Anti-AQP4 (+) NMO spectrum disorder associated with central nervous system tuberculosis

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Introduction

Neuromyelitis optica spectrum disorder (NMOsd) is an inflammatory astrocytopathy that has both genetic and environmental cause. The exact etiology and pathogenesis of NMOsd is partially known, complex interactions between genetic and environmental factors are thought to be involved in its development. Infectious diseases have received particular attention since they have long been considered as triggers of many autoimmune disorders. Here we report two cases of positive aquaporin 4 (AQP4) serostatus NMOsd in relation to granulomatous infection of the central nervous system

Case 1

47-year-old woman attended to the emergency room (ER) with dysarthria, disorientation, fever and drowsiness in the previous 36 hours. CSF reported 667 cells (91% MN), 604 mg/dl of proteins and 16 mg/dl of glucose. The infectious evaluation showed a positive adenosine deaminase (ADA) in CSF of 20 IU (nl 0-9 IU). CSF and serum viral PCR panel including *M. tuberculosis* was negative. Meningoencephalitis secondary to MTB was concluded and treatment with antituberculous drugs (isoniazide, rifampicin, pirazinamide and ethambutol) and corticosteroids was initiated 5 days after initial assessment.

On day 3 of hospital-stay, the patient developed acute left sided body paresthesia and ipsilateral hemiparesis; cervical-thoracic MRI was performed showing longitudinally extense transverse myelitis at the cervical level. Anti-AQP4 IgG was requested and reported as positive by immunofluorescence. A course of 5 days intravenous methylprednisolone was administered, and anti-tuberculosis treatment was continued. Her mental status improved but the hemiparesis remained. A follow up LP was conducted showing improvement in the CSF parameters (214 cells , 117 mg/dl of proteins and 48 mg/dl of glucose). She was discharged after 5 weeks of hospital-stay still unable to walk. Rituximab was proposed as a maintenance therapy.

