

BILATERAL RECURRENT AUTOIMMUNE OPTICAL NEUROPATHY IN CHILDHOOD

NEUROPATÍA ÓPTICA AUTOINMUNE RECIDIVANTE BILATERAL EN LA INFANCIA

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ABSTRACT

Clinical case: A ten year-old girl, after a *Yersinia* gastroenteritis, developed an optic neuritis in the left eye. She was not treated and resulted ultimately in optic atrophy on the affected side. Six months later a similar episode occurred in the contralateral eye. On this occasion corticosteroid therapy was given. During this therapy the neuritis diminished; however the patient had three relapses, so it was decided to give her immunosuppressive treatment with azathioprine and continue this indefinitely.

Discussion: After considering the differential diagnoses of bilateral recurrent optical neuritis in childhood, we concluded that it was most likely to have an autoimmune basis. After considering the benefits and risks of the long-term treatment, we believe immunosuppressive therapy is most useful in controlling the disease allowing corticosteroid therapy to be reduced (*Arch Soc Esp Ophthalmol* 2006; 81: 607-610).

Key words: Autoimmune optic neuritis, post-infectious optic neuritis, bilateral optic neuritis, childhood optic neuritis, Azathioprine.

RESUMEN

Caso clínico: Niña de 10 años, que tras gastroenteritis por *Yersinia* debuta con neuritis óptica en ojo izquierdo. No recibe tratamiento y evoluciona a atrofia óptica. A los 6 meses presentó un episodio en el ojo contralateral, instaurándose tratamiento corticoideo. Durante su disminución progresiva sufre tres recaídas. Se decide instaurar tratamiento con inmunosupresores, manteniéndose estable desde entonces sin efectos secundarios.

Discusión: Tras descartar las múltiples causas de neuritis óptica bilateral recidivante en una niña, se concluye que la etiología era autoinmune. Valorando los beneficios y riesgos del tratamiento con inmunosupresores creemos que permiten el control de la enfermedad y el ahorro corticoideo.

Palabras clave: Neuritis óptica autoinmune, neuritis óptica postinfecciosa, neuritis óptica bilateral, neuritis óptica infancia, Azatioprina.

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INTRODUCTION

The optic neuritis most frequently found in children is the post-infectious one, which is bilateral and has an excellent visual prognosis (1). However, in the presence of a bilateral and prolonged condition with higher functional repercussions, it is necessary to exclude other causes of optic nerve involvement. One of these, after discarding demyelinating, metabolic, toxic and compressive causes, is autoimmune etiology. Self-immune optic neuropathy can appear in isolation, its development is relapsing and its origin uncertain. Corticoids play a crucial role in its treatment. In children, the side effects of prolonged use of corticoids, particularly on the growth curve, calls for the use of immunosuppressants.

This paper presents the case of a 10-year old girl with autoimmune bilateral optic neuropathy, with severe relapse evolution, discussing the diagnostic strategy, the use of azathioprine to spare corticoids and the hypothesis of a Gram-negative bacteria, *Yersinia enterocolitica*, as inducer of the optic nerve immune response.

CASE REPORT

A ten-year old girl without relevant antecedents who, two weeks after *Yersinia* gastroenteritis referred visual acuity (VA) reduction and pain with movement of the left eye (LE). Diagnosed with left optic neuritis, a Brain Nuclear Magnetic Resonance (RNMR) was carried out with normal results. No treatment was prescribed.

Six months later, she exhibited loss of eyesight in the right eye (RE), diagnosed as papillitis. The RNMR exhibited an inflammatory lesion in the optic nerve (signal hyperintensity in T2). She was treated with intravenous pulses of methylprednisolone (1 gram/day for 3 days) and subsequently with oral corticoids, beginning with 1 mg/kg/day for 1 week with progressive reduction.

The patient returned to our practice one month after being diagnosed with RE papillitis, exhibiting a corrected VA in the RE of 0,8, and the LE with hand movements, relative afferent pupillar defect in LE, red-green dichromatopsia in RE, achromatopsia in LE and reduced sensitivity to contrast. Funduscopy revealed papillitis in the RE (fig. 1A) and papillar atrophy in the LE (fig. 1B). The visual field

(VF) of the RE was normal, with an absolute diffuse scotoma in the LE for Humphrey's stimulus III. Optic Coherence Tomography (OCT) revealed a diffuse loss in the LE fiber layer and focal in the RE (fig. 2A).

The study was completed with a hemogram, VSG, coagulation, basic biochemistry, serous viric serologies (cytomegalovirus, herpes, HIV, measles, mumps, Epstein Barr, Herpes 6), treponemic tests (FTA-Abs), non-treponemic tests (VDRL), *Borrelia* and *Bartonella* serologies, levels of lead, vitamin B12, with negative results. A genetic analysis of the mitochondrial DNA was made without finding mutations matching Leber's disease. Lumbar puncture revealed two oligoclonal strips.

The ECG gave normal results and visual evoked potential altered. Antinuclear antibodies (ANA) and antiphospholipids were positive.

