Eyes and Inflammatory Bowel Diseases

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Abstract

Inflammatory Bowel Disease (IBD) is a chronic systemic disease which includes Crohn’s disease (CD) and Ulcerative Colitis (UC). Extra-intestinal manifestations (EIMs) in IBD are very common but the pathophysiology is not well understood. It is most likely mediated by the inflammatory nature of the disease. Ocular manifestations represent the third most frequent EIMs and they may proceed the diagnose of the intestinal disease or occur after the diagnose, even if the disease is in remission. In this review we present the most uncommon ocular manifestations of CD and UC.

Keywords: Inflammatory Bowel Disease; CD; UC; Extra Intestinal Manifestations; Ocular Inflammation

Introduction

Extra intestinal manifestations in inflammatory bowel disease are frequent and may occur before or after IBD diagnosis. Up to 50% of patients with IBD experience at least one extraintestinal manifestation or complication. These extra-intestinal manifestations have an impact in the quality of the patients’ lives and can involve any organ system including the musculoskeletal, dermatologic, hepatobiliary, ocular, renal and pulmonary systems. The most common include type 1 peripheral arthritis, erythema nodosum, oral aphthous ulcers and episcleritis which are associated with the disease activity and pyoderma gangrenosum, uveitis, axial arthropathy and Primary Sclerosing Cholangitis (PSC) which are predominantly independent of disease activity [1].

Ocular complications directly related to IBD are categorized as primary and secondary. Primary complications are usually temporally associated with IBD exacerbations and tend to resolve with systemic treatment of the intestinal inflammation. These include keratopathy, episcleritis, and scleritis. Secondary complications arise from primary complications [2].

Examples include cataract formation due to treatment with corticosteroids, scleromalacia due to scleritis, and dry eye due to hypovitaminosis. Some ocular manifestations of IBD can lead to significant visual morbidity and temporally associated complications can also be a sign of disease control [3].

A systematic search of PubMed was performed and rare cases of ocular manifestations of IBD are presented in this review.

Epidemiology

The prevalence of the EIMs ranges between 16% and 40% considering that the occurrence of one EIM predisposes to the development of additional EIMs. A large cohort study of Greek patients with IBD showed that in general, EIMs are more common in women, patients

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with CD, smokers, patients born or living in urban areas, patients with extensive UC and those with a history of major IBD surgery. The frequency of EIMs in Greek population was 33.1%. Among the manifestations, the most common was peripheral arthritis seen in 16.7% of patients with its prevalence being similar in CD and UC, whereas ankylosing spondylitis seen only in 2.1% of the patients, being more prevalent in males and CD patients. Ocular manifestations represented the third most frequent group of EIMs [1].

Nearly, 2% to 5% of patients with IBD experience ocular manifestations. These manifestations are reported more frequently in patients with CD (3.5% - 6.3%) than patients with UC (1.6% - 4.6%). Patients older than 40 years have more likely iritis/uveitis than those younger than 40 years [2].

Ocular Manifestations
Orbital pseudotumor and orbital myositis

Orbital pseudotumor is a rare extra intestinal manifestation of IBD. All the evidence and information that we have is gathered from case reports. Therefore we have not made an exact association with the clinical characteristics of the intestinal disease and the prevalence on the patients Lakatos, et al. in a 25-year follow-up study of 873 patients with IBD found only one case of orbital pseudotumor in a woman with severe ulcerative pancolitis [4].

Orbital myositis represents a subgroup of the ‘orbital pseudotumour syndrome’, which defines inflammation within any structure in the confines of the orbit and is a noninfectious, inflammatory process primary involving extraocular eye-muscles, likely represents a process of impaired immunoregulation related to the underlying intestinal inflammation. It can involve a single muscle or the entire orbital musculature and can be acute or recurrent and chronic. It is most often described as idiopathic, but has been associated with a number of systemic inflammatory diseases [5,6].

This rare manifestation of IBD is mimicking thyroid ophthalmopathy, so IBD should be considered in the differential diagnoses, especially if all thyroid tests are negative. Clinical physicians should be alert in order to recognize orbital myositis as an extra intestinal manifestation of CD so that the diagnosis can be made and appropriate therapy commenced. Seventeen cases of CD associated orbital myositis and 3 cases of ulcerative colitis associated orbital myositis have been reported in the published literature since 1970. Orbital myositis has been described to occur prior to the development of Crohn’s related gastrointestinal symptoms and when the CD is in remission [8].

