



Case Report

Anti-aquaporin-4 Antibody Positive Relapsing Neuromyelitis Optica in a Patient With Systemic Lupus Erythematosus

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Abstract

Neuromyelitis optica (NMO) is a rare inflammatory disorder of the central nervous system characterized by optic neuritis and myelitis. NMO may rarely be accompanied by systemic autoimmune disease including systemic lupus erythematosus (SLE). This immunological overlap may reflect the predisposition of patients with NMO to systemic autoimmunity. We report a young female with relapsing NMO and SLE. The patient was seropositive for anti-aquaporin-4 autoantibody, a highly sensitive and specific marker for NMO. Our case highlights the importance of testing for the anti-aquaporin-4 autoantibody in the case of relapsing myelitis or optic neuritis in patients with SLE for making correct diagnosis and choosing the appropriate management.

Keywords: Systemic lupus erythematosus; neuromyelitis optica; anti-aquaporin 4 antibody

Sistemik Lupus Eritematozuslu Bir Olguda Anti-aquaporin-4 Antikor Pozitifliği ile Seyreden Relapsing Nöromiyelitis Optika

Özet

Nöromiyelitis optika (NMO) santral sinir sisteminin optik nörit ve miyelit ile karakterize nadir bir inflamatuvar bozukluğudur. NMO'ya ender olarak sistemik lupus eritematozusun (SLE) da aralarında bulunduğu sistemik hastalıklar eşlik edebilir. Bu immünolojik birliktelik NMO hastalarının sistemik otoimmüniteye yatkınlığını yansıtabilir. Relapslarla seyreden NMO ve SLE'li bir olgu sunulmaktadır. Hasta NMO için yüksek derecede sensitif ve spesifik olan anti-aquaporin-4 otoantikoru için seropozitif. Olgumuz, SLE'li bir hastada relapslarla seyreden miyelit veya optik nörit tablosunda anti-aquaporin-4 otoantikoru tayininin, doğru tanı konması ve uygun tedavinin seçilmesindeki önemini vurgulamaktadır.

Anahtar Kelimeler: Sistemik lupus eritematozus; nöromiyelitis optika; anti-aquaporin 4 antikoru

INTRODUCTION

Neuromyelitis optica (NMO), or Devic's disease, is an idiopathic inflammatory disease of the central nervous system that preferentially affects the optic nerves and the spinal cord^(4,8). The disease has a devastating course with progression to functional blindness or wheelchair dependence within 5 years of onset in more than 50% of cases⁽⁹⁾. Patients with NMO often have accompanying autoimmune diseases including systemic lupus

erythematosus (SLE) and Sjögren syndrome (SS)⁽⁷⁾. Although these diseases may also cause central nervous system involvement, this coexistence may reflect a predisposition of patients with NMO to multiple autoimmune diseases⁽⁵⁾. Seropositivity for anti-aquaporin-4 antibody which is a highly sensitive and specific marker for NMO, can help differentiating between SLE nervous system manifestations and NMO^(1,3,10).

We present a patient in whom SLE was complicated by anti-aquaporin 4 antibody positive relapsing NMO.

CASE PRESENTATION

A 30-year-old woman presented with a two days history of urinary retention and leg weakness progressing to its nadir in the first 24 hours. The patient had a history of arthritis, malar rash with photosensitivity and anemia, and a diagnosis of SLE was made four years before. The patient was under hydroxychloroquine treatment. Her family history was unremarkable.

On admission, the patient had no fever; her pulse was 89 beats per minute (bpm) and regular, blood pressure was 110/70 mmHg, and respiratory rate was 18 bpm. Neurological examination revealed neck stiffness, flaccid paraplegia, areflexia in the lower limbs, a sensory deficit below the level Th4, extensor plantar responses on both sides and urinary and bowel retention.

Complete blood cell count analysis showed a hemoglobin level of 10.7 g/dl (normal range 12-16 g/dl), leukocyte count of 16.100/mm³ (normal 4.000-11.000/mm³) and platelet count of 391.000/mm³ (150.000-400.000/mm³). Erythrocyte sedimentation rate was elevated (50 mm/h). Antinuclear antibody (ANA) was positive at 1/320 granular pattern. Anti-double stranded and anti-single stranded DNA were also positive. Anti-cardiolipin IgM and IgG antibodies were positive. VDRL/RPR was positive. However, TPHA and FTA Abs were negative. There were no abnormal findings in other laboratory data including serum levels of glucose, electrolytes, liver enzymes, urea, creatinine, vitamin B12, folate, C-reactive protein, complements 3 and 4, rheumatoid factor, tumor markers and qualitative urine analysis. Serological tests were negative for hepatitis viruses, HIV, brucella and syphilis. Analyses for histones, SS-A, nucleosomes and, Ro-52 were positive. Cerebrospinal fluid analysis revealed hypoglycorrachia (13 mg/dL, simultaneous

serum glucose level 103 mg/dL), increased protein level (650 mg/dL, normal 10-40 mg/dL) and pleocytosis (4500 cells/mm³, 90% polymorphic) and no oligoclonal bands. However, CSF culture for bacterial, viral, parasitic and fungal infections yielded no positive result. Spinal MRI showed longitudinally transverse myelitis extending longitudinally from the point of the medulla oblongata-cervical spinal cord junction to Th8 with marked cord edema and gadolinium enhancement.