After a period of 6 months of corticoids treatment without changes, the patient suffered two relapses

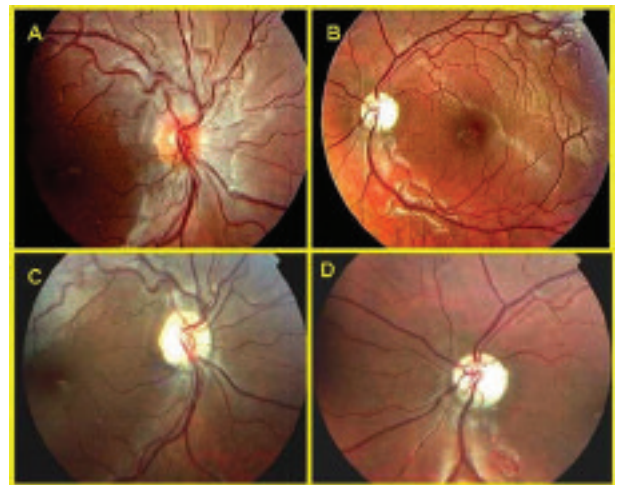


Fig. 1: Funduscopy image of both eyes. 1A and 1B correspond to the patient's first visit. 1C and 1D are from the third relapse. The RE optic atrophy evolution can be seen.

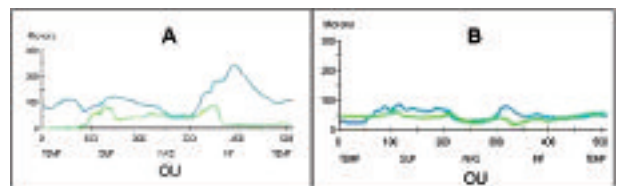


Fig. 2: OCT image of the fiber layers of both eyes: RE in blue, LE in green. 2A: First visit. 2B: During the third relapse. Progressive loss of fibers in the RE.

in 14 months and it was decided to add Azathioprine (50 mg/day the first month, increasing to 100 mg/day, controlled by means of enzymatic study TPMT). One year later the patient suffered a new relapse in the RE which reduced VA to 0,12, showing a CV alteration (fig. 3), optic atrophy in funduscopy (fig. 1C) and the OCT revealed generalized loss of the fiber layer in both eyes (fig. 2B).

Since then, after 24 months, the patient exhibits a stable VA (0,1), with azathioprine treatment being maintained at the maximum dosage of 3 mg/kg/day.

DISCUSSION

The case presented in this paper is a recurring bilateral optic neuropathy evolving to optic atrophy in a girl after gastroenteritis due to *Yersinia*. According to the clinical development (1) (bilateral and recurring) and funduscopy (papillar edema), inflammatory causes were discarded (connective tissue diseases due to virus or vaccines) as well as infectious or demyelinating diseases (RMNC and multiple viral and bacterial serologies gave negative results) and Lebers optic neuropathy (normal analysis of mitochondrial DNA primary mutations). We excluded other causes such as leukemia or disseminated erithematous lupus, and toxic, metabolic and hereditary degenerative causes.

In the light of the above results, this case might involve a *Yersinia* post-infection optic neuritis (for: appearance 1-3 weeks after infection, bilateral, age, existence of 2 oligoclonal bands in LCR and negative neuroimage. Against: poor visual recovery and absence of antibodies in serum or LCR, which are

detected up to 8 months after the appearance of symptoms due to a persistent type IgA humoral response. No HSP60 or thermal shock proteins were requested, which are white for immune response in multiple inflammatory diseases) or a self-immune demyelinating optic neuritis where the *Yersinia* infection would be the precipitating factor (for: corticoid dependency, positive ANA, signal hyperintensity in T2 of the optic nerve and absence of demyelinating disease data in CNMR).

At present, it is known that *Yersinia* is involved in infectious spondiloarthritic diseases, acting as an infectious agent (2) against which the body produces an immune response. In this case, *Yersinia* could be the trigger of the immune response against the optic nerve, producing a demyelination thereof (the patient does not exhibit any other immune symptoms).

For the confirmation of the immune condition a cutaneous biopsy could be performed with immunofluorescence (3) although, as the patient does not exhibit lactic acidosis, the test had a reduced diagnostic capacity.

OCT is of interest in the follow-up to confirm the damage in the nervous fiber layer in patients in whom conventional campimetry loses reliability due to the low rate of cooperation by the child. In self-immune optic neuropathies where the response to corticoids is lessened by relapses when reducing dosages, oral corticoid treatment is indicated for long periods of time (4). The immunosuppressing treatment aims at reducing the dosage of corticoids in these recurring, chronic conditions. In Myers review (5), 79% of patients exhibited clinical benefits (stable VA and absence of side effects) with a therapy saving on corticoids. For this economy, azathioprine was utilized instead due to the lower rate of side effects and to its utilization in diseases where the activation of humoral immunity and the subsequent demyelination of the optic nerve seem to play a relevant role (Devie's optic neuromyelitis and self-immune optic neuropathies).

On the basis of the above studies and taking into account the chronic and progressive development of our case, it was decided to initiate treatment with Azathioprine (Imurel®) with initial dosage of 50 mg/day the first month and, in view of the low response and absence of side effects, with prior TPMT control, the dosage was increased to 3 mg/kg/day (150 mg) which was adequately tolerated and halted the relapses.

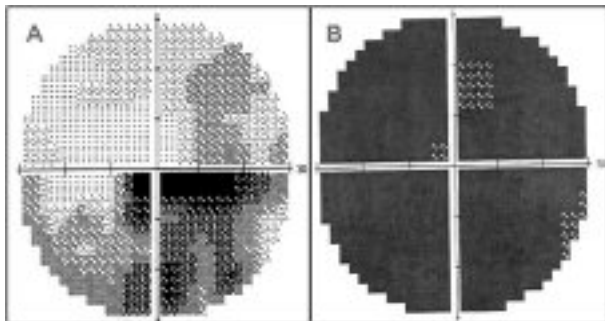


Fig. 3: Image of the patient's 30-2 visual field after the third relapse: RE centro-cecal scotoma. 3B Absolute diffuse scotoma in LE.

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