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Neuromyelitis Optica with Negative Anti-Aquaporin-4 Antibodies: About an Observation

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Abstract: Devic's Neuromyelitis Optica (NMO) is a rare demyelinating disorder affecting the optic nerves and spinal cord, with a relative brain saving. The diagnosis involves optic neuropathy and acute myelitis. The dosage of anti-aquaporin-4 autoantibodies is generally positive, but its negativity does not call into question the diagnosis. We report the case of a 34-year-old woman admitted to the Department of Neurology at the Fann University Hospital in Dakar for visual impairment and motor deficiency in the lower limbs of rapidly progressive onset in which clinical examination has revealed right monocular blindness and transverse myelitis. Medullary MRI and VEP enabled us to make the definitive diagnosis of optic neuromyelitis despite the negativity of AQP4 antibodies.

Keywords: Neuromyelitis Optica, Anti-AQP4, Antibodies

1. Introduction

Described for the first time in 1894 by Eugène Devic and Fernand Gault, Devic's Neuromyelitis Optica (NMO) is a severe demyelinating inflammatory disease of the central nervous system that affects essentially the optic nerve and the spinal cord [1], it can also associate the presence of specific antibodies (Anti-NMO antibodies) [2]. However, the diagnosis of an NMO can be retained despite the initial negativity of AQP4/NMO-IgG [3, 4]. Long regarded as a particular form of multiple sclerosis (MS), NMO is now recognized as a separate entity, differentiated from clinical, epidemiological, immunological and pathological MS. Its prevalence is higher in non-Caucasian populations with a female predominance [1, 2, 5].

Recent anatomopathological studies and the discovery of disease-specific antibodies support the role of humoral immunity in its pathogenesis. The best therapeutic option seems to be the combination of corticosteroids or plasma exchange during an outbreak and an immunosuppressive treatment for the prevention of relapses [6].

The authors report a case of a young woman with monocular blindness associated with transverse myelitis in which cerebral MRI showed extensive lesion on more than three vertebrae. The visual evoked potential (VEP) revealed a demyelinating involvement of the right optic nerve. The diagnosis of NMO was made despite the negativity of anti-AQP4 antibodies.

2. Observation

Patient SR 34 years old, married and primary school teacher, with no known pathological history, received at the neurological clinic of the Fann University Hospital of Dakar for a motor deficit of the lower limbs of progressive installation over a month, associated with back pain.

The clinical examination found a right monocular blindness, a complete medullary syndrome, associating a symmetrical bilateral sensitivomotor deficit (spastic paraplegia, hyperesthesia in the two lower limbs), a symmetrical sensory level, sphincteric disorders of urinary incontinence type. The hypothesis of transverse myelitis was emitted, associated with right monocular blindness. Visual evoked potential (VEP) revealed severe demyelinating

involvement of the right optic nerve. Medullary MRI (figures 1, 2 and 3) showed an extensive hypersignal over more than three vertebrae, suggestive of transverse myelitis. The assay of anti-aquaporin-4 autoantibodies on transfected EU90 cells was negative.

We concluded with an Optical Neuromyelitis with negative anti-aquaporin-4 autoantibodies.

The patient received corticosteroid therapy (Prednisone) at a dose of 1 mg / kg / day in combination with an immunosuppressant (Azathioprine: 150 mg / day) and functional rehabilitation. The evolution was towards progressive improvement with partial recovery of the motor deficit.

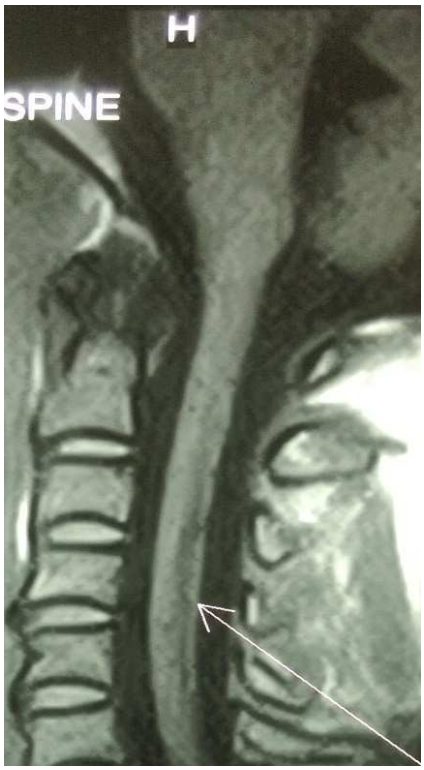

Figure 1. *Medullary lesion: hyposignal T1 on more than three vertebrae.*

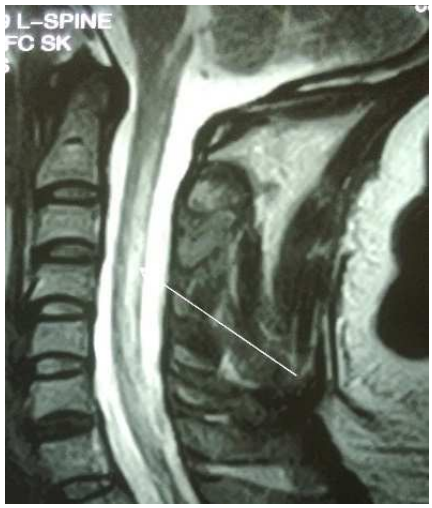

Figure 2. *Medullary lesion extending over more than three vertebrae. Hypersignal T2.*

