Devic's neuromyelitis optica associated with active pulmonary tuberculosis, Tunisia

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Abstract

Devic's Optic neuromyelitis (OND) is a very rare disease defined as a central nervous system (CNS) inflammation resulting in optic neuritis and/or myelitis. The discovery of a highly specific serum autoantibody biomarker for the diagnosis has triggered a great interest in conducting further research into this disease. The association of OND with Tuberculosis (TB) is even rarer and could be an entirely random conjunction. To our knowledge, we reported the first case of Neuromyelitis Optica associated with pulmonary TB in Tunisia.

Keywords: Neuromyelitis Optica, Devic's Syndrome, demyelination, tuberculosis, Tunisia

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To the Editor,

Considered for a long time as a form of multiple sclerosis [1], Devic's optical neuromyelitis, also called neuromyelitis optica (NMO), is a rare anatomic and clinical entity that involves the optic pathways and spinal cords, without causing severe brain injuries [2]. It is an inflammatory demyelinating disease of the central nervous system [2]. The association of NMO with tuberculosis (TB) is scarce and could be an entirely random conjunction. To our knowledge, only a few case reports associating these two diseases exist in medical literature [3–6]. We provide the first detailed Tunisian case report of NMO associated with pulmonary TB.

Case report

We report the case of a 28-year-old man with no medical history. He presented to the emergency room complaining of ocular pain, blurred vision, gait disorders and dysuria. He also sought care for respiratory symptoms including cough with a small amount of haemoptysis, fever and a decrease in general condition over the preceding few months. At admission, he developed complete urinary retention and a spastic paraplegia. Brain and spinal cord MRI showed a transverse myelitis extending from C5 to T10 (Fig. 1a) with optic nerve and optic chiasma contrast recording. Ophthalmological examination revealed the presence of bilateral papilloedema. Visual evoked potential indicated a significant prolongation of the latency of the P100 wave. Lumbar puncture showed clear cerebrospinal fluid (CSF) with albumin cytological dissociation (white blood cell count of 7/mm^3 with elevated protein concentration of 3.23 g/L) and low glycorrhachia (ratio of 1/3). Direct examination and CSF culture were negative. In addition, PCR analysis of the CSF was negative for herpes simplex virus, varicella zoster virus, enteroviruses, *Listeria monocytogenes* and *Mycobacterium tuberculosis*. Molecular detection was carried out using the FilmArray® Meningitis/Encephalitis (M/E) Panel from bioMérieux (Marcy l'Étoile, France) and by conventional tests.

The diagnosis of NMO was confirmed on clinical presentation (simultaneous transverse myelitis with an optic nerve damage) and immunological data (presence of anti-NMO or anti-aquaporin 4 antibodies in the CSF) all based on the criteria of Wingerchuk et al. [1].

Chest X-ray showed a bilateral micronodular infiltrate (Fig. 1b). A thoracic CT revealed bilateral acinar nodes more prevalent in the upper left lobe, associated with several cavitating lesions.

Tuberculin skin test (Mantoux test) was negative. Direct examination of the sputum did not identify any acid-resistant bacilli. *Mycobacterium tuberculosis* colonies did finally grow in the culture of the endotracheal aspirate. Human immunodeficiency virus serology was negative. Active pulmonary TB diagnosis was based on clinical and radiographic findings but was

