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RECURRENT NEUROMYELITIS OPTICA WITH DIFFUSE CENTRAL NERVOUS SYSTEM INVOLVEMENT

Case report

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ABSTRACT - Several demyelinating disorders can affect children. The differential diagnosis between these diseases is usually an arduous task. Diagnostic criteria have been proposed for some of these disorders, however most of them have not yet been clinically and prospectively validated. Here we present a case of a ten year-old boy with recurrent bilateral optic neuritis and spinal cord involvement. Clinical and cerebrospinal fluid data have fulfilled diagnostic criteria for Devic´s neuromyelitis optica (NMO). The differential diagnosis with multiple sclerosis (MS) has become troublesome since not only optic nerves and spinal cord were involved. In one of the relapses a left hemiparesis with facial involvement was registered. Magnetic resonance imaging was also compatible with MS. This case illustrates that CNS demyelinating disorders can fulfill diagnostic criteria for more than one demyelinating disease, making the clinical judgment an important tool in the management of these patients.

KEY WORDS: neuromyelitis optica, Devic´s disease, multiple sclerosis.

Neuromielite óptica recorrente com envolvimento difuso do sistema nervoso central: relato de caso

RESUMO - Diversas doenças desmielinizantes podem ocorrer em crianças, sendo muitas vezes o diagnóstico diferencial entre elas difícil. Critérios diagnósticos têm sido propostos para algumas destas entidades, entretanto nenhum deles pode ser considerado definitivo. O objetivo deste trabalho é apresentar o caso de um paciente de 10 anos de idade, com quadro recorrente de neurite óptica bilateral e mielopatia. Os dados clínicos e liquóricos preencheram critérios para o diagnóstico de neuromielite óptica de Devic. O diagnóstico diferencial foi especialmente difícil em relação à esclerose múltipla, pois não apenas os nervos ópticos e medula foram acometidos, visto que em um dos surtos registrou-se hemiparesia, com acometimento facial. A ressonância magnética foi também compatível com esclerose múltipla. Este caso ilustra que pacientes com doenças desmielinizantes do SNC podem preencher critérios diagnósticos para mais de uma delas, o que torna o julgamento clínico uma ferramenta ainda importante na abordagem e condução clínica destes casos.

PALAVRAS-CHAVE: neuromielite óptica, doença de Devic, esclerose múltipla.

Neuromyelitis optica (NMO) (Devic´s syndrome) is an association of optic neuritis with myelitis. The neuropathological features and the clinical evolution of NMO suggest that this is a distinct disease. Several other diseases such as multiple sclerosis (MS), collagen diseases, and infections can present with myelitis and optic neuritis[1]. As the result of the difficult distinction between NMO and other diseases sharing the same clinical features some diagnostic criteria have been proposed, however, none of them have been prospectively validated so far[1,2]. The evolution of NMO can be monophasic or recurrent. The prognosis is usually worse than in MS. The relapses can be confined in the optic nerve or spinal cord, however, they can be found in different areas of central nervous system (CNS)[2]. In such cases the differential diagnosis with MS can become more troublesome because clinical diagnostic criteria for MS and NMO may be superposed.

Here we report the clinical and diagnostic features of a patient with recurrent NMO who fulfilled diagnostic criteria for both MS and NMO.

CASE

A ten year-old boy has presented with acute bilateral visual loss, gait abnormality, and urinary retention. No recent histories of fever,

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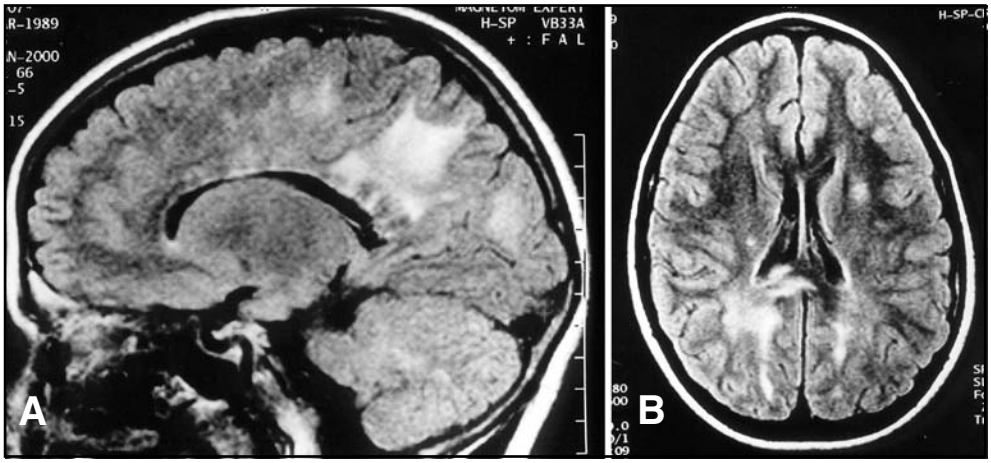

Fig 1A. Sagittal Fast-FLAIR MRI scan shows multiple hyperintense lesions, some of them coalescent, in the periventricular white matter extending to the pericallosum region, with minimal mass effect. B. Axial Fast-FLAIR brain images shows several hyperintense white matter lesions, in the corona radiata and corpus callosum splenium.

respiratory symptoms, or diarrhea have been reported. The patient had no previous history of neurological disorders, and had received regular immunizations against B hepatitis, tuberculosis, tetanus, diphtheria, pertussis, measles, mumps, rubella, and poliomyelitis.

