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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Orbital Myositis in a Patient With Ileal Crohn's Disease in Remission on Vedolizumab

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ABSTRACT

Orbital myositis (OM) is an extremely rare ocular extraintestinal manifestation of inflammatory bowel disease. Acute or chronic inflammation of one or more extraocular muscles leads to symptoms related to the mass effect including orbital pain, swelling, ophthalmoplegia, proptosis, and diplopia. Although the use of steroids typically leads to rapid resolution of symptoms, recurrence is common, necessitating long-term steroid-sparing therapies. Given the rare presentation of OM, its pathogenesis and optimal therapy are not well established. We present a young woman with Crohn's disease in remission on vedolizumab who developed OM, and we discuss our management approach.

INTRODUCTION

Orbital myositis (OM) is a rare ocular extraintestinal manifestation (EIM) of inflammatory bowel disease (IBD) characterized by acute or recurrent inflammation of one or more extraocular muscles. Although other ocular EIMs, such as episcleritis, scleritis, and uveitis, are more common, present in up to 10% of patients with IBD, the development of OM is extremely rare and its true prevalence is unknown.[1] Initially reported in a patient by Greenstein in 1976, OM has since only been described in isolated case reports.[2] OM is most often idiopathic and presents an independent entity; however, it has also been associated with inflammatory bowel diseases. When seen in association with IBD, most cases described occurred in women with Crohn's disease (CD). It typically presents as a unilateral disease with involvement ranging from a single muscle to the entire orbital musculature. The exact pathogenesis of IBD-associated OM is unknown. OM can lead to a myriad of acute ophthalmologic symptoms related to the mass effect and can potentially lead to permanent visual damage if left untreated.[3] Although a few therapeutic strategies have been trialed and published in case reports, strong evidence to inform treatment decisions does not exist, and therefore, management should be individualized.

CASE REPORT

A 26-year-old woman with a 3-year history of nonstricturing, nonpenetrating ileal CD, with a history of primary nonresponse to infliximab, and currently in remission on vedolizumab for the past 3 years, presented with a 2-day history of progressively worsening left eye pain, swelling, and erythema. Her primary nonresponse to infliximab in the past was determined by persistent uncontrolled disease despite appropriate drug levels and lack of antidrug antibody formation. She denied any current changes in vision. She was seen by optometry and was prescribed topical prednisolone drops for presumed scleritis. Few days later, she presented to the ER because of the persistence of symptoms. Examination revealed left periorbital swelling, erythema, and marked tenderness on palpation. C-reactive protein was normal. Laboratory workup for sarcoidosis, immunoglobulin G4 disease, and Grave's disease was negative. Magnetic resonance imaging (MRI) of orbits revealed an abnormal enhancement of the left medial rectus, consistent with inflammatory myositis (Figure 1). She was seen by an ophthalmologist who performed a slit lamp examination which was unremarkable, and her clinical presentation was felt to be consistent with OM. IV methylprednisolone 250 mg 4 times daily was started for 3 days, which led to marked improvement. She was transitioned to an oral prednisone taper down to 20 mg daily, which was

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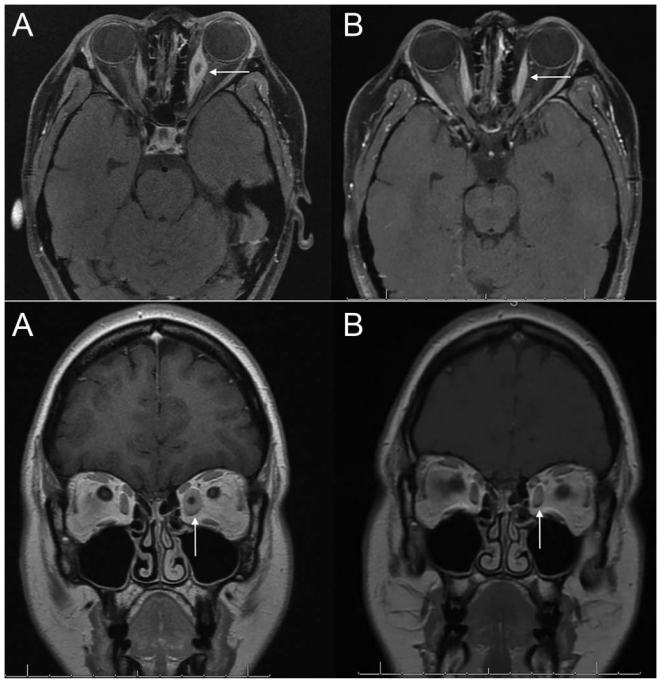