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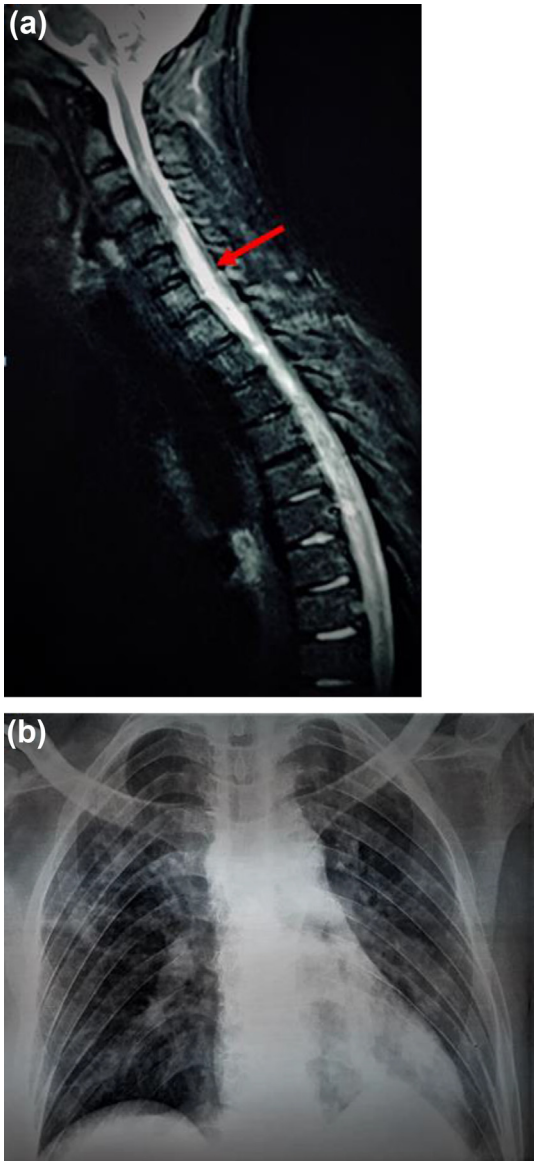

FIG. 1. (a) Spinal cord MRI (sagittal T2 sequence) showed a longitudinally extensive transverse myelitis extending from C5 to T10 (red arrow). (b) Posteroanterior chest radiograph showed bilateral micronodular infiltrate without peripheral consolidation or pleural effusion.

not supported by microbiological data. So, the diagnosis of Devic syndrome revealing associated pulmonary TB was confirmed.

The patient was treated with parenteral corticosteroid therapy along with immunoglobulins. Anti-tubercular therapy was also given for 6 months. The outcome was only partially favourable with persistent paraplegia.

The ophthalmological examination of the left eye at follow up (4 months later) showed optic neuritis. The patient had no light perception and a quiet anterior chamber. His pupillary light reflex was absent with a positive Marcus Gunn sign. The crystalline lens was transparent and the conjunctiva was pale with clear edges. He had a normal spontaneous venous pulsation.

Discussion

Devic's neuromyelitis optica is characterized by the onset of concomitant visual impairment and myelitis due to optic nerve and spinal cord demyelination [1,7]. The pathophysiological mechanism is still uncertain but is probably of immunological origin. During NMO, the immune system produces autoantibodies that target a protein called aquaporin-4, which is expressed by astrocytes. Thereafter a cascade of reactions leading to damage of the entire nervous tissue is triggered.

These reactions cause an inflammatory response that destroys the myelin sheath covering the neurons, and also the neuron itself, which explains the neurological symptoms of the disease.

Although the association of NMO with active pulmonary TB has been reported and might not be a simple coincidence, a causal relation between the two conditions has not been demonstrated [3]. Moreover, pulmonary and central nervous system TB must be ruled out before making the diagnosis [8].

Anatomopathological study of spinal cord injuries has demonstrated that the humoral immunity dysregulation is triggered by an infectious agent [7]. In fact, *M. tuberculosis* surface antigens might initiate the production of reactive antibodies against aquaporin-4 proteins leading to the acute demyelination [9].

Another argument supporting this causative association between NMO and active TB is the onset of demyelination clusters being far from infectious clusters. Moreover, in experimental studies, demyelination occurred after an intracisternal injection of antigenic *Mycobecterium tuberculosis* or tuberculin extracts [10].

Anti-bacillary treatment toxicity leading to NMO is another hypothesis that has been discussed. However, it remains inconclusive, considering the possibility of neuro-ophthalmological damage before the initiation of TB treatment and the beneficial impact of anti-tubercular therapy in patients suffering from steroid-refractory NMO [4].

