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OPHTHALMIC COMPLICATIONS IN INFLAMMATORY BOWEL DISEASE

Key Takeaways

- Ocular EIMs are more common in CD than UC
- Episcleritis and uveitis are the most common ocular EIMs
- All patients living with IBD must check their eyes regularly and be aware to consult a physician if experiencing ocular redness, pain, light sensitivity or blurred vision
- When ocular manifestations are present, prompt treatment can avoid blindness, and patient awareness and education contribute enormously to this
- Ocular complications may arise from the natural history of the disease, from treatment or from non-related but concurrent conditions. Awareness is the key for proper management.
- Collaboration between gastroenterologists and ophthalmologists is essential when selecting therapy for patients with ocular inflammation and IBD

Introduction

The prevalence of inflammatory bowel disease (IBD), estimated at 843 per 100,000 people (95% PI 828-859) (i.e., 0.843% of the population) in 2023 is increasing in Canada and is expected to reach 1.1% of the Canadian population by 2035.[1] Consequently, extraintestinal manifestations and complications will also increase. Up to 50% of patients suffering from IBD will develop an extraintestinal manifestation (EIM) during the course of their disease, patients with Crohn's disease (CD) being more often affected then those with ulcerative colitis (UC).[2] Ocular manifestations are the third most common EIM after articular and dermatological involvements.[3] Ocular complaints in patients with IBD can represent an EIM, a complication of systemic treatment or an unrelated affection. All patients presenting with a red eye, light sensitivity, loss of vision or any acute ocular symptom(s) should be promptly evaluated by an eye specialist. Early detection of ophthalmologic diseases and appropriate management require collaboration between specialists and are of utmost importance to avoid permanent visual loss.

The most common ocular manifestations reported in IBD patients are episcleritis (2-5%) and anterior uveitis (0.5-3.5%).[3] Other less common manifestations include scleritis, intermediate and posterior uveitis, retinal vasculitis, retinal vascular occlusions, orbital inflammatory syndrome, and optic neuritis.[4] Ocular manifestations can also be associated with malabsorption syndromes encountered in some patients with IBD.[5] Secondary vitamin A deficiency can result in night blindness and keratoconjunctivitis sicca.[6,7]

Episcleritis and Scleritis

Episcleritis, the most common ophthalmic complication of IBD, consists of an inflammation of the superficial episcleral vessels. It presents as sudden eye discomfort, sectorial or diffuse redness, tearing, minimal or no pain, and no change in visual acuity. It is generally unilateral and can also present in its nodular form. In episcleritis, redness will blanch with the diagnostic test consisting of instillation of a drop of phenylephrine 2.5%. Like other ocular manifestations, episcleritis can present before or after the diagnosis of IBD. Episcleritis is associated with active CD and can be considered an indicator of intestinal disease activity.[8] Treatment of active IBD is generally sufficient to resolve episcleritis but some topical treatment can be added, such as lubricants, topical corticosteroids or topical non-steroidal anti-inflammatories (NSAIDs). Sometimes oral NSAIDs are needed but should be used cautiously because of their effect on intestinal inflammation.

Scleritis

Scleritis is a rare manifestation of IBD, occurring in less than 1% of cases[3] **(Table 1)**. Contrary to episcleritis, scleritis is not considered an index of IBD activity and may develop even when the intestinal disease is inactive. Scleritis has a more severe presentation than episcleritis. Patients with scleritis typically complain of severe redness and deep pain (typically wakening up at night due to pain). Redness will not blanch with topical phenylephrine. There is generally no discharge or photosensitivity and visual acuity remains normal unless it is a severe form of the condition or there is an associated posterior component. Scleritis can be associated with multiple systemic diseases, some life-threatening. Due to its severity, scleritis needs to be treated aggressively to avoid blindness. Treatment requires systemic therapy, initiating with NSAIDs and frequently requiring systemic corticosteroids and immunosuppression.

	Uveitis	Episcleritis	Scleritis
Presentation	Perilimbal flush, photosensitivity, blurry vision	Red eye, minimal pain, blanches with phenylephrine	Red eye, deep pain, violet hue, does not blanch with phenylephrine
First-line Treatment	Topical steroids	Observation, NSAIDs, topical corticosteroids	Systemic NSAIDs, systemic corticosteroids
Differential diagnosis for underlying disease	Idiopathic, trauma, HLA-B27 associated systemic diseases like IBD, other systemic conditions, postoperative	Idiopathic, herpes zoster, rarely systemic disease	Connective tissue disease, herpes zoster, syphilis, gout

Table 1: Uveitis versus episcleritis versus scleritis; courtesy of Marie-Lyne Belair, MD, FRCSC and Evangelina Esposito, MD CHM

