Devic-like syndrome in the course of pulmonary tuberculosis

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Summary

Introduction Optic neuromyelitis or Devic’s syndrome is a very rare disease affecting the optic tracts and the spinal cord. Its association with evolving pulmonary tuberculosis has been reported in a handful of case reports.

Case report: The authors report two cases of Devic’s syndrome associated pulmonary tuberculosis (48 and 43 years old men). The first patient was experiencing evolving pulmonary tuberculosis. The two patients were admitted for bilateral blindness followed by paraplegia and sphincter disturbance. Clinical examination and investigations excluded direct tuberculous involvement of the nervous system or a reaction to antituberculous therapy and Devic’s syndrome was diagnosed, based on Wingerchuck’s criteria. Following treatment with corticosteroids and antituberculous chemotherapy, we noted partial recoverery of motor symptoms and sphincter control but the patients remained completely blind.

Conclusions: Throughout this case report, the authors emphasize the rarity of this association and discuss the pathophysiological mechanism, which appears to be an immune dysfunction triggered by mycobacterium infection.

Key-words: Devic’s Syndrome; Devic’s Disease; Neuromyelitis optica; Pulmonary tuberculosis.

Introduction

The Neuromyelitis optica (NMO) or Devic syndrome is a very rare neurological dysimmune disease characterized by an acute and extensive demyelization demyelization of the optic nerves and spinal cord. Long regarded as a form of multiple sclerosis, it now appears as a separate entity. The recent discovery of NMO antibody (IgG) increases the specificity of disease diagnostic criteria and supports the role of humoral mediation in the pathophysiology. His association with infectious diseases including tuberculosis, was reported by some authors.

Case report

Case 1

M. CN, 48 years, followed for one year (23/02/07) for positive pulmonary tuberculosis. Patent was prescribed anti-bacillary (protocole 2SRH/4RH (2 months of combined streptomycin, rifampicin, isoniazid and pyrazinamid followed by 4 month of combined rifampicin and pyrazinamid) according to the national program (Moroccan health ministry 1995). Treatment was discontinued (by patient himself) after 2 months. Three months before his hospitalization, the patient presented a significant bilateral decline in visual acuity followed, one month later, by a total functional impairment of the lower limbs associated with sphincter dysfunction. Physical examination diagnosed bilateral blindness. Neurological examination found a spinal cord section syndrome with a T4 sensory level. The spinal MRI revealed an extended T3 to T5 hyposignal T1, hypersignal T2 image (Fig. 1A). Brain MRI was normal. The CSF study objectified increased cells (30 cells/mm3 lymphocytes). Bacteriological (search for BK) and chemical were normal (glucose at 0.4g/l in CSF and 0.94 g/l in serum, protein at 0.68g/l). Electrophoresis was normal. Chest radiography objectified an excavated cave in the left apex (Fig 1B) and the BK search in sputum was still positive. Anti-NMO antibodies were negative. These clinical and
para-clinical exams permitted the exclusion of a tuberculous localization in the nervous system and the retention of of the Devic’s syndrome diagnosis, associated with pulmonary tuberculosis, according to the Wingerchuk diagnostic criteria (Table I). The patient was retreated with antibacillary drugs (2 SRHZ/9RH) associated a methylprednisolone pulse (5 days, 1g/d) relayed by oral corticosteroids at 1 mg / kg / day (6 weeks) with gradual digression.

Outcome was unfavorable with worsening motor deficit, persistent sphincter disorders. Ophthalmologic control showed bilateral optic atrophy.

**Case 2**

A 43-year-old male patient without history of tuberculosis, experienced, 4 months previous to his hospitalization, sudden right blindness followed one month later by a contra lateral blindness with heaviness of the four members leading to an absolute dysfunction after 15 days, with urinary incontinence and constipation. Furthermore, the patient was also experiencing anorexia and generalized asthenia. The neurological examination has disclosed a spinal cord section syndrome with a T2 sensory level. The ophthalmologic examination revealed bilateral blindness. Brain MRI was normal, and spinal cord MRI objectified cord lesion in hyposignal T1 and T2 hypersignal range C2 to T1 (Fig. 2A and 2B). CSF study objectified increased protein (0.80g/l) with glucose at 0.41g/l (in serum at 0.89g/l) but was normal in the cytological, Bacteriological exams and in electrophoresis. A review in search of a condition associated including a chest X-ray which disclosed a right apical excavated lesion (Fig. 2C), the search for BK in sputum and tuberculin IDR were positive. Anti-NMO antibodies study remains negative. The diagnosis of Devic’s syndrome associated with pulmonary tuberculosis was retained. The patient was treated with a methylprednisolone pulse (1g/d for 5Day) relayed by oral corticosteroids at 1 mg/kg/day, combined to antibacillary treatment (2SRHZ/9RH). The patient kept quadriplegia. Ophthalmological Control objectified bilateral optic atrophy.

