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Case report

Optic neuritis in juvenile idiopathic arthritis patient

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ABSTRACT

Optic neuritis (ON) was rarely reported in juvenile idiopathic arthritis (JIA) patients, particularly in those under anti-tumor necrosis factor alpha blockage. However, to our knowledge, the prevalence of ON in JIA population has not been studied. Therefore, 5793 patients were followed up at our University Hospital and 630 (11%) had JIA. One patient (0.15%) had ON and was reported herein. A 6-year-old male was diagnosed with extended oligoarticular JIA, and received naproxen and methotrexate subsequently replaced by leflunomide. At 11 years old, he was diagnosed with aseptic meningitis, followed by a partial motor seizure with secondary generalization. Brain magnetic resonance imaging (MRI) and electroencephalogram showed diffuse disorganization of the brain electric activity and leflunomide was suspended. Seven days later, the patient presented acute ocular pain, loss of acuity for color, blurred vision, photophobia, redness and short progressive visual loss in the right eye. A fundoscopic exam detected unilateral papilledema without retinal exudates. Orbital MRI suggested right ON. The anti-aquaporin 4 (anti-AQP4) antibody was negative. Pulse therapy with methylprednisolone was administered for five days, and subsequently with prednisone, he had clinical and laboratory improvement. In conclusion, a low prevalence of ON was observed in our JIA population. The absence of anti-AQP4 antibody and the normal brain MRI do not exclude the possibility of demyelinating disease associated with chronic arthritis. Therefore, rigorous follow up is required.

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Neurite óptica em paciente com artrite idiopática juvenil

Palavras-chave:
Neurite óptica
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Anticorpo antiaquaporina 4

RESUMO

A neurite óptica (NO) raramente é relatada em pacientes com artrite idiopática juvenil (AIJ), especialmente naqueles que utilizam tratamento com bloqueador de fator de necrose tumoral-alfa. No entanto, até onde se sabe, a prevalência de NO em pacientes com AIJ ainda não foi estudada. Acompanharam-se 5.793 pacientes no Hospital Universitário desta instituição. Destes, 630 (11%) tinham AIJ, e apenas um (0,15%) apresentava NO. O paciente com NO, de 6 anos de idade e do sexo masculino, foi diagnosticado com AIJ oligoarticular estendida. Foram introduzidos naproxeno e metotrexato, posteriormente substituídos por leflunomida. Aos 11 anos de idade, ele foi diagnosticado com meningite asséptica, seguida de convulsão motora parcial com evolução para generalização secundária. A ressonância magnética do encéfalo e o eletroencefalograma evidenciaram desorganização difusa da atividade elétrica do encéfalo. A lefluomida foi suspensa. Após 7 dias, o paciente apresentou dor ocular aguda, baixa acuidade visual para cores, visão turva, fotofobia, hiperemia e amaurose progressiva no olho direito. No exame de fundo de olho, foi detectado edema de papila unilateral sem exsudatos retinianos. A ressonância magnética de órbita sugeriu neuropatia óptica à direita. O anticorpo antiaquaporina 4 (anti-AQP4) foi negativo. O paciente foi submetido a pulsoterapia com metilprednisolona por cinco dias, seguida de prednisona, apresentando melhora clínica e laboratorial. Em suma, foi observada baixa prevalência de NO em pacientes com AIJ. A ausência do anticorpo antiaquaporina 4 e a ressonância magnética normal do encéfalo não excluem a possibilidade de doença desmielinizante associada a esta artrite crônica. Logo, é importante que seja feito um acompanhamento rigoroso.

Introduction

Optic neuritis (ON) is characterized by acute visual loss and optic nerve inflammation. The most common clinical manifestations of this disease are sudden vision loss, disturbance of color vision and periorbital, and retro-orbital pain mainly during eye movement.[1] This visual abnormality may be associated with infections, vaccinations, drugs and autoimmune diseases, particularly multiple sclerosis (MS) and neuromielitis optic (NMO).[2,3]

Of note, ON was rarely reported in juvenile idiopathic arthritis (JIA) patients, particularly in those under tumor necrosis factor alpha (TNF-α) blockage.[3–6] However, to our knowledge, the prevalence of ON in JIA population has not been studied.

Therefore, from January 1983 to July 2013, 5793 patients were followed up at the Pediatric Rheumatology Unit of the Children's Institute, Faculdade de Medicina da Universidade de São Paulo. Out of those, 630 (11%) fulfilled the International League of Associations for Rheumatism (ILAR) classification criteria for JIA.[7] Only one (0.15%) had acute visual loss due to ON during the disease course and was reported herein.

