Retrobulbar optic neuritis in a patient with enteropathic spondyloarthritis treated with tumor necrosis factor inhibitors

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Abstract

We report a case of a 62-year-old-woman with a 17 year-history of axial and peripheral spondyloarthritis associated to a crohn disease, treated with tumor necrosis alpha inhibitors, who developed an asymetric retrobulbar optic neuritis that promptly responded to a high dose of steroids. Key Words: optic neuritis, crohn disease, spondyloarthritis

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Abstract: We report a case of a 62-year-old-woman with a 17 year-history of axial and peripheral spondyloarthritis associated to a crohn disease, treated with tumor necrosis alpha inhibitors, who developed an asymetric retrobulbar optic neuritis that promptly responded to a high dose of steroids.

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Key Clinical Message: Optic neuritis is a rare ocular manifestation of inflammatory bowel diseases and spondyloarthritis. It should be suspected in case of painful loss of central visual field. The incrimination of tumor necrosis alpha inhibitors reminds possible.

Introduction: Retrobulbar optic neuritis (RBON) is an inflammatory condition of the optic nerve in which the disease process occurs behind the lamina cribrosa (1). It is frequently associated to demyelinating diseases as Multiple Sclerosis (MS) (2), autoimmune disorders and infections (3). However, many other rare causes were identified. We report the case of a patient with enteropathic spondyloarthritis treated with tumor necrosis alpha inhibitors (TNF alpha inhibitors) presenting a RBON.

Case Presentation: Our patient was a 62-year-old-woman with a family medical history of MS, a 17 year-history of axial and peripheral spondyloarthritis associated to a Crohn disease (CD), with no previous neurologic or ocular manifestation. She was initially treated with a 20mg/week of oral Methotrexate which failed to bring her symptoms under control. Then, she received Infliximab, discontinued after 8 courses for secondary non-response, Etanercept, discontinued for lymphopenia, and lastly 40 mg/2 weeks of Adalimumab. One year after the switch to Adalimumab, anti-nuclear anti-double stranded and anti-histone antibodies were positive, consistent with a drug induced lupus. Adalimumab was discontinued for 6 months then reintroduced after an immunologic remission.

Two years later she presented with an occipital headache, blind spots and pain with her left eye movement. At the time of presentation, the neurologic physical examination found a quadripyramidal syndrom, a convergent strabism on the left eye and a normal accommodation reflex. Her visual acuity was 20/20 in the two eyes. Formal visual field showed a central scotoma in the left eye and full field in the right eye. Dilated fundoscopic examination was unremarkable.

Laboratory tests demonstrated normal levels for complete blood count and no B12 vitamin deficiency was detected. The Neuromyelitis optica (NMO) antibodies were negative. A visual evoked potential showed a prolonged latencies consistent with bilateral demyelinating RBON. Non-specific frontal white matter hyperintensities (wMH) lesions were found on the T2/FLAIR brain magnetic resonance imaging (MRI).

The diagnosis of an asymetric bilateral RBON was made. Both anti-TNF therapy and inflammatory diseases (CD and spondyloarthritis) were incriminated. The patient received 1 g intravenous Methylprednisolone per day on 3 successive days with a dramatic improvement of blind spots and eye pain. The decision was to discontinue Adalimumab.

An ophthalmic and a neurologic follow-up were recommended. No signs of relapse were noted during follow-up visits.

Discussion: The frequency of ophthalmic involvement in CD features 6.8% (4). It is more frequently seen in the first year of the following-up, during activity of the bowel disease, in colonic localisation and in the case of coexistence of articular manifestations (entheropathic arthritis)(5).

Episcleritis and acute anterior uveitis are the most frequent ocular complications (5). This latter is also reported as the most common extra-articular manifestation of Spondyloarthritis, affecting more than 20% of the patients (6). Many other ophthalmic manifestations have been described in relation to inflammatory bowel disease (IBD) such as glaucoma, keratitis and dry eyes(5). However, the reported incidence of posterior segment involvement ranges between less than 1% to 30%, depending upon the series (4). Optic neuritis (ON), which is an inflammation or demyelination or a degeneration of the optic nerve, may be present in up to 4% of adult IBD patients(4). To our knowledge, only 6 documented cases of ON with CD were reported in the literature (7)(table 1). The co-existence of ankylosing spondylarthritis (AS) and ON were only reported in three cases(8) (Table 2).