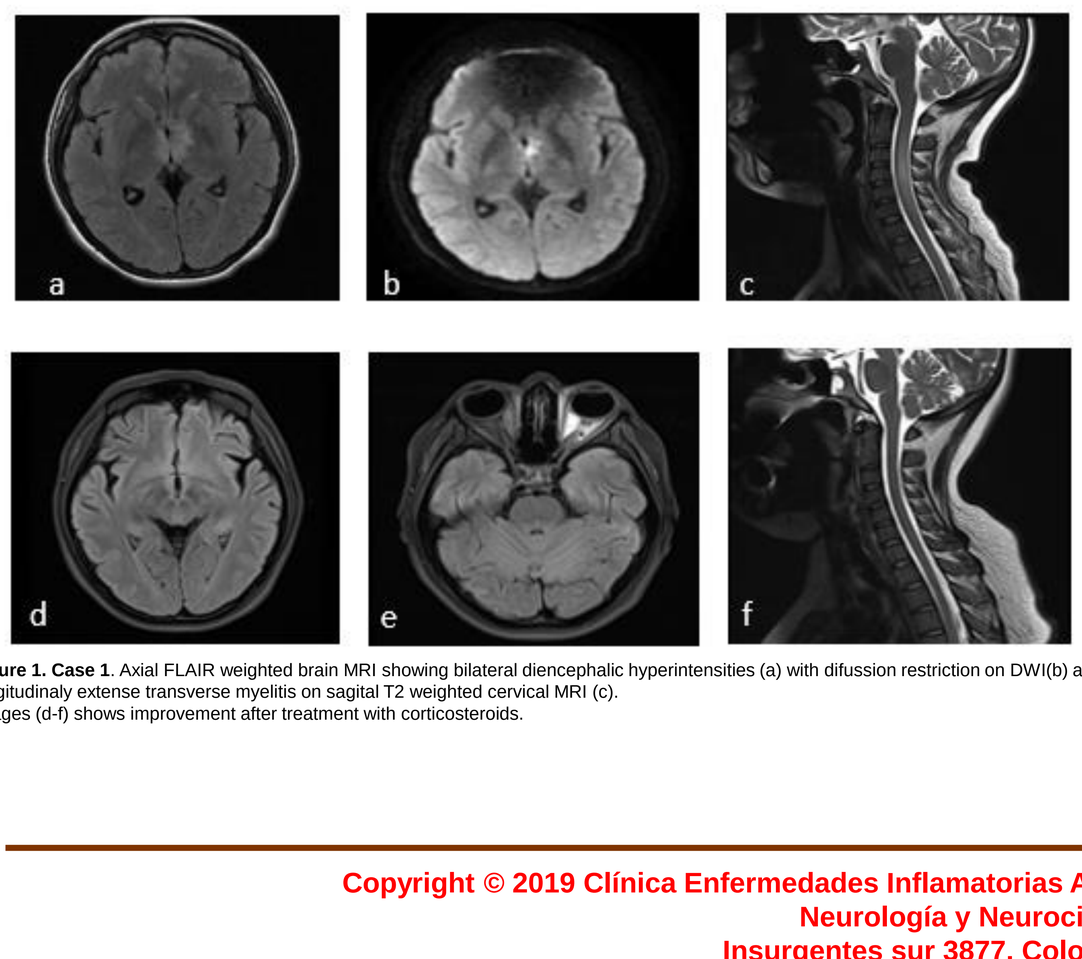

Figure 1. Case 1. Axial FLAIR weighted brain MRI showing bilateral diencephalic hyperintensities (a) with difussion restriction on DWI(b) and longitudinaly extense transverse myelitis on sagital T2 weighted cervical MRI (c).
Images (d-f) shows improvement after treatment with corticosteroids.

Case 2

A 28-year-old man with episodes of headache and fever in the 2 months prior. Confusion and drowsiness appeared so he attended the hospital where neuroinfection was considered. CSF reported 136 cells (64% MN), 79 mg/dl of protein, 52 mg/dl of glucose, and a positive PCR for *M. tuberculosis.* Antituberculous drugs and prednisone was started. 2 weeks after discharge the patient was readmitted because of the presence of fever and confusional state. At the new admission, CSF analysis showed 23 mg/dl glucose, 98 mg/dl proteins and 352 cells count (66% PMN 34% MN) and ADA level of 96 IU (nl 0-9 IU. He started treatment with intravenous steroid and continued with ATD.

During the second week of hospitalization, the patient showed improvement of the initial symptoms, however, he developed subacute paraparesis, a sensory level and urinary retention; we suspected transverse myelitis and cervical-thoracic MRI was perform showing longitudinaly extense transverse myelitis at C5-T2 level, with secundary sirinx (fig. 2). Serum anti-AQP4 IgG was performed and reported as positive by immunofluorescence technique. A course of 5 days intravenous methylprednisolone was administered and treatment with ATD was continued with significant clinical improvement, he was able to walk with no assistance at day 3 of IV steroids and bladder catheter was removed. After discharged he remained on oral steroids with no relapses.

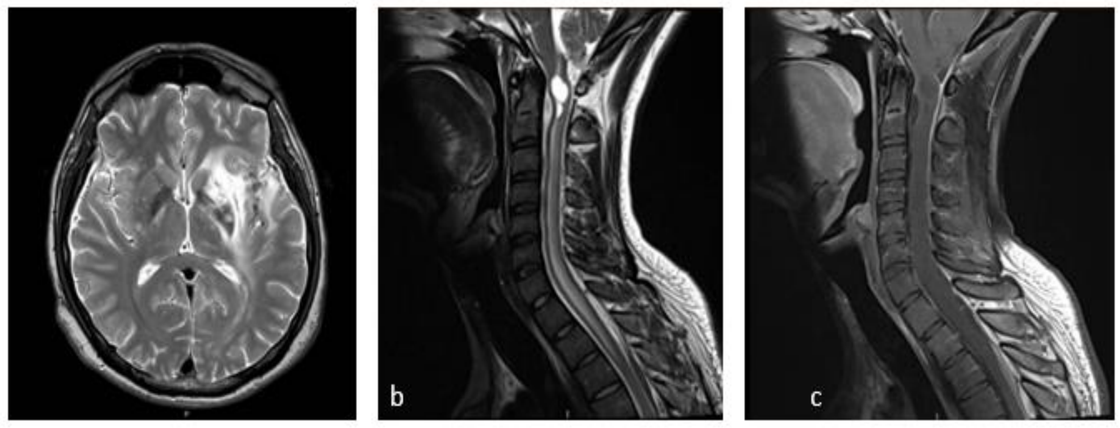

Figure 2. Case 2. Axial T2 weighted brain MRI imaging showing left diencephalic hyperintensity with cortical and subcortical extension (a). Sagital T1 and T2 weighted cervical MRI showing longitudinaly extense transverse myelitis at C5-T2 with secundary sirinx and no contrast enhancement.

Conclusion

Infection with *M. tuberculosis* may act as a trigger factor in NMOsd. Many of the antigens expressed by mycobacteria share homologous sequences with human cellular structures and with some of the loops of AQP4. Therefore, a proposal regarding the pathophysiology of this type of autoimmune disease in the CNS is the phenomenon of spreading or extension of these epitopes and the subsequent production of antibodies and secondary immune response.

References

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