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Case report

Devic's disease in an adolescent girl with juvenile dermatomyositis



Neuromielite óptica em uma adolescente com dermatomiosite juvenil

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Introduction

Devic's disease, also known as neuromyelitis optica, is classified as an autoimmune inflammatory demyelinating disorder of the central nervous system, distinct from multiple sclerosis, that mainly affects the optic nerve and spinal cord.¹ Devic's disease was demonstrated to be the result of antibodies against the water channel aquaporin-4 in the blood-brain barrier.²

There have been reports of Devic's disease in infancy,^{3,4} but there are few reported associations of Devic's disease with other diseases. The association of Devic's disease with dermatomyositis has not yet been described in the literature.

Case report

A female patient sought our service at 7 years of age, presenting with bipalpebral edema with ocular hyperemia over the previous 4 months. She also presented edema of the hands and feet; pain in the wrists, elbows and knees; and muscular weakness. She also had, on that occasion, an intermittent fever lasting 15 days.

The physical exam revealed heliotrope, Gottron's sign, arthritis in the left knee and ankle, and muscular weakness in the upper and lower limbs (childhood myositis assessment score of 14/52).⁵

General exams were performed with the following results: hemoglobin of 10.4 g/dl, 4400 leucocytes with a normal

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differential, erythrocyte sedimentation rate of 70 mm in the first hour, and an increase in muscular enzymes (aspartate alanine transferase 712 [normal value 10 up to 35], creatine kinase 187 [normal value 10 up to 155] and lactate dehydrogenase 1150 [normal value 240 up to 480]).

Assays for antinuclear antibodies, anti-DNA antibodies, anti-ENA (extractable nuclear antigens) antibodies and anti-cardiolipin antibodies were negative, and the complement level was normal. A muscle biopsy showed perifascicular atrophy typical of dermatomyositis. The videodeglutogram was normal, and a nailfold capillaroscopy demonstrated a scleroderma pattern with significant capillary deletion and ectasia. A diagnosis of juvenile dermatomyositis was made.⁶

Over two years, the patient received 11 pulse therapies of methylprednisolone, prednisone and methotrexate until clinical and laboratory control of the dermatomyositis was achieved. The patient abandoned treatment for 4 years, then she returned to the pediatric rheumatology clinic four years ago, at age of 13, with no clinical (childhood myositis assessment score 41/52)⁵ nor laboratory evidence of juvenile dermatomyositis activity and no medication was needed.

Two years ago, at age of 15, the patient had numbness in the left arm without muscular weakness that lasted for 10 days and resolved spontaneously. After two months, the patient developed paresthesia with proximal and distal muscular weakness in all four limbs, and difficulty in walking and carrying out daily activities. The neurologist ordered a brain computerized tomography that was normal and no medication was prescribed. The patient lost the follow up again and after nine months of these initial symptoms, the patient had an episode of blurred vision and distal weakness in all four limbs.

The neurological examination revealed hyperactive deep tendon reflexes in right upper limb and legs, without weakness, and a severe loss of vision in the right eye (VA 20/800) with fundus examination showing optic disk atrophy. The expanded disability status scale (EDSS)⁷ that quantifies disability in eight functional systems (pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral and others) was 4 from a scale of 0 to 10.

Laboratory tests including cerebrospinal fluid analysis showed no abnormalities. A neurological consultation suggested central nervous system demyelination, and the neuraxis magnetic resonance image showed a long intraspinal lesion from C3 to T4 (Figs. 1 and 2). A proposed diagnosis of Devic's disease (neuromyelitis optica) was made. The positive test for anti-aquaporin 4 antibody confirmed the diagnosis. The patient was started immediately on pulse therapy with methylprednisolone followed by azathioprine plus prednisone as maintenance therapy.

The patient remained stable for eight months with the initial therapeutic regimen. A year ago, the patient presented a new outbreak of severe optic neuritis without muscular weakness but with impaired urinary sphincter function. Cerebrospinal fluid analysis and brain magnetic resonance imaging were repeated. She was treated with intravenous immunoglobulin. Pulse therapy with methylprednisolone and the use of prednisone 0.1 mg/kg/day and azathioprine 3 mg/kg/day were maintained for four years up to now. After



Fig. 1 – Sagittal magnetic resonance image. T2-weighted cervical spinal cord showing a long hyperintense spinal cord lesion (black arrow) in an adolescent girl with juvenile dermatomyositis.

immunoglobulin treatment, the patient's urinary and visual symptoms improved.

