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Neuromyelitis Optica Immunoglobulin G in a Child

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Abstract

Neuromyelitis optica or Devic's syndrome is an uncommon demyelinating disorder that preferentially attacks the spinal cord and optic nerves. Although it is well described in adults, childhood neuromyelitis optica has rarely been reported in the literature and is frequently misdiagnosed as severe multiple sclerosis. Recently, a serum immunoglobulin G test for neuromyelitis optica has become available which may clarify and accelerate the diagnosis. This report describes a child with recurrent myelitis and an elongated spinal cord lesion who was found to have positive neuromyelitis optica autoantibody. We believe that neuromyelitis optica autoantibody testing should be performed in cases of pediatric transverse myelitis with multiple vertical segments or recurrence.

Introduction

Neuromyelitis optica, or Devic's syndrome, is a rare and aggressive demyelinating disease of the spinal cord and optic nerves that usually spares the brain. Recently, a serum autoantibody immunoglobulin G marker for neuromyelitis optica with a sensitivity of 73% and specificity of 91% in patients with clinically defined neuromyelitis optica has become available [1]. This autoantibody allows early detection of neuromyelitis optica before fulfillment of formal diagnostic criteria, and may allow earlier institution of immunosuppressive therapy. Compared with multiple sclerosis, neuromyelitis optica usually has a later age onset and even greater preponderance of female cases [2], but rare pediatric cases have been described. Neuromyelitis optica antibody has not been previously reported in children. This report presents the case of a child with recurrent transverse myelitis and a large cervical spinal cord lesion responsive to intravenous methylprednisolone with a positive neuromyelitis optica immunoglobulin G.

Case Report

An 8-year-old female subacutely developed bilateral upper extremity paresthesias. Over the next 5 days, she manifested weakness and clumsiness of all four limbs with gait instability.

She denied visual, sensory, or sphincter involvement. She had no recent infectious illnesses. Gestational, birth, past medical and family history were unremarkable. On examination, she was alert and oriented with normal cranial nerve function. She had weakness to resistance in all four extremities, more on the left. Tone was moderately increased in the bilateral lower extremities. Reflexes were pathologically brisk in all four limbs with clonus at the ankles. Plantar reflexes were extensor. Sensation to pain, temperature, vibration, and position sense was modestly diminished in the lower extremities with an indistinct sensory level in the upper thorax and normal sensation in the arms. There was both finger/nose and heel/shin ataxia. She could not walk unassisted and had a spastic-ataxic gait. Rectal tone was normal.

Magnetic resonance imaging of the entire spinal cord revealed increased T2 signal from the cervicomedullary junction to C₇ with associated swelling and modest enhancement at the level of C₃ (Fig 1). Magnetic resonance imaging of the brain and optic nerves was normal. Visual evoked potentials were normal. Complete blood counts, electrolytes, and liver function tests were normal. A lumbar puncture demonstrated three nucleated white blood cells, 450 red blood cells, glucose of 45 mg/dL, and protein of 29 mg/dL. Immunoglobulin G synthesis and index were normal in the cerebrospinal fluid, but greater than five oligoclonal bands were present.

Polymerase chain reaction for enterovirus, *Mycoplasma*, varicella zoster virus, cytomegalovirus, *Bartonella*, and herpes simplex virus in the cerebrospinal fluid were all negative. Venereal disease research laboratory test for syphilis was negative, and antibodies to human immunodeficiency virus were not detected. Antinuclear antibody was negative, erythrocyte sedimentation rate was 4 mm/hr, C-reactive protein was less than 0.2 mg/dL, and anti-streptolysin O titer was elevated at 864 Todds units/ml. Neuromyelitis optica antibody (Mayo Medical Laboratories) was positive in serum. She received 1 gm of intravenous methylprednisolone every day for 5 days followed by a 2-week prednisone taper. In 10 days, strength and coordination returned to baseline. Four weeks later, a magnetic resonance imaging scan of her cervical spine indicated near complete resolution of the lesion.

Three months later, the patient developed lower back pain, urinary urgency and frequency, and paresthesias in the legs. A thoracic and lumbar spine magnetic resonance imaging revealed a conus lesion less than one segment long. She received 1 gm of intravenous methylprednisolone every day for 3 days and had resolution of all symptoms.

Discussion

Transverse myelitis is well recognized in children, with nearly 400 cases annually in the United States [3]. Prognosis in children is variable, but Knebusch estimated 44% had good recovery, 33% had persistent deficits but could walk unassisted, and 23% manifested severe neurological impairment in gait, micturition, and defecation [4]. Our patient had a fairly typical episode consistent with transverse myelitis, but with a lesion greater than three vertebral segments long. The second episode was associated with a shorter lesion in a new location. To date, the patient has not had a clinical episode of optic neuritis, and her visual evoked potentials were normal. A variety of potential causes were investigated, but none other than neuromyelitis optica was identified. Oligoclonal bands are evident in approximately 30% of patients with neuromyelitis optica [5], and the elevated anti-streptolysin O titer is nonspecific and does not point to a different underlying disease or explanation for recurrent transverse myelitis.

For the diagnosis of neuromyelitis optica, the patient reported herein meets two of the three absolute criteria (acute myelitis and absence of clinical disease outside the optic nerve or

spinal cord), and two major supportive criteria (negative brain magnetic resonance imaging at onset and spinal cord magnetic resonance imaging with signal abnormality extending over three vertebral segments) [5]. By suggested revised criteria [6], she would still be considered only “at risk” for developing neuromyelitis optica, and, in this context, 56% of patient are neuromyelitis optica antibody positive [1]. The positive neuromyelitis antibody and the long spinal cord lesion, however, are two minor diagnostic criteria which support the theory that these were the first two attacks of neuromyelitis optica, making this the first detailed case report of positive neuromyelitis antibody in a child.

The course of neuromyelitis optica in adults may be monophasic; however, in over 90% of cases, as here, it is relapsing [5]. The prognosis for neuromyelitis optica in adults is variable, but compared with multiple sclerosis, leads to more severe neurologic impairment [2]; this outcome is particularly true for patients with relapsing disease [5]. Neuromyelitis optica has been reported in children [7,8], and, based on a small review of patients diagnosed after a viral syndrome, they may have a more favorable prognosis [8]. These patients may have had a monophasic illness consistent with acute disseminated encephalomyelitis. Distinguishing neuromyelitis optica from routine transverse myelitis or acute disseminated encephalomyelitis with autoantibody testing may allow for early surveillance of neurologic recurrence and initiation of more aggressive immunosuppressive therapy.

A nonrandomized, prospective trial supports the use of intravenous methylprednisolone for acute management of relapses, but there is little consensus on long-term treatment options designed to delay or reduce the severity of relapses [9]. Some agents which have been reported to have efficacy include azathioprine, prednisone, and intravenous immunoglobulin. As neuromyelitis optica appears to be caused by an antibody that binds to the aquaporin-4 water channel [10], treatment with rituximab, which binds to the CD20 protein on B lymphocytes, may be the most logical approach [11].

Some have suggested revision of neuromyelitis optica diagnostic criteria to include antibody testing [6] and, in this case, antibody testing did help with early diagnosis and appropriate treatment. The present report suggests that neuromyelitis optica antibody testing may be useful in cases of pediatric transverse myelitis with long spinal cord lesions.

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Figure 1.

A sagittal cervical magnetic resonance imaging (TR/TE = 3510/109 ms) demonstrates increased T₂ signal and swelling extending from the cervicomedullary junction down to C₇.