On the other hand, a possible association between IBD and MS was hypothesized and an approximately 3-fold increased risk of MS in IBD patients was suggested (9). A retrospective study performed to examine the relation between the two diseases in the era before TNF alpha inhibitors showed a small but a significant association(9). Patients with CD and ulcerative colitis were 54% and 75% more likely than community controls to have been diagnosed with MS, ON or other demyelinating conditions(4). ON was recorded in 6 of 7988 CD patients (0.08%) and in 17 of 12 185 ulcerative colitis patients (0.14%), in comparison with 50 of 80 666 controls (0.06%) (9).

TNF alpha inhibitors which are commonly used for the treatment of IBD and refractory rheumatic diseases are incriminated in increasing the risk of developing MS and ON. By 2001, the Food and Drug Administration had received more than 20 reports of MS or other demyelinating conditions in patients treated with these medications. In 2004, clinician and patient warnings were updated on 3 major anti-TNF α therapies: Etanercept, Adalimumab, and Infliximab (9). The mechanism of this complication is not still well elucidated. A hypothesis suggests that systemically administered anti-TNF agents may inhibit the apoptosis of self-reactive T cells but fail to penetrate and reach the central nervous system, inducing an autoimmune demyelinating process(10). The other hypothesis suggests an activation of infecting microorganisms which may result in a demyelinating process(11).

In our case, the incrimination of anti-TNF α therapy remained possible, but it is less likely to be the sole cause of the RBON.

Conclusion: ON is rarely the ocular manifestation of AS or CD. To date, the reported cases of demyelination after anti-TNF therapy suggest a possible causal relationship. Further research should be conducted to

elucidate the mechanism of this complication which is a serious adverse event.

Table 1: cases of co-existence of crohn disease and optic neuritis in the absence of anti-TNF therapy reported in the literature

Authors year	Patient characteristics	Presenting symptoms	Treatment	Systemic steroid response
Ernst, B et al.(12) 1991 Van de Scheur et al. (13) 2002	A 25-year-old woman A 39-year-old man	Blurred Visual acuity in the right eye Bilateral visual loss	Pulse methylprednisolone 2 intermittent courses of systemic steroids for 3 weeks in doses of up to 60 mg	yes yes
Sung H et al.(14) 2006	A 22-year-old man	Loss of visual acuity	High dose steroid treatment	yes
Taxiarchis F et al.(15) 2009	A 32-year-old man	Not mentioned	Intravenous methylprednisolone (1g/day for 3 days)	Not mentioned
-Barabinoet et al.(4) 2011	An 11-year-old boy	Bilateral visual loss	Intravenous methylprednisolone (30mg/kg/day for 3 days) followed by an oral prednisone taper	yes
-McClelland et al.(7) 2012	A 42-year-old man	Painless loss of the entire visual field in the left eye	Intravenous methylprednisolone (1g/day for 1 week) followed by an oral prednisone taper and corticosteroid eye drops	yes

Table 2: Cases of co-existence of ankylosing spondylarthritis and optic neuritis in the literature

Authors year	Patient characteristics	Presenting symptoms	Treatment	Systemic steroid response
Menon et al.(16) 2001	A 20-year-old man	Sudden diminution of vision in the right eye	Intravenous methylprednisolone (1g for 3 days) followed by 60 mg oral prednisolone/day for 10 days	2 attacks of optic neuritis in the left eye after one year
Y-S Chou et al.(17) 2011	A 31-year-old woman	Sudden pain and decreased vision in the right eye	Pulse steroid therapy for 3 days	No obvious visual field defect on the third day

Authors year	Patient characteristics	Presenting symptoms	Treatment	Systemic steroid response
Zhao et al. (18) 2015	A 31-year-old man	Sudden decreased vision in two eyes	Intravenous methylprednisolone (1 g/day for 3 days) followed by 1mg/kg oral prednisolone for 10 days and tapered	Improvement of the Visual acuity in the right eye after a follow-up period of 2 years/ No improvement of the visual acuity in the left eye after a follow-up period of 2 years

Conflict of interest: None.

Author contribution :

Ben Ayed H: conceptualization, data curation and writing-original draft

Fazaa A: visualisation, data curation, wrinting-review and editing

Miladi S and Sellami M: data curation

Souabni L, Kassab S and Chekili SS: data curation and methodology

Ben Abdelghani K and Laater A: validation

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