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 neuritis⁴. As a 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 far¹,². 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,
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 pericallosal region involvement (Figs 1A e 1B). Neither gadolinium-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 gadolinium enhancement in spinal cord lesions.

Cerebrospinal fluid (CSF) analysis has revealed pleocytosis (165 cells/mm³), 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 isoelectric 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 cyclophosphamide (500 mg, once) were given. After a few days a complete recovery of spinal signs and partial visual recovery were seen. About a month la-

![Fig 1A. Sagittal Fast-FLAIR MRI scan shows multiple hyperintense lesions, some of them coalescent, in the periventricular white matter extending to the pericallosal 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.](image1)

![Fig 2. Fast Spin Echo Heavy T2-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.](image2)
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 reg-
istered. At this time a left hemiparesis was registered. M ethylprednisolone (1000 mg a day for three days) and intravenous
immunoglobulin (IVIG, 0.4 g/day for five days) were given. A com-
plete recovery was seen except for the visual acuity deficit. Prednisone
(40 mg a day) and azathioprine (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 methylpred-
nisolone plus IVIG. The preventive schedule was altered and present-
ly the patient is using subcutaneous glatiramer acetate 20 mg a day,
mitoxantrone, 5 mg/m², 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 ecocar-
diography has been performed every three months, in order to assess
mitoxantrone side effects.

DISCUSSION

Diagnostic criteria for NM O have been recently proposed
by Wingerchuck and col.2. According to such criteria, diagno-
sis 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 ver-
tebra1 segments, 3) CSF pleocytosis of >50 WBC/mm³ or
>5 neutrophils/ mm³, or two of the following minor support-
ive 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 cri-
teria, two major supportive criteria, and three minor support-
ive criteria were present. Laboratory tests have excluded oth-
er diseases, such as collagen and vascular diseases, auto-anti-
bodies syndromes, and infections. Therefore, the signs and
symptoms initially displayed by our patient are consistent
with the diagnosis of NM O 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 monopha-
ic and our patient had a multiphasic disease. Although recur-
rent 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.4-5. Diffuse sclerosis was ruled
out since this is a rapidly progressive disease with white mat-
ter lesions with mass effect4-5. The differential diagnosis with MS is more difficult in this
instance. MS can be found in children and usually presents with
attacks reflecting white matter involvement6-8. 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 juxtacortical lesion, and 4) at least three periven-
tricular lesions9. Recommended diagnostic criteria for MS
were recently proposed by M cDonald and col10. According to
these criteria, if there are two attacks compatible with MS, doc-
umented 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 hemi-
paresis. 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 juxta-
cortical lesion.

NM O 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 ver-
tigo, and one had cerebellar tremor. These authors have per-
formed MRI studies in 28 patients with NM O. Brain parenchy-
ma was normal in 22, but three (11%) have satisfied the cri-
teria for MS diagnosis.

Our case points to the difficult differential diagnosis of recur-
rent demyelinating CNS diseases. Clinical criteria have provid-
ed a more uniform clinical approach to these patients11.
However, they still require future refinements because some
overlapping can still occur. It is possible that more overlap-
ning situations can presently be documented because
M cDonald’s and cols. criteria are more sensitive than Poser’s
criteria. In M cDonald’s and col. criteria it is stressed that there
should be no better explanation than MS for the clinical pic-
ture to define MS diagnosis12. In our patient we believe that
NM O is a better explanation for the whole clinical picture than
MS. This conclusion was strongly based on clinical judgment
since clinical criteria for both NM O and MS were fulfilled.

The diagnostic problems can have therapeutic implica-
tions. NM O is a distinct disease with more severe prognosis
than MS. There are few studies addressing NM O treatment.
The combination of prednisone and azathioprine have reduced
the attacks frequency in an uncontrolled series12,13. Plasma
exchange has been tried with good results. Interferons and
immunosuppressive drugs efficacy have not yet been proved
to be effective in preventing new attacks. Our patient has not
presented new recurrences since g latiram er acetate and
mitoxantrone have been introduced. Because NM O patients
can improve spontaneously this may be just a coincidence, how-
ever, future trials should address the role of such drugs in NM O.
treatment.

REFERENCE