As the immune response against active TB infection is commonly cell-mediated rather than a humoral response, the combination of the two entities could be a pure coincidence and still needs to be proven [4].

Neuromyelitis optica is generally associated with pulmonary TB. Lungs are most often infected by the bacilli when compared with other sites. Nevertheless, further TB localizations have been reported such as abdominal TB [5] and renal TB [6].

The treatment is based on corticosteroids and anti-tubercular therapy. A partial recovery of motor symptoms, restored sphincter control and permanent blindness are seen in the majority of cases [11].

The long-term clinical efficacy of anti-tubercular therapy in patients with steroid-refractory NMO has been proved. It reduces the disease's activity and progression, resulting in significant recovery of neurological function [12].

Neuromyelitis optica-like disorders are an important diagnosis to consider in patients treated for active TB who present with acute neurological and ocular disorders such as transverse myelitis and optic neuritis, once neurological TB has been ruled out. Anti-aquaporin-4 antibody screening should be part of the investigation of these patients [3].

Further studies are required to assess whether this association is random or is caused by a dysregulated immune response.

Conflict of interest

All authors declare that there is no conflict of interest.

Authors' contributions

SZ and AZ made substantial contributions to conception, analysis and interpretation of data. SZ, AZ and HH contributed to drafting the manuscript and revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

[1] Wingerchuk DM, Hogancamp WF, O'Brien PC, Weinshenker BG. The clinical course of neuromyelitis optica (Devic's syndrome). Neurology 1999;53:1107–14.
[2] Jindahra P, Plant T. Update on neuromyelitis optica: natural history and management. Eye Brain 2012;4:27–41.
[3] Zatjirua V, Butler J, Carr J, Henning F. Neuromyelitis optica and pulmonary tuberculosis: a case-control study. Int J Tuberc Lung Dis Off J Int Union Tuberc Lung Dis 2011;15:1675–80.
[4] Sridhar S, Chan JF-W, Yuen K-Y. Fatal anti-aquaporin-4 seropositive neuromyelitis optica spectrum disorder in tuberculosis. BMC Infect Dis 2014;14:470.
[5] Bhatty SA, Lal H, Talib A, Mahmood K, Naqvi I, Zaidi SS. Neuromyelitis optica (NMO) with abdominal tuberculosis (TB). J Coll Phys Surg Pak 2015;25(Suppl. 2):S102–4.
[6] Iorio R, Monforte M, Pierconti F, Iodice F, Sabatelli M. Tuberculous nephritis accompanying neuromyelitis optica: causal or coincidental association? J Neurol 2014;261:1028–30.
[7] Zhong X, Zhou Y, Lu T, Wang Z, Fang L, Peng L, et al. Infections in neuromyelitis optica spectrum disorder. J Clin Neurosci Off J Neurosurg Soc Australas 2018;47:14–9.
[8] Li R, Zhong X, Qiu W, Wu A, Dai Y, Lu Z, et al. Association between neuromyelitis optica and tuberculosis in a Chinese population. BMC Neurol 2014;14:33.
[9] Pohl M, Fischer M-T, Mader S, Schanda K, Kitic M, Sharma R, et al. Pathogenic T cell responses against aquaporin 4. Acta Neuropathol (Berl) 2011;122:21–34.
[10] Bradl M, Lassmann H. Experimental models of neuromyelitis optica. Brain Pathol 2014;24:74–82.
[11] Jarius S, Wildemann B, Paul F. Neuromyelitis optica: clinical features, immunopathogenesis and treatment. Clin Exp Immunol 2014;176:149–64.
[12] Feng Y, Guo N, Huang F, Chen X, Sun Q, Liu J. Anti-tuberculosis treatment for Devic's neuromyelitis optica. J Clin Neurosci Off J Neurosurg Soc Australas 2010;17:1372–7.