The patient had a diagnosis of longitudinally extending transverse myelitis associated with SLE and she was treated with 1 gr/d intravenous methylprednisolon for five days followed by oral prednisolone 1 mg/kg/d and intravenous cyclophosphamide (1000 mg/m²). The clinical manifestations of the patient did not respond to the treatment and flaccid paraplegia and sphincter disturbances persisted.

After a six-months of follow-up, the patient was readmitted with the complaints of binocular vision loss and retro-orbital pain that worsened with eye movements. Neuroophthalmological examination revealed dilated pupils unreactive to light stimuli, absolute vision loss on both sides and bilateral swollen discs. The patient had persistent flaccid paraplegia as a sequella of the myelitis episode. In addition to the above-mentioned laboratory abnormalities, the patient developed microalbuminuria as demonstrated by quantitative urine analysis. Visual evoked potentials could not be elicited. Spinal MRI revealed severe thoracic cord atrophy. Brain MRI was normal. Serum NMO-IgG antibody detected by immunofluorescence was positive.

The diagnosis of SLE was confirmed based on the diagnostic criteria proposed by The American College of Rheumatology, as the patient fulfilled 6 of the 11 criteria for diagnosis of SLE: (1) arthritis, (2) malar rash, (3) photosensitivity, (4) anemia, (5) positive ANA and (6) positive anti-DNA

antibody⁽²⁾. The diagnosis of NMO was also made as the patient had optic neuritis and myelitis in addition to the three supportive diagnostic features; longitudinally extending transverse myelitis, seropositivity for NMO-IgG and brain MRI non-diagnostic for multiple sclerosis⁽⁸⁾. The patient was treated with intravenous methylprednisolone 1 g/d over ten days followed by oral prednisone 1 mg/kg/d and monthly pulses of intravenous cyclophosphamide 1000 mg/ m². After the treatment, the visual acuity of the both eyes was 20/200.

DISCUSSION

We presented a case of SLE and anti-aquaporin-4 antibody positive relapsing NMO. Our case fulfilled the revised diagnostic criteria for NMO⁽¹⁰⁾. Although non-organ-specific autoantibodies such as antinuclear antibodies are frequently detected in patients with NMO, as our case had other symptoms and signs indicative of SLE besides immunological abnormalities, the diagnosis of SLE was undoubtful in our patient⁽⁵⁾. NMO may coexist with SLE, SS, autoimmune thyroiditis, type 1 diabetes mellitus, or myasthenia gravis⁽⁵⁾. This coexistence may reflect the predisposition of patients with NMO to multiple autoimmune diseases⁽⁵⁾.

In recent years, a highly sensitive and specific marker for NMO, anti-aquaporin-4 antibody has been discovered^(3,10). However, in Turkish patients with NMO, anti-aquaporin-4 antibody was positive in only 60%⁽¹¹⁾. In 2007, Birnbaum et al.⁽¹⁾ reported the first case of anti-aquaporin-4 antibody positive NMO in a patient with SLE. Pittock et al. reported that the antibody was not detected in any patient with SLE or SS who did not have any symptoms indicative of NMO⁽⁵⁾. This finding suggests that seropositivity for anti-aquaporin-4 antibody in patients with SLE is highly specific for NMO and this autoantibody is not a nonspecific accompaniment of SS or SLE⁽⁵⁾. As detection of the anti-aquaporin-4 antibody

positivity during the longitudinally extending transverse myelitis attack could have predicted the relapsing course of the disease, our case should have undergone anti-aquaporin-4 antibody testing at her first attack⁽¹²⁾. The case highlights the importance of testing for the anti-aquaporin-4 antibody in the case of a longitudinally extending transverse myelitis or optic neuritis in a patient with SLE.

Our case had CSF findings indistinguishable from bacterial meningitis. Therefore, differential diagnosis included central nervous system infections. However, CSF culture for bacterial, viral, parasitic and fungal infections was negative. Similarly, Birnbaum et al.⁽¹³⁾ reported that CSF findings in gray matter myelitis in patients with SLE was characterized by inflammatory features including neutrophilic pleocytosis, increased protein level and decreased glucose level resembling the pattern expected for bacterial meningitis except for sterile cultures. In addition, Lepur et al.⁽¹⁴⁾ reported two patients with NMO in whom CSF findings suggestive of bacterial meningomyelitis. These findings suggest that CSF findings may resemble bacterial central nervous system infections in patients with NMO.

Treatment options include intravenous methylprednisolone or plasmapheresis for acute attacks and maintenance immunosuppression to prevent relapses⁽¹²⁾. Azathioprine, cyclophosphamide, methotrexate, mitoxantrone, mycophenolate mofetil, intravenous immunoglobulin, and rituximab have been reported to reduce relapses in patients with NMO^(6,12). The longitudinally extending transverse myelitis and optic neuritis attacks of our case was unresponsive to treatment with intravenous methylprednisolone. Attacks unresponsive to intravenous methylprednisolone should be treated with plasmapheresis⁽¹²⁾.

In conclusion, myelitis or optic neuritis in patients with SLE should alert the clinician regarding the coexistence of NMO and lead to testing for the presence of anti-aquaporin-4 antibody.

Conflict of interest: The authors declare that they have no conflict of interest.

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