Devic Disease With Brainstem Lesions

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We describe a patient who suffered from an unusually severe form of neuromyelitis optica with a hyperacute time-course evolution requiring mechanical ventilation within 3 days. The patient died after 72 days and autopsy showed major spinal cord, optic nerve, and brainstem necrosis, and multifocal necrotic lesions on the cerebellum and cerebral white matter.

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Devic disease or neuromyelitis optica (NMO) is characterized by the association of an acute or subacute demyelinating myelitis and unilateral or bilateral optic neuritis.1 This uncommon syndrome is sometimes considered a particular form of multiple sclerosis, especially in East Asia.2 Devic disease may have a stepwise progression during several years leading to severe disability. Immunosuppressive treatments remain ineffective and the prognosis is usually poor. By definition, NMO spares the brainstem from degeneration.1 However, our patient demonstrates that brainstem involvement and hyperacute course may occur in this potentially devastating disease.

REPORT OF A CASE

A 45-year-old man presented to the emergency department on November 2003, for febrile acute urinary retention for 24 hours. His medical history was relevant for pulmonary tuberculosis and active alcohol and tobacco consumption.

On day 2, he experienced a meningeal syndrome and paraparesia, which rapidly progressed to tetraplegia and coma. On examination, there was a flaccid motor deficit and areflexia of the 4 limbs, abolition of brainstem reflexes (corneal and oculomotor), and bouts of hypotension and bradycardia. On day 3, mechanical ventilation was required. A cerebrospinal fluid (CSF) tap revealed 18 leukocytes/mm³ (89% lymphocytes and 11% polymorphonuclear leucocytes), 350 red blood cells/mm³, and total protein level of 2.4 g/L with normal IgG index and normal glucose levels. Brain and spinal cord computed tomographic scans and spinal cord magnetic resonance images (MRI) showed no abnormalities. The cerebral MRI showed a signal hyperintensity in fluid-attenuated inversion recovery weighted images in the corpus callosum, attributed to alcohol intoxication. An electroencephalogram showed diffuse slow waves and somatosensory evoked potentials were abolished. Electrophysiological study of peripheral nerves showed axonal changes consistent with critical illness polyneuropathy confirmed by a neuromuscular biopsy.

Empirical therapy with acyclovir, amoxicillin, antituberculous drugs, and corticosteroids (prednisolone, 1 mg/kg per day) was initiated on day 2.

On day 7, neurologic status was unchanged. A new CSF tap showed increased pleocytosis (660 leukocytes/mm³, 88% lymphocytes; 21 100 red blood cells/mm³; total protein level, 2.35 g/L; glucose level, 1.7 mmol/L [31 mg/dL]). Subsequent CSF examination results showed progressive normalization. No abnormalities were seen on a second brain MRI performed on day 11.

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Dysautonomic disorders had worsened since day 14, which necessitated intravenous norepinephrine infusion, while the neurologic status remained unchanged. The following diagnostic test results remained negative: CSF cultures for common pathogens and mycobacteria, serologic testing for human immunodeficiency virus type 1 and 2, human T-lymphotrophic virus type 1 and 2, cytomegalovirus, herpes simplex viruses 1 and 2, human herpes virus 6, influenza A and B viruses, human adenovirus, enterovirus, Coxsackie B virus, West Nile virus, flavivirus, poliomyelitis virus, tetanus, diphtheria, mycoplasma Streptococcus pneumoniae, Campylobacter jejuni, syphilis, Rickettsia rickettsii, leptospirosis, Histoplasma capsulatum, and screening for rabies virus on saliva, urine, blood, and CSF by polymerase chain reaction. Antinuclear antibodies, anti-DNA antibodies, antineutrophil cytoplasmic antibodies, antiganglioside antibodies, rheumatoid factor, and anti-Hu antibodies were not detected. Blood concentration levels of thyroid-stimulating hormone, cortisol, acute intermittent porphyric metabolism, arsenic, and lead were normal or negative.

A brain MRI on day 67 showed a major brainstem atrophy, a linear hyperintensity of the optic nerves, scattered T2-weighted signal hyperintensities in the left and right temporal white matter, and a diffuse periventricular leukoapthy (Figure 1).