One week after symptoms have begun he was brought to our attention. No abnormalities were found on general examination. The patient was fully oriented. He had no problems with fluency, comprehension, and repetition. Visual acuity was severely affected on both sides. Fundoscopic examination disclosed bilateral optic atrophy. He had full extraocular movements. Facial sensation and musculature were intact. Swallowing was normal. Arms strength and tone were normal, but there was a severe weakness of his legs (+++/4+), with spasticity. Babinski sign was present bilaterally. Sensory examination revealed spinal cord level at T4.

A brain magnetic resonance imaging (MRI) has shown more than nine T2-hyperintense lesions, most of them in periventricular white matter, but also with juxtacortical and pericallosum region involvement (Figs 1A e 1B). Neither gadolinuim-enhancing nor infratentorial lesions were seen. Spinal MRI has shown multiple hyperintense T2 lesions in the upper cervical region, predominating in the dorsal region. A large T2 hyperintense lesion with mild mass effect was seen extending from the low cervical level through the conus medularis (Fig 2) There was not gadoliunium enhancement in spinal cord lesions.

Cerebrospinal fluid (CSF) analysis has revealed pleocytosis (165 cells/mm^3), with polymorphonuclear predominance (65%), protein and glucose concentration were 165 and 63 mg⁄dl, respectively. No oligoclonal bands were found by agarose gel electrophoresis or isoleletric focusing. Antinuclear antibodies, anti-SSA, anti-SSB, hepatitis B surface antigen, hepatitis C antibodies, p-ANCA, anticardiolipin antibodies were all negative. IgM antibodies against HSV, VZV, CMV, and EBV were not found. Complement levels were within normal values.

The hypothesis of NMO, acute disseminated encephalomyelitis (ADEM), or MS were initially raised and high doses of methylprednisolone (500 mg a day for five days) followed by ciclophosphamide (500 mg, once) were given. After a few days a complete recovery of spinal signs and partial visual recovery were seen. About a month later a new attack was registered with isolated visual involvement. Methylprednosolone was given again, and the patient was maintained with prednisone 40 mg a day with further reduction of prednisone and azathiprine introduction (2-3 mg/Kg/day). Visual acuity at this

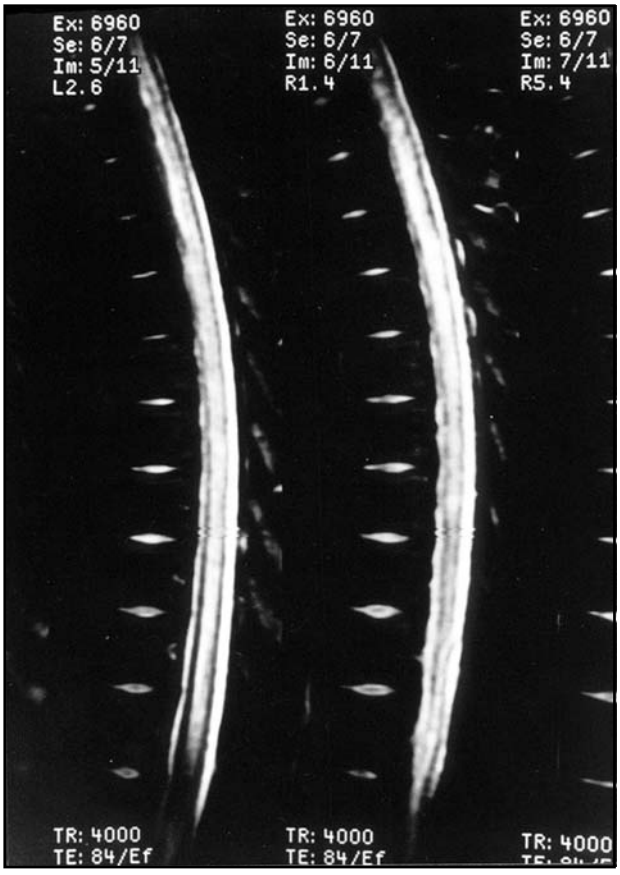

Fig 2. Fast Spin Echo Heavy T_2-Weighted sequence shows an extensive hyperintense lesion involving the spinal cord from the low cervical level (not shown) to the conus with mild mass effect.

time was 20/40 at left and he was able to count fingers at 30 cm of distance with his right eye. Three months later a new attack was registered. At this time a left hemiparesis was registered. Methylprednosolone (1000 mg a day for three days) and intravenous immunoglobulin (IVIG, 0.4 g/day for five days) were given. A complete recovery was seen except for the visual acuity deficit. Prednisone (40 mg a day) and azathiprine (2-3 mg/Kg/day) were maintained. Several months later there was a new relapse after an attempt to reduce prednisone. Paraparesis plus bilateral optic worsening were registered. This new attack was treated again with methylprednisolone plus IVIG. The preventive schedule was altered and presently the patient is using subcutaneous glatiramer acetate 20 mg a day, mitoxantrone, 5 mg/m^2, every three months, and oral prednisone 20 mg/day. Since this schedule was introduced no other attack has been registered. Blood cell counts have been ordered monthly and echocardiography has been performed every three months, in order to assess mitoxantrone side effects.