### Table I

<table>
<thead>
<tr>
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<th>Revised diagnostic criteria for acute Devic’s optico-neuro-myelitis (Wingerchuk DM <em>et al</em>. 2006) (NB: in our case, only the anti-NMO antibodies are missing)</th>
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</thead>
<tbody>
<tr>
<td>1.</td>
<td>Acute transverse myelitis</td>
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<td>2.</td>
<td>And optic neuritis</td>
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<td>3.</td>
<td>And at least two of the following criteria:</td>
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<tr>
<td>a.</td>
<td>Brain MRI normal (or not suggestive of MS);</td>
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<tr>
<td>b.</td>
<td>Spinal cord MRI with lesion ≥ 3 vertebral segments;</td>
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<tr>
<td>c.</td>
<td>Positive NMO-IgG Serology.</td>
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</table>
Neuromyelitis optica (NMO) or Devic’s syndrome was first described in 1894 by Eugène Devic (Devic et al., 1894). It is a rare disease characterized clinically by a spinal cord and optic nerves involvement, and at pathological level by demyelization, necrosis and axonal loss. The brain was macroscopically normal (Devic et al., 1894; Lucchinetti et al., 2002; Mandler et al., 1993).

The pathophysiological mechanism is still not clearly understood, however, the discovery of specific antibodies supports the role of humoral immunity in its pathogenesis (De Seze et al., 2007; Papeix et al., 2007).

In its typical form, as in our patients, Devic NMO is characterized by attacks of optic neuritis followed after a few days or months by myelitis. Visual Impairment may be bilateral (Wingerchuk et al., 1999), but is more often unilateral. It is usually acute (Papeix et al., 2007). There are two clinical forms of Devic’s NMO: a single-phase with a time lag between optic neuritis and myelitis (less than or equal to one month) and a relapses form (Wingerchuk et al., 1999).
Wingerchuk et al defined criteria for the diagnosis of Devic’s disease: diagnosis is clinical and paraclinical (Wingerchuk et al., 1999) (Table I). However, MRI brain, spinal cord and analysis of cerebrospinal fluid (CSF) often add a contribution to the diagnosis. Indeed, there is frequently an important hypercellularity (sometimes more than 50 elements), combined with an increased CSF protein (greater than 1 g). In addition, MRI shows (in 60% of the cases) spinal extensive damage to several levels. However, brain MRI is usually normal (De Seze et al., 2007). Recently, a NMO specific antibody was identified (Lennon et al., 2004). This antibody, directed against aquaporin and called “anti-NMO” was found in over 50% patients with NMO, while it was present in none of the healthy control subjects or the patients with MS (Lennon et al., 2004). This discovery has led to propose new criteria, including anti-NMO (Wingerchuk et al., 2006) (Table I).

Several diseases have been reported in association with the Devic’s NMO: autoimmune diseases, – especially endocrine and infectious – (Wingerchuk et al., 1999). The association with active extra-neurological tuberculosis has already been described (Barbizet et al., 1980; Wingerchuk et al., 2006). However, neurological localization must be excluded before. In our patients, the normal brain MRI has eliminated an optic nerve compression cause. Similarly, the bacteriological normality of CSF excluded the infectious nature of myelitis. The occurrence of NMO in a context of pulmonary tuberculosis can be explained by an acute demyelization demyelization secondary to the immune dysfunction caused by the BK (Barbizet et al., 1980). Several elements support this mechanism including the finding of foci of demyelization away during tuberculosis encephalitis and the experimental reproduction of demyelization by cistern injection of BK or tuberculin antigenic extracts. It’ interesting to note that all cases reported in the literature, (including our observations) show pulmonary tuberculosis. This could be explained by the profusion of bacillary population in this location.

Two other diagnosis must be discussed: acute disseminated encephalomyelitis (ADEM) and multiple sclerosis (MS) with onset presentation as Devic’s syndrome, but the brain and spine imaging are not compatible with this two situations (diffuse brain lesions in ADEM and less than one vertebral lesion for spine MRI in MS).

Therapeutic options in Devic’s syndrome are numerous; they are mainly based on high doses of corticosteroids, possibly associated with plasma exchange or immunoglobulin. Therefore the association of NMO to another pathology including Tuberculosis is a serious therapeutic problem. The treatment combines a corticosteroid bolus with oral relay and antibacillary drugs (Barbizet et al., 1980). A favorable evolution in this association was first reported by Barbizet (Barbizet et al., 1980).

NMO is usually regarded as having an unfavourable outcome. In some series, the mortality rate in the acute phase may reach 20%, particularly in monophasic forms (De Seze et al., 2007; Wingerchuk et al., 1999), due to the higher risk of death by associated dysautonomia (cardio-respiratory attack, hypotension). However, a recent study showed that long-term disability was more pronounced in remitting forms (De Seze et al., 2007; Wingerchuk et al., 1999).

A number of predictive criteria of poor outcome are known. They are, in decreasing order, gender, associated autoimmune disease, most significant interval between the first two episodes and the frequency of episodes during the first years of disease (De Seze et al., 2007).

The prognosis of the combination between Devic’s syndrome and pulmonary tuberculosis varies in the literature. The first seven cases published before 1980 were fatal (death caused by the dysautonomic and respiratory consequences of the myelitis). Since then, other authors (Barbizet et al., 1980) have reported some cases of good outcome. In our patients, the evolution was unfavorable in terms of motor and visual symptoms (with quadriplegia and total blindness). This poor prognosis may be partially explained by the delay of corticosteroid treatment at onset. However, the prognosis in Devic’s syndrome is generally poor on the long term and 20 to 60% of patients develop blindness (Papeix et al., 2007).

**Conclusion**

Devic’s syndrome is rare. Its combination with pulmonary tuberculosis is anecdotally reported and raises several pathophysiological questions. The prognosis of this co-morbidity is not uniform, but is often reported as poor and fatal.

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To Asmaa Bendahmane MD and Hicham Bendahmane MD

**REFERENCES**


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