Ocular manifestations have been reported in up to 10% of patients with CD, including uveitis, episcleritis, scleritis and chorioretinitis. Orbital myositis is rare. A case report in 2008 presented a 23-year-old woman with a seven years history of terminal ileal CD who presented with typical signs of posterior scleritis. An immediate response was achieved with high dose of oral steroids (prednisolone 40 mg/day) followed by a six week stapering. Over the next three months she experienced three episodes of symptomatic posterior scleritis, affecting first the right then the left eye. Her intestinal disease was active. She was given infliximab for the intestinal activity, and the ocular pain resolved immediately.

One year later she presented with typical signs of orbital myositis in her left eye. The intestinal disease was active. Infliximab was discontinued. She was admitted to a hospital for pulsed methyl prednisolone (1 gr. on three consecutive days) and intravenous cyclophosphamide (15 mg/kg every two weeks, six doses). Two months after completion of the cyclophosphamide infusions, she experienced a recurrence in symptomatic CD. She was commenced on adalimumab and she remains in remission [5].

In Spain, the authors presented a case of recurrent orbital myositis in a patient with a history of CD which treated successfully with adalimumab. With this medication the doctors managed to achieve remission of the intestinal disease and control of the orbital inflammation [6].

Until this point we have described orbital myositis only in patients with CD. At 2012 Bennion, et al. presented a case of bilateral, diffuse, orbital myositis associated with ulcerative colitis in a patient treated with infliximab with this being only the third report of ulcerative colitis-associated orbital inflammatory disease by the time of the article. The orbital inflammation was treated with iv methyl prednisolone and had a dramatic improvement in the first 72 hours. The inflammation resolved after 8 weeks of prednisone [7].
In 2013 Sanam Verma, et al. describe a case of a 35-year-old male who presented in the ER with typical signs of orbital myositis 13 weeks after he discontinued infliximab due to intolerance. As the authors were concerned, this was the first case of orbital myositis occurring in a patient in clinical and biochemical remission after discontinuation of anti-TNFα therapy. The orbital inflammation was treated successfully with prednisone and adalimumab. The inflammation occurred 13 weeks after discontinuing infliximab because of its known pharmacokinetics [8].

**Retinal vasculitis**

The authors present a case of a 38-year-old woman with unilateral retinal vasculitis, branch retinal artery occlusion and a following retinal neovascularization with a four years old history of CD. The treatment included argon green laser which lead to successful regression of retinal neovascularization along with oral corticosteroids and salazopyrine. Physicians should be alert of this rare EIM of CD, because it may result in retinal neovascularization and the necessity of laser photocoagulation [9].

**Proptosis in the left eye**

Proptosis of the eye is a rare manifestation of the IBD.

The literature presents two cases of unilateral proptosis of the eye and specifically of the left eye.

In 2005 the authors present a case report of a 32-year-old male with a three year old history of ulcerative colitis, who presented with a 2-month history of progressive proptosis in his left eye with no visual impairment nor diplopia. All the examination results were negative for ocular or systemic disease. The patient was treated with systemic steroids and his ocular and gastrointestinal pathologies were quickly improved. After a 1-year follow up, the orbital myositis remains unchanged and the ulcerative colitis in remission with the use of mesalazine [10].

In 2013 a different team described the case of a young woman, presenting for the first time with abdominal pain, diarrhea and proptosis of her left eye. The woman was diagnosed with CD and her ocular symptoms were quickly improved after the treatment of the underlying CD [11].

**Dacryoadenitis**

Dacryoadenitis is a very rare EIM of CD. Although there are a few case reports of acute dacryoadenitis in the literature, there is not of a recurrent one. In 2012 Boukouvala, et al. presented a case report of a recurrent dacryoadenitis; a 41-year-old woman with a three year medical history of CD (proctocolitis) in remission with sulphasalazine and azathioprine was diagnosed with right acute dacryoadenitis. The inflammation was treated with iv broad spectrum antibiotics and subsequently with oral antibiotics. However, 8 months after the first diagnose, she was diagnosed again with acute dacryoadenitis, this time at the left eye. The initial treatment with antibiotics was followed by oral prednisolone, with the thought of a possible relation between the recurrent inflammation and the CD. No recurrence had been noted after a period of 6 months [12].

**Optic neuropathy**

Ocular manifestations of IBD are, in general, localized to the anterior chamber but rarely can involve the posterior chamber, orbit and optic nerve [14].

The literature presents two cases of optic neuropathy associated with IBD

In 2001, Romero., et al. presented a case of a 27-year-old woman with abdominal pain, bloody diarrhea, arthralgia and acute bilateral loss of vision. The woman was diagnosed with bilateral optic neuritis. After the diagnose of ulcerative colitis and the treatment with systemic mesalamine the ocular manifestations had entirely settled [13].