The patient has been in remission for juvenile dermatomyositis activity for the last four years but still with activity of the neuromyelitis optica.

Discussion

Recurrent neuromyelitis optica is typically characterized by visual and spinal cord relapses. Clinical and laboratory neuroimaging data and the immunopathology suggest that neuromyelitis optica differs from multiple sclerosis and presents a poorer prognosis, making early diagnosis of paramount importance for the initiation of aggressive immunosuppressive therapy.⁸

New diagnostic criteria have been proposed by Wingerchuk et al., and these include optic neuritis, acute myelitis,

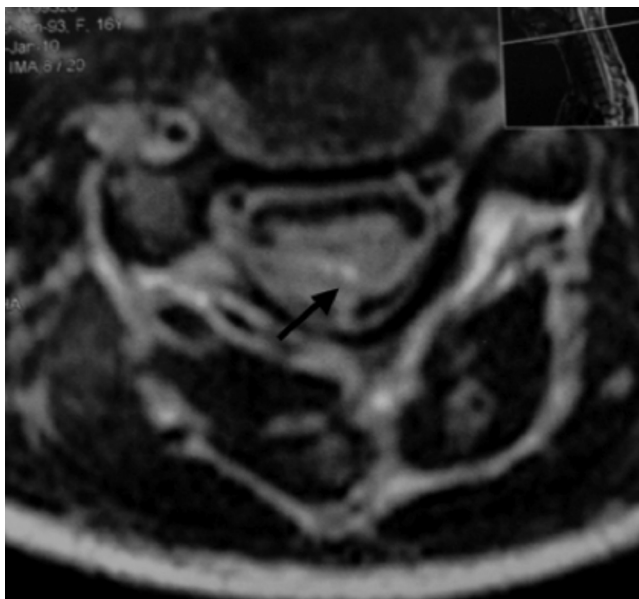


Fig. 2 – Axial magnetic resonance image of the cervical spine (C3) showing a long hyperintense spinal cord lesion (black arrow) in an adolescent girl with juvenile dermatomyositis.

and at least 2 of the 3 following criteria: lesions in the spinal cord spanning at least three segments on magnetic resonance images, brain magnetic resonance images incompatible with multiple sclerosis and a positive neuromyelitis optica IgG test (serum marker: auto-antibody directed against aquaporin-4).⁹

Anti-aquaporin 4 is an autoantibody (IgG) targeted against the water channels of the blood–brain barrier, and the SNC lesion distribution corresponds to the areas where there is a high concentration of such channels. Therefore, anti-aquaporin-4 may be considered a biomarker for neuromyelitis optica, although the extent of the correlation between the titer of the antibody and the relapse severity is not clear.⁹

Luccinetti et al. demonstrated the deposition of complement and perivascular IgM and the presence of an intense inflammatory infiltrate composed predominantly of macrophages, granulocytes and eosinophils in demyelinating lesions in neuromyelitis optica autopsy cases, confirming the importance of humoral immunity in the pathophysiology of neuromyelitis optica.¹⁰

In a retrospective study covering a 15-year period, Jeffery et al. evaluated nine children with neuromyelitis optica. All children had had a viral infection prior to neuromyelitis optica symptoms. Bilateral optic neuritis was a common finding, observed in 89% of children, and all children exhibited a monophasic course.³ However, antibody-positive Devic's disease is not typically associated with a monophasic illness but does display a very rapid progressive course.

Our patient presented the clinical characteristics described above, magnetic resonance imaging abnormalities and the presence of antibody anti-aquaporin-4. She has the recurrent form of the disease and already has irreversible visual impairment.

Neuromyelitis optica findings may appear in patients with other autoimmune, inflammatory and infectious diseases with some reports in adults and children.¹¹ Although the authors do not suggest a possible explanation for these associations, infectious agents can trigger the autoimmune process.