Uveitis

Uveitis is the second most common ocular manifestation of IBD (0.5-3.5%) and is twice as frequent in patients with CD than in patients with UC.[9,10] Uveitis signifies acute inflammation of the uveal tract or middle layer of the eye, which includes the iris, ciliary body and choroid. It is classified as anterior, intermediate, posterior or panuveitis. Anterior uveitis (also referred as iritis or iridocyclitis) occurs when the inflammation is predominantly in the anterior chamber; intermediate uveitis when the vitreous is involved; posterior uveitis when it affects the retina and/or choroid; and panuveitis when the inflammation is equally present in all three parts of the eye.[11] In patients with IBD, uveitis is typically anterior and does not correlate with gastrointestinal tract activity.[12] However, anterior uveitis might be considered a marker of a more severe disease course.[13] Anterior uveitis is often associated with other EIMs such as erythema nodosum and arthralgias. There is a well-established association between CD, ankylosing spondylitis and anterior uveitis. These patients tend to be HLA-B27 positive.[4] Clinically, anterior uveitis symptoms are redness, light sensitivity, pain, and decreased vision. If severe, anterior uveitis can present with an accumulation of inflammatory cells in the anterior chamber called a hypopyon (**Figure 1**). Treatment of an anterior uveitis episode need to be initiated promptly to avoid potential blinding complications such as posterior synechiae, glaucoma, macular edema, cataracts, band keratopathy, and retinal involvement. Initial treatment is with topical corticosteroids and cycloplegic drops. Periocular injection or systemic corticosteroids may be required for more severe cases. In cases of multiple recurrences or chronic evolution, or if topical treatment leads to intolerable side effects, immunosuppression therapy may be considered.

Special considerations must be taken in the pediatric population. Often, children do not complain of blurred vision and uveitis can be less symptomatic. It is particularly important in this age group to proceed to regular ophthalmic follow-up. The prevalence of ocular manifestations of IBD in children is reported to be 0.62-1.82%, uveitis being the most common.[14]

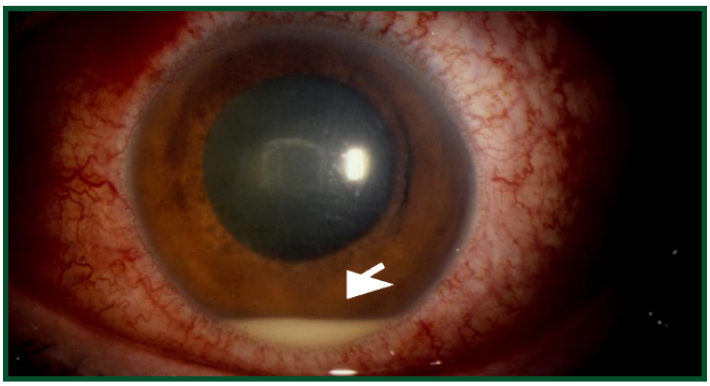

Figure 1. Photo showing the presence of a hypopyon (white line – arrow): sign of severe anterior uveitis ; courtesy of Marie-Lyne Belair, MD, FRCSC and Evangelina Esposito, MD CHM

Differential Diagnosis

Uveitis can be associated with inflammatory diseases other than IBD. The most common association is with ankylosing spondylitis, a type of inflammatory arthritis associated with HLA-B27. It is important not to assume that all cases of IBD presenting with uveitis are from inflammatory causes. Infectious and other non-infectious causes need to be kept in mind and investigated appropriately. Among infectious causes are syphilis, herpetic group (HSV, VZV, CMV), Lyme disease, and tuberculosis. Ocular redness can also be associated with some non-urgent pathologies such as blepharitis, conjunctivitis and keratitis sicca, or more urgent pathologies such as corneal ulcer (a pathology that should always be considered in contact lens wearers), ocular trauma or endophthalmitis (in patients with recent ocular surgery or therapeutic injection for other causes).

Importance of Collaboration in Treatment Decision-making

As mentioned previously, most cases of ocular EIM can be treated with local or periocular corticosteroids. More severe cases or chronic ocular inflammation must be treated more aggressively and with a long-term approach. Uveitis with a chronic course or multiple recurrences requires immunosuppressive therapy to avoid prolonged use of corticosteroids and their associated side effects.[15] Various immunosuppressive agents are used in uveitis treatment. Anti-metabolites such as methotrexate, mycophenolate mofetil and azathioprine are frequently used for severe non-infectious uveitis. When a patient with IBD requires systemic therapy, the choice of the immunosuppressive agent should also consider the presence or absence of ocular EIM. Biological anti-tumor necrosis factor (anti-TNF) agents (mainly infliximab and adalimumab) are effective in treating both IBD and uveitis. These agents are approved for the treatment of isolated non-infectious intermediate, posterior and panuveitis forms of uveitis. In cases of anterior uveitis associated with ankylosing spondylitis, anti-TNF agents have been proven effective in reducing flares of uveitis and improving the control of chronic uveitis.[16,17] Vedolizumab has been introduced recently for the treatment of IBD but its gut-selective inflammatory control appears to limit its effect on EIM prevention as described in a study where patients receiving it were more likely to develop EIMs vs those receiving anti-TNF therapies.[18]

Conclusion

Ocular involvement is prevalent in CD and active IBD. Ophthalmologists must be aware that ocular inflammation can precede the diagnosis of IBD. Physicians treating patients with IBD must be aware of the presenting symptoms of ocular extra-intestinal manifestations. Patients must be informed to seek

medical attention if experiencing such symptoms. They should also have regular ocular examinations to detect eye involvement and potential side effects of IBD treatment. Timely diagnosis and treatment are important to prevent irreversible visual loss.

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