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SHORT REPORT

Reversible bilateral optic neuritis after Infliximab discontinuation in a patient with Crohn's disease

Taxiarchis Felekis [a], Konstantinos Katsanos [b,1], Dimitrios Christodoulou [b], Ioannis Asproudis [a], Epameinondas V. Tsianos [b,*]

[a] Department of Ophthalmology, University Hospital of Ioannina, Ioannina, Greece
[b] 1st Department of Internal Medicine and Hepato-Gastroenterology Unit, University Hospital of Ioannina, Ioannina, Greece

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Abstract

A relationship between inflammatory bowel disease and multiple sclerosis is supported by a higher than expected coexistence of these diseases among families and individuals.
A 32 year-old male with Crohn's disease of the terminal ileum diagnosed 4 years ago and HLA-B27 negative bilateral sacroiliitis diagnosed 2 years ago, was admitted in our hospital because of an acute episode of blurred vision. In addition the patient complained for urine incontinence. Before this admission the patient was administered methylprednisolone and Infliximab induction treatment. During admission the diagnosis of multiple sclerosis-associated bilateral optic neuritis was made and Infliximab was discontinued. The patient was started on therapy with interferon-beta for multiple sclerosis, prednizolone and azathioprine for Crohn's disease and oxybutynin hydrochloride for urine incontinence. After 8 weeks of Infliximab discontinuation patient recovered totally from optic neuritis.
This is a rare case of totally reversible bilateral optic neuritis associated with multiple sclerosis in a patient with Crohn's disease and sacroiliitis receiving also Infliximab induction therapy.

1. Introduction

A relationship between inflammatory bowel disease and multiple sclerosis (MS) is supported by a higher than expected coexistence of these diseases among families and individuals.[1] Furthermore, a possible relationship especially between Crohn's disease (CD) and MS has been widely documented, both sporadically and at a familial level.[2] Albeit in the absence of precise experimental data, it is legitimate to presume that the two diseases may share some common pathogenetic traits.

Tumor necrosis factor (TNF) is a cytokine secreted by white blood cells and plays an important role in mediating

Abbreviations: CD, Crohn's disease; IFX, Infliximab; MS, Multiple sclerosis; TNFa, Tumor necrosis factor a.

* Corresponding author. 1st Department of Internal Medicine and Hepato-Gastroenterology Unit, Medical School, University of Ioannina, 451 10 Ioannina, Greece. Tel.: +30 26510 97501; fax: +30 26510 97016.
E-mail address: etsianos@uoi.gr (E.V. Tsianos).

[1] Equal contribution to the first author.

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the inflammation in Crohn's disease. TNFa inhibitors such as Infliximab, neutralize the activity of this molecule thus resulting in the healing of the bowel's inflammatory process.[3] Given the fact that over the last years there have been some reports concerning demyelinating adverse effects possibly associated with the administration of anti-TNFa agents[4] it is of importance to understand the mechanism(s) of their interference in the normal function of the nervous system and the optic nerve. By this way we could be able to properly screen high-risk groups before the initiation of such therapies.

We report herein a Crohn's disease patient with HLA-B27 negative sacroiliitis who was subsequently diagnosed with multiple sclerosis-associated bilateral optic neuritis that was totally reversed after Infliximab discontinuation.

2. Case report

A 32 year-old male with Crohn's disease (CD) of the terminal ileum diagnosed 4 years ago and HLA-B27 negative bilateral sacroiliitis diagnosed 2 years ago, was admitted to our hospital because of a sudden decrease in vision in both his eyes also associated with pain during ocular movements.

The patient also mentioned that he suffered recently from numbness of the upper limbs, weakness, instability and urine incontinence. Of notice, patient had a family history of Crohn's disease (aunt and grandfather).

Endoscopy, histology and radiology exams that patient ileal CD was of luminal type with no penetrating or structuring features.

Since diagnosis patient refused azathioprine and was started on mesalamine 3gr/d while during relapses 32 mg/d of methylprednisolone tapered within a 3-month period was co-administered. Patient relapsed six times since diagnosis and required hospitalization twice.

Four months ago and due to a severe CD relapse patient was administered elsewhere only three doses of Infliximab (induction scheme) and methylprednisolone 16 mg/day and responded well.

The first neurological symptoms appeared 6 weeks after the end of Infliximab induction scheme and were followed by ophthalmological symptoms 2 weeks afterwards.

On admission patient except of his neuro-opthalmological complains was otherwise in good clinical status with CDAI at 110 and no symptoms suggestive of CD relapse.