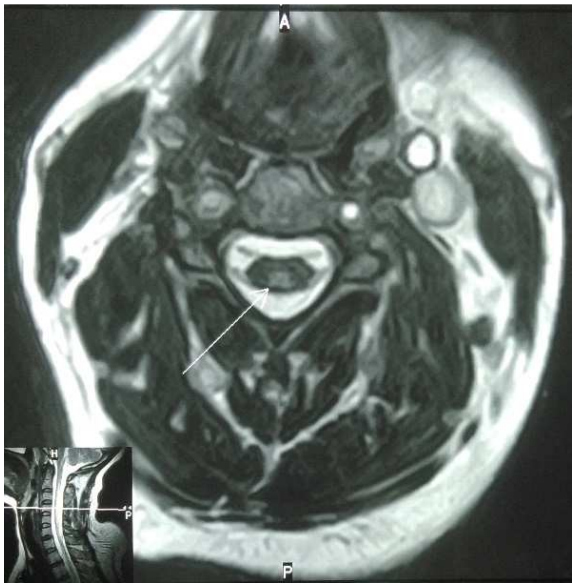

Figure 3. *Medullary lesion in axial section.*

3. Discussion

NMO is a rare demyelinating disease of the central nervous system (CNS) [1, 7]. It is characterized clinically by CNS involvement limited to the spinal cord and optic nerves, and pathologically by demyelination, necrosis and axonal loss of the spinal cord and optic nerves, the brain being macroscopically normal [6]. Optic neuritis can be bilateral (30% in the series of Wingerchuk *et al.* [8]), But is more often unilateral. It is generally acute with severe prognosis. Myelitis during Devic's disease is also most often acute onset associated with back pain [6, 9]. In our case, the patient presented a unilateral neuritis, and this neuritis as well as the transverse myelitis were of acute installation associated with dorsalgia. Very fragmented epidemiological data suggest an inequality of the disease at the expense of women and a higher incidence in black populations [2, 6, 9]. This disease mainly affects young women. Prevalence is higher in non-Caucasian populations [2]. Cabre *et al.* [9] in the Caribbean basin found a mean age of 30.9 years and sex ratio F / H of 9.8. The incidence of NMO in the French West Indies is 0.20 / 100,000 inhabitants for the period from July 2002 to June 2007. The mortality of the NMO in the French West Indies, previously equivalent to its incidence, has gradually collapsed enabling the continuous increase in its prevalence reaching 4.20 / 100,000 inhabitants in June 2007. The prevalence of the NMO in Cuba in 2004 is 0.52 / 100,000 inhabitants [9]. Unlike MS, the NMO also affects Caucasians but also West Indians and Japanese [1, 10].

The discovery in 2004 of the immunoglobulin G neuromyelitis optic (NMO-IgG), an autoantibody directed against aquaporin 4 (AQP4), made it possible to understand the pathogenic mechanism of the NMO [1]. The NMO, described for the first time by Eugene Devic in 1894, is characterized by the association of unilateral or bilateral blindness and paraparesis, or even paraplegia [11, 12]. In our case, the patient had a right monocular blindness and

paraplegia.

The diagnosis of NMO is therefore based on the presence of optic neuritis and transverse acute myelitis plus the existence of two of the following three signs: magnetic resonance imaging (MRI) detection of a marrow lesion Spinal cord covering at least three vertebrae, normal cerebral MRI and seropositivity to NMO-IgG [13]. However, the diagnosis of an NMO can be retained despite the initial negativity of the AQP4 / NMO-IgG [3, 4], as was the case with our patient. Theoretically this is related to the fact that the AQP4 / NMO-IgG Antibodies are specific but not very sensitive. Their positivity prejudices recurrence or aggressiveness of NMO and leads to immunosuppressive therapy [14].

Brain MRI is normal in most cases [6, 10]. In our case it was normal, but spinal MRI showed a presence of a T2 hypersignal extending over more than three vertebrae. To date, no treatment has been demonstrated to be effective. Potentially effective treatments are known, however, evidence of their efficacy has not been made, partly because of the rarity of the disease. A prospective, open, uncontrolled study of 7 patients conducted by Mandler [15] showed clinical stabilization over at least 18 months under azathioprine and corticosteroids. Our patient received corticosteroid therapy (Prednisone) at a dose of 1 mg / kg / day in combination with an immunosuppressant (Azathioprine: 150 mg / day) and functional rehabilitation. The evolution was towards progressive improvement with partial recovery of the motor deficit.

4. Conclusion

NMO is a rare demyelinating condition with a particular tropism for the spinal cord and the optic nerve. Negativity of AQP4 antibodies does not formally exclude the diagnosis of NMO because these antibodies, although they are specific to the disease, are not very sensitive. Its prognosis is severe. Clinical stabilization can be achieved by the combination of azathioprine and corticosteroids.

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