Case report

A 6-year-old male was diagnosed with extended oligoarticular JIA based on chronic arthritis of left knee with progression to the wrists and ankles. The initial laboratory exams revealed hemoglobin 12.9 g/dL, hematocrit 38.1%, white blood cell count 17,700 mm^3 (73% neutrophils, 23% lymphocytes, 0% eosinophils and 4% monocytes), platelet count 401,000 mm^3, erythrocyte sedimentation rate (ESR) 30 mm/1st, C-reactive protein (CRP) 98.4 mg/dL (normal range 5.0), rheumatoid factor and antinuclear antibody (ANA) were negative. Naproxen (20 mg/kg/day) and methotrexate (0.5 mg/kg/week) were introduced and subsequently changed for leflunomide (20 mg/day) due to gastric intolerance. At 11 years old, no arthritis or limitations were present and he had been treated with leflunomide (20 mg/day). At that moment, he presented headache and vomits without fever, followed after four days by a partial motor seizure affecting the right arm with secondary generalization. The laboratory findings showed cerebral spinal fluid (CSF): slightly muddy, 127 cells/mm^2 (32% lymphocytes, 19% monocytes, 1% plasmocytes, 43% neutrophils, 2% eosinophils, 1% basophils and 2% macrophages), red blood cells 0/mm^2, protein 61 mg/dL, glucose 58 mg/dL and adenosine deaminase 0.7 IU/l (normal range <4). ESR was 30 mm/1st hour and CRP was 10.1 mg/dL. The DNA detections by polymerase chain reaction in CSF for adenovirus, cytomegalovirus, herpes simplex type I/II, *Toxoplasma gondii*, *Mycobacterium tuberculosis* and *Treponema pallidum* were negative, as well as aerobic, anaerobic, fungus and mycobacteria CSF cultures. Brain magnetic resonance imaging (MRI) was normal and electroencephalogram showed diffuse disorganization of the brain electric activity. Therefore, aseptic meningoencephalitis was diagnosed and leflunomide was suspended. Seven days later, the patient presented acute ocular pain, low visual acuity for colors, blurred vision, photophobia and redness in the right eye, progressing to unilateral visual loss. Fundoscopic exam detected right papilledema and dry macula, without macular exudates. Orbital MRI

showed thickening and hyperintensity on T2 associated with enhancement of the intraorbital, intracanalicular and cisternal segments of the right optic nerve, strongly suggested right ON. Immunological tests showed antinuclear antibodies ANA 1:160 (fine speckled pattern), negative anti-double-stranded DNA, anti-Sm, anti-RNP, IgG and IgM anticardiolipin, anti-Ro and anti-La negatives. The serum anti-aquaporin 4 (anti-AQP4) antibody by indirect immunofluorescence was negative. Pulse therapy with methylprednisolone (1.0 g/day) was administered for five consecutive days and subsequently prednisone (60 mg/day). After a 30-day treatment with prednisone, clinical, laboratory and fundoscopic, the exams were normal. Currently, he is on corticosteroid tapering.

Discussion

ON with reversible visual loss in JIA population was infrequently described in our pediatric rheumatology service for 30 consecutive years.

Of note, this ophthalmic disease occurs most commonly in young patients[8] and without gender predominance.[9–11] The diagnosis is based on clinical features secondary to optic nerve damage,[9–11] resulting in sudden vision loss, color vision impairment and periorbital pain in eye movement. Papilledema may be observed in the fundoscopic exam in one third of patients,[1] as a result of papillitis, perineuritis or neuroretinitis. In our patient, the presence of swollen disk without macular star exudates suggests a papillitis associated with a retrobulbar neuritis. Interestingly, retrobulbar neuritis and papillitis are mainly related with MS, whereas perineuritis and neuroretinitis are more often associated with infectious or inflammatory etiologies.

The orbital MRI is not required to confirm the diagnosis. However, it is necessary to exclude other disorders, that can mimic ON, such as compressive or inflammatory orbital lesions.[12,13] Importantly, nearly 50% of the patients with isolated ON develop MS over a period of 15 years. Consequently, brain MRI should be performed to find early symptoms for demyelinating brain lesions and closely monitor the disease evolution.[12,14]

In addition, our patient had negative anti-AQP4 antibody. This autoimmune marker targeting the central nervous system has high specificity for the spectrum of NMO diagnosis.[15] However, 53% of sensitivity was detected by indirect immunofluorescence method.[16] Ten percent of seronegative patients that present recurrent ON will develop NMO within five years.[14] Therefore, the rigorous follow-up of our patient is of the utmost importance.

In JIA population, ON was rarely reported, usually associated with TNF-α inhibitors,[4] with a median of 8 months treatment.[3,6] Furthermore, this ocular abnormality was also described in adult patients with inflammatory arthritis.[17] The etiology for ON in our patient is unclear and possibly related to autoimmunity. To our knowledge, no ON case was reported under leflunomide therapy.

Intravenous methylprednisolone is an option of ON treatment, as indicated herein.[19] A recent review, including randomized trials in adult populations, evidenced similar recovery of normal visual acuity in patients treated with intravenous or oral corticosteroids.[18]

In conclusion, a low prevalence of ON was observed in our JIA population. The absence of anti-AQP4 antibody and the normal brain MRI do not exclude the possibility of demyelinating disease associated with this chronic arthritis. Therefore, rigorous follow up is required.

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Conflict of interest

The authors declare no conflict of interest.

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