Ophthalmological examination showed that corrected visual acuity was 6/10 for the right eye and 4/10 for the left one. A relative afferent pupillary defect and disorder in colour perception were present. Both kinetic and static perimetry revealed a large paracentral scotoma in his right eye and a central scotoma in his left eye. MRI scan of the brain, orbits and spine revealed areas of high signal in the midlobe and C1–C5 spinal cord. Those findings in combination with evoked potentials set the diagnosis of multiple sclerosis (MS) associated bilateral optic neuritis and Infliximab was immediately discontinued. The patient was started on therapy with interferon-beta for MS, azathioprine (100 mg/day) for Crohn's disease and oxybutynin hydrochloride (10 mg/day) for urine incontinence.

Resolution of neurological and visual field defects was associated with improvement of visual acuity, muscular power and neurological tests. In detail, corrected visual acuity was 10/10 for both the eyes and electromyography was much ameliorated at the 2-month follow up.

On the six-month follow up patient is in excellent clinical status with remission of his neurological symptoms and visual field defects.

3. Discussion

We presented herein a rare case of a patient with Crohn's disease (CD) with multiple sclerosis (MS)-associated bilateral optic neuritis that totally subsided after Infliximab (IFX) discontinuation.

Based on the review of Simsek et al.[4], there are only two cases of CD patients treated with IFX who were diagnosed with optic neuritis.[5,6] Both cases were unilateral and reversible after IFX discontinuation within 3 months and 6 weeks respectively.

There is intriguing controversy regarding whether the development of demyelinating disorders such as multiple sclerosis (MS) and optic neuritis is connected to of anti-TNFa agent use or it is only based on one or more genetic factors, acting in conjunction with other presumably exogenous factors and triggering HLA antigens to lead to the one or the other disease.

Anti-Tumor Necrosis Factor (anti-TNFa) agents, constitute a new generation of biological agents used in the treatment of IBD and of a variety of autoimmune diseases.[7] There are several theories suggesting a potential mechanism for demyelinating side effects of these agents.[8–13]

In our case, the restoral of the patient's visual acuity and visual fields after IFX discontinuation, could indicate a possible inculpatory role of IFX in the pathogenesis of demyelinating process in this patient. According to Simsek et al.[4], the median interval from the first administration of TNFa inhibitors to the onset of optic neuritis was 7,5 months (range 2 months to 1,5 years). This observation is in accordance with our case report, as our patient developed ophthalmologic manifestations 8 weeks after Infliximab induction treatment. However it is questionable whether in this particular patient only three doses of IFX induction were the only factor able to induce severe bilateral optic neuritis resulting in loss of vision. The complete reversibility of the case after IFX discontinuation points towards IFX as a triggering factor to a strongly predisposed individual for optic nerve dysfunction.

It is impossible to provide a pathology confirmation regarding possible subclinical alterations in the optic nerve, which might precede the clinically evident loss of vision in this patient. On the other hand, a potential contribution of interferon-beta to clinical improvement should not be disregarded. In this view, early screening in visual acuity parameters in patients needing biologicals may be of importance to identify high-risk individuals.

Finally, although chronically strongly related to IFX administration, the symptomatic appearance of an MS-associated optic neuritis as an additional to sacroiliitis silent extraintestinal manifestation cannot be excluded. In fact, the spectrum and frequency of ophthalmologic manifestations in Crohn's disease has not been extensively studied[14] and some CD patients with latent symptoms from their eyes,

including optic nerve dysfunction may escape proper diagnosis and early treatment. These patients may represent high-risk groups for anti-TNFa or other immunosuppressive treatment.[15]

A study from Denmark showed that IBD patients have a four-fold increased risk of demyelinating diseases independent of medical treatment.[16] In our cohort of 910 IBD patients this was the only case of demyelinating disease independent of any type of treatment while in the Leuven cohort the long-term use of Infliximab was efficacious and safe.[17]

It is difficult to thoroughly investigate for all therapies in CD — including anti-TNFa agents — their effect(s) in the optic nerve, also in the view of the largely unexplained nature of multiple sclerosis. Genetic predisposition, age of disease onset and other concomitant extraintestinal manifestations seem to be of capital importance in this group of CD patients. However, the ability of safe prediction is a chimera at the moment and careful patient selection for biological or immunomodulator as well as regular follow up can promptly diagnose and possibly reverse such episodes.

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T.F. and K.K. drafted the manuscript, D.C reviewed the literature, I.A and E.V.T. critically revised the manuscript and approved the final version.

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