In 2012 McClelland., et al. presented a case of a 42-year-old man who was diagnosed with CD after been diagnosed with optic perineuritis when presenting with acute loss of vision [14]. You may notice that in both cases optic neuropathy occurred at the same time of the symptoms of the IBD and in one case actually lead to the diagnose of the underlying disease.

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The term uveitis describes a heterogeneous group of diseases characterized by inflammation of intraocular structures. It is typically grouped into anterior uveitis (iritis and iridocyclitis), intermediate uveitis which affects the vitreous, and posterior uveitis which affects the retina. Anterior uveitis is the most frequent ocular manifestation in chronic inflammatory bowel disease: approximately 1.9 - 4.9% in CD and 1.6% in UC [16].

In 2005 Chaoui, et al. presented three cases of anterior uveitis in patients with history of IBD. Specifically the first two cases describe the treatment of bilateral anterior uveitis in two patients with ulcerative colitis, whereas the third case describes a recurrent anterior uveitis in a patient with CD. In this case neither topical nor systemic corticosteroids provided control of the ocular inflammation so a gonio-surgery was required [16].

In 2007 Tappeiner, et al. described a rare case of posterior uveitis in a patient with CD. The ocular manifestations were followed by a recurrence of the intestinal symptoms [17].

Also in 2007, a different group described a case of subretinal fibrosis and panuveitis syndrome in a patient with ulcerative colitis. By the time of the ocular manifestations the colitis was inactive. The ocular inflammation was controlled after a one year treatment with immnosuppressive agents (methotrexate) [18].

Keratopathy

Corneal disease (keratopathy) is a rare manifestation of IBD, but if it does occur the patient will present with eye pain, foreign body sensation, irritation, and very occasionally decreased vision [3].

We quote three cases of keratopathy in patients with IBD.

In 1998 Kodjikian, et al. described a rare case of nummular keratopathy of the left eye in a 58-year-old woman with active CD. The symptoms were improved with local steroids a spontaneous decrease in bowel activity [19].

In 2007 Paroli, et al. described a case of bilateral ring keratopathy in a patient with ulcerative colitis and psoriatic arthritis which did not respond in topical nor systematic anti-inflammatory medication [20].

In 2013 Federica Fasci-Spurio and her associates described a paradox; the development of a severe form of bilateral keratopathy in a patient receiving anti-TNF treatment (infliximab) for CD. Also Infliximab did not manage to control the intestinal disease and it was replaced by adalimumab with a significant improvement of the active disease but a deterioration of the ocular manifestation. Eventually, adalimumab was also discontinued and replaced by methotrexate which achieved a clinical remission of his CD. The ocular manifestations remained in remission with the use of topical steroids and antibiotics [21].

Treatment

The management of ocular manifestations in IBD includes the use of topical steroids, cycloplegics, systemic steroids, immunosuppressive agents or anti-TNF biological treatment [15].

The first-line therapy for most ocular manifestations of IBD that do not improve with the treatment of the underlying disease are corticosteroids. They are used topically or systemically, depending on the severity of the inflammation. If corticosteroids fail to manage the inflammation, cytotoxic immunosuppressive agents such as azathioprine should be considered. This treatment can be particularly effective in patients who are HLA-B27 positive. Also anti-TNFs can be used, such us infliximab and adalimumab. Biological medication for IBD associated uveitis has been reserved for refractory or recurrent cases [3].

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In some cases, a surgical approach is required to treat eye complications, i.e. cataract or retinal neovascularization and to improve the patient’s quality of life. In severe cases associated with active bowel inflammation, colonic surgical resection may be required to control the ocular inflammation [3].

**Conclusion**

IBD is a chronic systemic disease with many extra-intestinal manifestations. The underlying pathophysiology leading to the ocular manifestations of IBD is still not well understood. Many ocular manifestations occur before the intestinal symptoms so it is very important for every clinical physician and ophthalmologist to ask patients with acute uveitis or recurrent eye inflammations for abdominal pain, diarrhea, fever, anemia and weight loss. Early diagnosis and effective treatment may avoid the onset and sometimes persisting complications. Most ocular manifestations respond to the treatment of the underlying disease; however some of them, such as retinal neovascularization may need surgery in order to resolve. Others, including optic neuritis and retinal vasculitis, have significant morbidity and are devastating if they are not immediately recognized and treated. Clinicians, Gastroenterologists and Ophthalmologists should be alert and promptly recognize and evaluate complications that can cause emergencies.

**Bibliography**


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