There is no consensus on the treatment of recurrent neuromyelitis optica. Several alternatives have been reported. Relapses are treated with oral prednisone, methylprednisolone, intravenous immunoglobulin and plasmapheresis.¹² Maintenance therapy involves monthly intravenous immunoglobulin¹³ and rituximab.¹⁴ Recently, two studies showed that treatment with azathioprine plus prednisone or mofetil mycophenolate halts disease progression.^{12,15}

After the first outbreak, this patient received pulse therapy with methylprednisolone and maintenance with prednisone and azathioprine. After the second outbreak, the use of methylprednisolone pulse therapy with monthly intravenous immunoglobulin, in addition to maintaining prednisone and azathioprine, was preferred.

Conclusion

The onset of atypical neurological symptoms during the course of a rheumatic disease should call attention to the possibility of an association with this autoimmune disease. In the case presented herein, the appearance of unusual visual and motor symptoms in a patient with juvenile dermatomyositis readily led to clinical suspicion, and laboratory tests confirmed the associated neurological disease.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Jacob A, Matiello M, Wingerchuk DM, Lucchinetti CF, Pittock SJ, Weinschenker BG. Neuromyelitis optica: changing concepts. *J Neuroimmunol.* 2007;187:126–38.
- Hino-Fukuyo N, Takahashi T, Haginoya K, Uematsu M, Tsuchiya S. Clinical features of Japanese pediatric patients with anti-aquaporin 4 antibody. *No To Hattatsu.* 2011;43:359–65.
- Jeffery AR, Buncie JR. Pediatric Devic's neuromyelitis optica. *J Pediatr Ophthalmol Strabismus.* 1996;33:223–9.
- Gokce G, Ceylan OM, Mutlu FM, Altinsoy HI, Koçlu T. Relapsing Devic's disease in a child. *J Pediatr Neurosci.* 2013;8:146–9.
- Lovell DJ, Lindsley CB, Rennebohm RM, Ballinger SH, Bowyer SL, Giannini EH, et al. Development of validated disease activity and damage indices for the juvenile idiopathic inflammatory myopathies. II. The Childhood Myositis Assessment Scale (CMAS): a quantitative tool for the evaluation of muscle function. *The Juvenile Dermatomyositis Disease Activity Collaborative Study Group. Arthritis Rheum.* 1999;42:2213–9.
- Bohan A, Peter JB. Polymyositis and dermatomyositis (two parts). *N Engl J Med.* 1975;292:344–7, 403–7.

7. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology*. 1983;33:1444-52.
8. O'Riordan JI, Gallagher HL, Thompson AJ, Howard RS, Kingsley DP, Thompson EJ, et al. Clinical and MRI findings in Devic's neuromyelitis optica. *J Neurol Neurosurg Psychiatry*. 1996;60:382-7.
9. Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitis optica. *Neurology*. 2006;66:1485-9.
10. Lucchinetti CF, Mandler RN, Mc Gavern D. A role for humoral mechanisms in the pathogenesis of Devic's neuromyelitis optica. *Brain*. 2002;125:1450-61.
11. Bichuetti DB, Oliveira EML, Souza NA, Rivero RL, Gabbai AA. Neuromyelitis optica in Brazil: a study on clinical and prognostic factors. *Mult Scler*. 2009;15:613-9.
12. Bichuetti DB, Oliveira EML, Oliveira DM, Amorin de Souza N, Gabbai AA. Neuromyelitis optica treatment. Analysis of 36 patients. *Arch Neurol*. 2010;67:1131-6.
13. Bakker J, Metz L. Devic's neuromyelitis optica treated with intravenous gammaglobulin (IVIg). *Can J Neurol Sci*. 2004;31:265-7.
14. Beres SJ, Graves J, Waubant E. Rituximab use in pediatric central demyelinating disease. *Pediatr Neurol*. 2014;51:114-8.
15. Falcini F, Trepani S, Ricci L, Simoncini G, De Martino M. Sustained improvement of a girl affected with Devic's disease over 2 years of mycophenolate mofetil treatment. *Rheumatology (Oxf)*. 2006;45:913-5.