Neuromyelitis optica spectrum disorder in the elderly associated with bronchiolitis obliterans organizing pneumonia

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Practical Implications

Neuromyelitis optica spectrum disorder should be investigated in patients with myelitis of uncertain origin, even in the elderly and without evidence of optic neuritis.

Neuromyelitis optica (NMO) spectrum disorder (NMOSD) is a rare, often severe, autoimmune condition defined by isolated optic neuritis or longitudinally extensive transverse myelitis with antibodies against aquaporin-4 (AQP-4).¹

NMOSD is more frequent in women in their 30s or 40s, although cases have been described in children and elderly patients.² The association with other autoimmune diseases and autoantibodies has been established, including systemic lupus erythematosus, myasthenia gravis, celiac disease, and Sjögren syndrome, among others. We report 2 elderly patients with transverse myelitis due to NMOSD and bronchiolitis obliterans organizing pneumonia (BOOP).³

Case 1

A 75-year-old man with a 6-month history of recurrent pulmonary infiltrates responsive to steroid therapy was admitted because of abdomen paresthesia for 72 hours, followed by unstable gait. Neurologic examination revealed a sensitive thoracic level (Th4–Th9), unstable walk, and a positive Romberg sign.

Spinal cord MRI showed an extensive centromedullary lesion from C4 to T10, suggestive of acute transverse myelitis (figure, A and B). CSF analysis showed 74.1 mg/dL proteins and lymphocytic pleocytosis (33 cells/mm³). Serum anti-NMO antibodies by indirect immunofluorescence were repeatedly positive. With the diagnosis of NMOSD, therapy with IV methylprednisolone was administered, with partial improvement.

Pulmonary CT scan showed the presence of bilateral patchy pulmonary infiltrates with a different location as compared to the initial CT scan, a finding consistent with a diagnosis of BOOP. Azathioprine was started and the patient had no further relapses in 5 years.

Case 2

An 83-year-old woman was admitted after experiencing weakness in the right lower limb. She had been diagnosed with BOOP in 2004, responsive to steroids. She presented a sensitive disturbance in her lower extremities in 2006, when spinal cord MRI showed 2 foci of centromedullary myelitis (C2–Th1 and Th7–Th9) (figure, C and D). CSF disclosed lymphocytic pleocytosis. She was treated with boluses of methylprednisolone and showed progressive improvement to normal.

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Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the **full text of this article** at Neurology.org/cp.

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Figure Spinal cord MRI of patients 1 and 2

(A, B) Patient 1 (sagittal, T2-weighted sequence, cervical and thoracic spinal cord): Centromedullary signal impairment (C4–Th10) consistent with longitudinally extensive transverse myelitis. There were no brain parenchyma abnormalities. (C, D) Patient 2 (sagittal, T2-weighted sequence, cervical and thoracic spinal cord): Multiple foci of centromedullary signal disturbance suggestive of longitudinally extensive transverse myelitis (C2–Th1 and Th7–Th9) with some foci of gadolinium enhancement. There were no brain parenchyma abnormalities.

In 2014, the patient was taken to another hospital because of weakness in the left lower limb. Cervical MRI showed multiple foci of abnormal, enhancing signal from C3 to C7, Th1 to Th3, and Th7 to Th12. She was treated with boluses of methylprednisolone and showed partial recovery, being able to walk with a walker.

In 2015, the patient was again admitted because of a right lower limb weakness that began 10 days prior and prevented her from walking. Spinal cord MRI showed multiple new intramedullary, enhancing foci (C2, C5–C7, Th1, Th9–Th11, L1–L2) and progression of the previous lesions. Brain MRI was normal. CSF contained 31 cells/mm³ and increased immunoglobulin G synthesis. Serum antibodies against NMO by indirect immunofluorescence were repeatedly positive. She was treated with boluses of corticosteroids with little recovery and was discharged on azathioprine.

DISCUSSION

The 2 patients described presented longitudinal extensive transverse myelitis in the context of NMOSD of very late onset, and had an associated bronchiolitis obliterans. Elderly patients with NMOSD are more prone to disability because of a decrease in repair mechanisms with a deficient anti-inflammatory response.⁴ In contrast with multiple sclerosis, relapse activity in NMOSD does not decrease with age, and delays in diagnosis and treatment often lead to relapses and fatal outcomes. Early treatment is essential but is difficult in the elderly due to comorbidities, less response to immunosuppressive therapies, and iatrogenic complications.⁵ In our patients, AQP4 seropositivity was performed by indirect immunofluorescence, which occasionally has yielded false-positive results. The fact that results were repeatedly positive is consistent with true positivity.

Patients with NMOSD have an increased predisposition to autoimmune disorders, and NMOSD can precede or appear later in the course of the autoimmune disease. The 2 patients presented had a previous diagnosis of BOOP, a chronic inflammatory lung disease characterized pathologically by the presence of granulation tissue in the bronchiolar lumen and alveolar ducts, associated with interstitial infiltration by mononuclear cells and macrophages.⁶ BOOP involves people of all ages, and responds to steroid therapy.

This condition can be associated with a variety of systemic disorders. Interestingly, AQP4 expression has been identified in lung tissue,⁷ which could explain the relation of BOOP with NMOSD. It could be argued that an immune response to pulmonary antigens might elicit an immune attack against cross-reactive nervous system antigens, in a similar manner to the mechanisms of autoimmune reaction in patients with small cell lung cancer and paraneoplastic disease.

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Received August 30, 2016. Accepted in final form November 15, 2016.

AUTHOR CONTRIBUTIONS

Aintzine Ruisanchez Nieva, Jose Luis Sanchez Menoyo, Ines Escalza Cortina, Nerea Fonca Beti, Marian Gomez Beldarrain, and Juan Carlos Garcia-Monco were involved in writing the manuscript and obtaining the data.

STUDY FUNDING

No targeted funding reported.

DISCLOSURES

The authors report no disclosures. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.