence of tumour-like white matter lesions showing concentric rings of demyelinated and relatively myelin-preserved fibers. The clinical course consists of an acute onset followed by a progression of symptoms that usually results in a permanent severe disability. The pathogenesis of BCS is still not completely understood even if the most common hypothesis is a distal oligodendroglialopathy mediated by hypoxia-like tissue damage and tissue preconditioning. We report a patient affected by NMOsd according to Wingerchuck 2006 criteria who developed a Baló's concentric lesion.

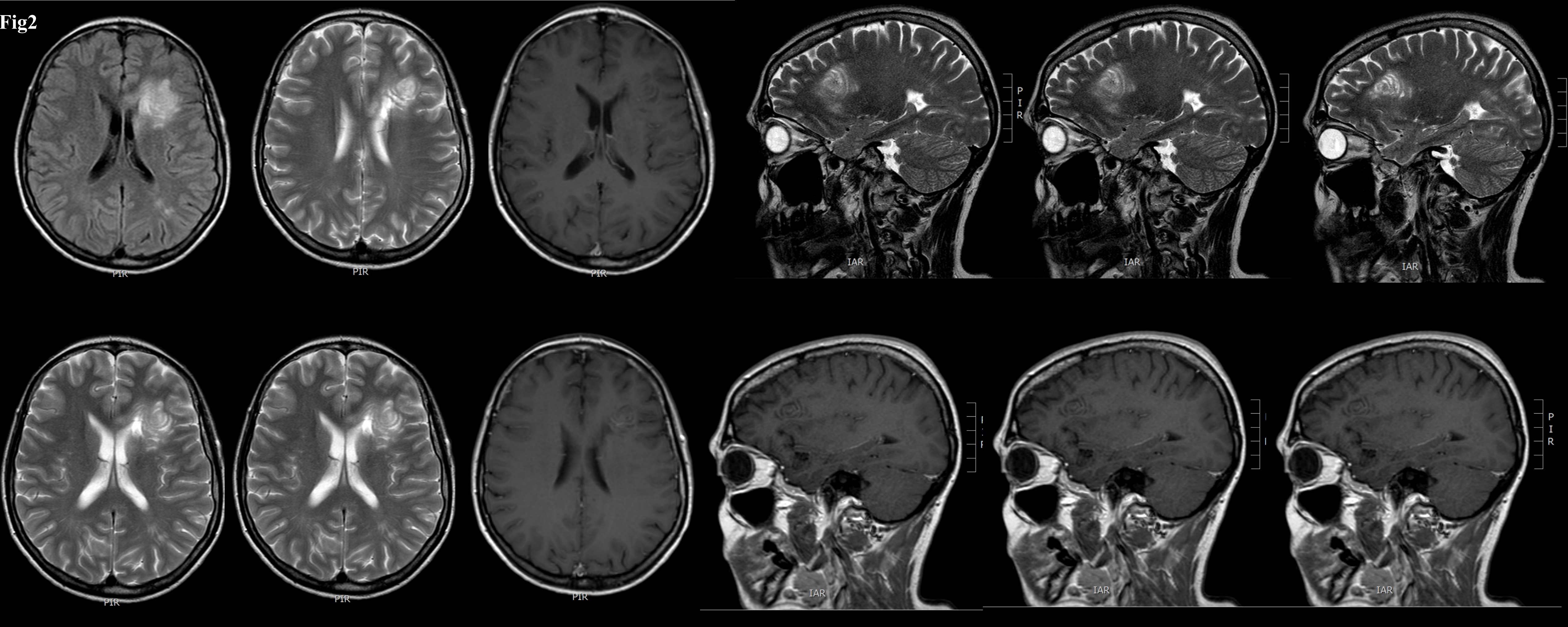
Results

Our patient is a 42 year old Caucasian woman who developed in November 2013 severe lower limbs hyposthenia and urinary retention. The spinal cord MRI revealed a LETM in the dorsal region. The brain MRI showed hyperintense T2 lesions in both the occipital regions (Fig1). A lumbar puncture showed hyperproteinorrachia and pleocytosis. NMO-IgG antibodies were positive. The patient underwent high dose i.v. steroids and i.v. immunoglobulins with partial recovery. A mild paraparesis persisted. The patient was treated with oral prednisolone until the beginning of July 2014. In August 2014 a new brain MRI showed a new tumor-like lesion with Gd enhancement in the subcortical left hemisphere. The spinal cord MRI confirmed the preexisting dorsal lesion. No symptomatology was reported. In September the patient complained of a mild left hemiparesis who worsened in the following weeks and right arm paresthesia. She was admitted to our hospital and the neurological examination revealed a severe left hemiparesis and a mild motor impairment of the right arm. The brain MRI showed an extension of the sub cortical tumor-like lesion with concentric rings involving the corpus callosum with perivenular enhancement (Fig 2). The spinal cord MRI revealed a new T2 lesion with Gd enhancement in the left portion of the cervical tract extended for three vertebral segments. NMO IgG were detected. She underwent plasma exchange and high dose i.v. Cyclophosphamide (Cy) with partial clinical recovery. Rituximab (RTX) treatment was started one week after Cy administration because of the persistence of Gd enhancement in the brain lesion. A brain and spinal cord MRI repeated three weeks after the first RTX course showed a partial reduction of the extension and of the enhancement of both brain and spinal cord lesions. At 6 months follow-up the patient presented a slight left hemiparesis and no new symptoms were reported.



Fig1

Fig2



Conclusions

Very few cases of concomitant BC lesions in NMO have been described. In only one case the presence of NMO-IgG antibodies was reported whereas in the other 2 cases NMO was suspected on the basis of the clinical characteristics. In a pathological study on four patients with BCS a selective AqP4 loss in both demyelinated and myelinated layers of BC lesions was described. However, no deposition of complement or immunoglobulins around vessels was found, differently from what is observed in NMO lesions. These findings, in association with clinical report of the absence of NMO-IgG antibodies in two of the patients reported in the literature, led to the hypothesis of a possible overlap of the two diseases that would be caused by different mechanisms not involving the humoral response. On the contrary, our patient showed a concomitant appearance of a BC lesion and LETM and NMO-IgG antibody positivity thus suggesting a common pathogenic mechanism. Moreover, the good response to plasma exchange and RTX supports the antibody-immunomediated nature of all the lesions. Further studies are needed to understand if BCS could be considered a variant of NMO or if the characteristic concentric lesions only reflect the patient's response to injury rather than a specific nature of the damage itself.