DISCUSSION

Diagnostic criteria for NMO have been recently proposed by Wingerchuck and col.[2]. According to such criteria, diagnosis requires three absolute criteria: 1) optic neuritis, 2) acute myelitis, and 3) no evidence of clinical disease outside the optic nerve or spinal cord; as well as at least one of the following major supportive criteria: 1) negative brain MRI at onset, 2) spinal cord MRI with signal abnormality extending over 3 vertebral segments, 3) CSF pleocytosis of >50 WBC/mm^3 or >5neutrophils/ mm^3, or two of the following minor supportive criteria: 1) bilateral optic neuritis, 2) severe optic neuritis, 3) severe, fixed, attack-related weakness in one or more limbs.

Our patient has initially presented with optic neuritis, myelitis, had pleocytosis with polymorphonuclear predominance, and MRI spinal cord abnormalities. Three absolute criteria, two major supportive criteria, and three minor supportive criteria were present. Laboratory tests have excluded other diseases, such as collagen and vascular diseases, auto-antibodies syndromes, and infections. Therefore, the signs and symptoms initially displayed by our patient are consistent with the diagnosis of NMO according to Wingerchuck's and col. criteria.

The possibility of other demyelinating CNS diseases were also raised. ADEM usually follows an infection or a vaccine. There were no histories of both. Also, ADEM is usually monophasic and our patient had a multiphasic disease. Although recurrent ADEM can occur, the recurrences are usually registered in the first six months and our patient had new attacks through the first 18 months of disease[3,4]. Diffuse sclerosis was ruled out since this is a rapidly progressive disease with white matter lesions with mass effect[4,5].

The differential diagnosis with MS is more difficult in this case. MS can be found in children and usually presents with attacks reflecting white matter involvement[6-8]. Only after years of disease a secondary progressive stage is usually seen. Some patients have a primary progressive disease but a relapsing-remitting course is the rule. MRI criteria for MS diagnosis require three of the following: 1) one gadolinium-enhancing or nine T2 hyperintense lesions, 2) one infratentorial lesion, 3) at least one jutacortical lesion, and 4) at least three periventricular lesions[9]. Recommended diagnostic criteria for MS were recently proposed by McDonald and col[10]. According to these criteria, if there are two attacks compatible with MS, documented by objective evidence of two lesions separated in time and necessarily separated in space may be sufficient to make an MS diagnosis solely on clinical grounds. Our patient had objective evidence of more than two lesions separated in space, such as optic neuritis, spinal cord lesion, and left hemiparesis. MRI findings were compatible with Barkhof and col. criteria, since there were more than nine T2 enhancing lesions, being more than three periventricular, and at least one juxtacortical lesion.

NMO can have a more diffuse brain involvement and relapsing course. In the series of Wingerchuck and col. there were five patients with recurrences not confined to optic nerves or spinal cord. Two of them had facial numbness, two had vertigo, and one had cerebellar tremor. These authors have performed MRI studies in 28 patients with NMO. Brain parenchyma was normal in 22, but three (11%) have satisfied the criteria for MS diagnosis.

Our case points to the difficult differential diagnosis of recurrent demyelinating CNS diseases. Clinical criteria have provided a more uniform clinical approach to these patients[11]. However, they still require future refinements because some overlapping can still occur. It is possible that more overlapping situations can presently be documented because McDonald's and cols. criteria are more sensitive than Poser's criteria. In McDonald's and col. criteria it is stressed that there should be no better explanation than MS for the clinical picture to define MS diagnosis[10]. In our patient we believe that NMO is a better explanation for the whole clinical picture than MS. This conclusion was strongly based on clinical judgment since clinical criteria for both NMO and MS were fulfilled.

The diagnostic problems can have therapeutic implications. NMO is a distinct disease with more severe prognosis than MS. There are few studies addressing NMO treatment. The combination of prednisone and azathioprine have reduced the attacks frequency in an uncontrolled series[12,13]. Plasma exchange has been tried with good results. Interferons and immunossupressive drugs efficacy have not yet been proved to be effective in preventing new attacks. Our patient has not presented new recurrences since glatiramer acetate and mitoxantrone have been introduced. Because NMO patients can improve spontaneously this may be just a coincidence, however, future trials should address the role of such drugs in NMO

treatment.

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