The combined anti-infective and steroid therapy was discontinued on day 48 because of the absence of clinical improvement. Intravenous immunoglobulin infusion (0.5 g/kg per day) was performed from day 7 to day 11 without efficacy. The patient died 72 days after admission.

Gross examination of the central nervous system revealed major necrosis of the whole spinal cord, which was reduced to a gelatinous grayish matter with no macroscopic lesion on the roots. This necrosis had also formed cavitations in the optic chiasma, the brainstem, and cerebellar white matter, but sparing the dentate nucleus. Focal demyelination of the temporal cerebral white matter was also observed.

Microscopic examination of the white matter showed loss of myelin with severe destruction and sparing few axon cylinders associated with axonal swellings. In the most injured areas, nervous tissue was replaced by countless macrophage infiltrations. In the relatively spared areas, demyelination occurred in a perivascular distribution and was associated with an astrocytic reaction with infiltration of mononuclear cells and lymphocytes forming perivascular cuffs. Bodian silver impregnation in the temporal white matter was consistent with severe demyelination and axonal damage (Figure 2). Immunohistochemistry confirmed the macrophage (using anti-CD68 antibodies) and CD8+ T lymphocytic infiltration (using anti-CD8 antibodies) and the reactive gliosis (using anti–glial fibrillary acidic protein antibodies). All these pathologic findings suggested Devic disease (neuromyelitis optica).

COMMENT

Our patient had a hyperacute myelitis associated with brainstem involvement and bilateral optic neuritis. Pathologic findings showed spinal cord, optic chiasma, and brainstem necrosis that was consistent with a severe demyelinating process and Devic disease. First described in 1894, NMO combines acute or subacute transverse myelitis and optic neuropathy that may occur at the same moment or separated by a variable period of time.1 Although pathologic features of our patient were characteristic of Devic disease, the clinical presentation, disease course, distribution of lesions, and severity of pathologic findings warranted further discussion.

Clinical presentation in this case was atypical with a coma and cranial nerve involvement secondary to an early
and severe brainstem involvement, which differs from the usual presentation of unilateral or bilateral vision loss and/or lower limb weakness. Moreover, the course of the disease was monophasic and hyperacute (disability peaked within 72 hours after onset of symptoms). Devic disease usually has a relapsing time-course evolution during 3 to 4 years, with incomplete regression of deficits between relapses. To our knowledge, such a hyperacute course is exceptional and has only been described twice. The first patient presented with an acute paraplegia with concomitant bilateral visual loss and died within 3 days of acute bulbar phenomena. The second patient initially experienced an isolated decrease of visual acuity and died within 7 days.

Commonly used diagnostic criteria of NMO exclude involvement of the peripheral and central nervous systems, but include the optic nerves and spinal cord. In our patient, clinical and pathologic examinations showed brainstem damage. In a clinicopathologic review of 22 cases of Devic disease, brainstem involvement was reported in 5 patients (23%). Death occurred in these 5 patients within 2.5 to 24 months (median, 4.5 months); the 17 other patients died within 3 days to 11 years (median, 4 months). Lesions described in the brainstem (demyelination, inflammation, or necrosis) were considered “a few to some,” inconsistently associated, and less severe in the brainstem than in the spinal cord. Although characteristic of the disease, pathologic findings in our patient were strikingly unusual because of their severity and extension. A major criteria for diagnosing Devic disease is an initial cerebral MRI, unlike what is recommended in acute disseminated encephalomyelitis. Initial brain and spinal cord MRIs taken of our patient did not show any demyelinating abnormalities except corpus callosum transient edema. Secondary multifocal demyelinating changes (Figure 1) were also consistent with previously described brain white matter MRI signal abnormalities in the course of NMO. To our knowledge, we report the first observation of brainstem necrosis on MRI in Devic disease (Figure 1).

Devic disease has a poor prognosis with severe neurologic impairment and a 5-year mortality rate near 30%. The various treatment options proposed have been disappointing both for acute episodes and for long-term prognosis. Recently, encouraging results have been reported with plasma exchange, intravenous immunoglobulins, and the monoclonal antibody rituximab. Taking into account the poor prognosis of the disease and the possibility of a hyperacute course, physicians should be alerted to this rare presentation and incited to start therapeutic treatment as soon as possible.

This observation emphasizes the fact that brainstem involvement is present in Devic disease, especially in the most severe cases.

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