Figure 1. (A) Magnetic resonance imaging of orbits demonstrating abnormal signal and enhancement of the left medial rectus muscle, consistent with inflammatory myositis. (B) Repeat magnetic resonance imaging 4 months later demonstrating near resolution of left medial rectus muscle inflammation.

continued for 4 months while further workup was obtained. Repeat MRI showed marked improvement (Figure 1). On discontinuation of the steroids, her symptoms recurred. Repeat evaluation including slit-lamp examination was performed by the ophthalmology team, and symptoms were deemed to be due to recurrent OM, and this necessitated repeat steroid courses over the next 2 months. Throughout this period, she had no gastrointestinal complaints, and objective re-evaluation of her disease activity which was all performed at the time of ocular symptoms revealed a fecal calprotectin of 30 μg/g, MR enterography was unremarkable, and ileocolonoscopy with biopsies did not demonstrate any active disease, all consistent with deep remission of CD. Given her persistent ocular symptoms and inability to wean off steroid therapy, decision was made in conjunction with ophthalmology to add 6-mercaptopurine (6-MP) 100 mg daily to vedolizumab. After 4 months of follow-up while on vedolizumab and 6-MP, both orbital myositis and CD remain in steroid-free remission.

DISCUSSION

OM occurs predominantly in women, with higher incidence in CD than ulcerative colitis, consistent with our patient's demographics.[4] Symptoms can include orbital pain, swelling, diplopia, and ophthalmoplegia. The development of OM seems to be mostly independent from bowel inflammation and can precede gastrointestinal symptoms or present during remission of IBD because it is the case of our patient.[5,6] Pathophysiology is poorly understood, although proposed mechanisms describe immune complex formation due to cross-reactivity between colonic mucoproteins and extraocular muscles.[7,8] Whether vedolizumab, a gut-selective anti-integrin, unmasked or triggered the development of OM in our patient, as it has been reported with other types of IBD extraintestinal manifestations in the literature, was considered but could not be proven.[18,19] The diagnosis of OM is best established by MRI, which displays hypersignal and contrast enhancement of the involved muscle. Biopsy is not necessary but can show histologic infiltration of polymorphous cells with variable fibrosis.[3,4] Although periorbital erythema and swelling can be present, OM typically lacks scleral injection as seen in other ocular manifestations of IBD such as episcleritis, scleritis, and anterior uveitis. Eye pain and visual changes can be overlapping symptoms in OM, scleritis, and anterior uveitis. Although other ocular EIMs may often respond to topical steroids, a hallmark of OM is a drastic response only to systemic steroids. Slit-lamp examination and ophthalmoscopy can help identify the more common EIMs, and we suggest these be obtained before pursuing an orbital MRI given the relatively higher incidence of other ocular EIMs.[9]

The first-line treatment of OM is high-dose systemic steroids with a prolonged taper. Initiation of steroids characteristically results in rapid resolution of symptoms.[10,11] Although some patients may have a single episode, most cases have reported recurrence rates of up to 52%, which can lead to steroid dependence.[12] Thus, OM has been described as a chronic and recurrent disease. Given the adverse effects of long-term corticosteroid use, treatment with steroid-sparing agents is necessary for optimal long-term maintenance therapy. Multiple approaches have been published including the use of systemic biologic agents, antimetabolites, cytotoxic drugs, intravenous immunoglobulin, and local radiation therapy.[11,13–16]

Biologic therapies, specifically anti-TNF agents, have been associated with high rates of remission of OM. Systemic therapy with agents including infliximab and adalimumab has been shown to be effective in both resolution of OM and prevention of recurrence.[4,17,18] Our patient had a history of primary nonresponse to infliximab despite adequate trough levels and lack of antidrug antibodies. Her CD was proved to be in deep remission with gut-selective vedolizumab, yet her OM was untreated. Rather than switching vedolizumab to a biologic with systemic effect, we decided to add a thiopurine to treat the OM given the risk of IBD flare with discontinuation of successful therapy. In the case of nonresponse to this measure, we considered that our next step would have been ustekinumab over likely a second anti-TNF given earlier mechanistic failure.

Antimetabolites, such as methotrexate (MTX) and thiopurines, have also been shown to be a safe and effective steroid-sparing treatment. There have been fewer cases described in the literature on the use of antimetabolites for chronic OM treatment.[20] The duration of treatment required in OM is also currently unknown. A total duration of 6–24 months has been reported in rare cases

to lead to 3 years of sustained resolution of symptoms.[16] Owing to the high recurrence rates and the chronic nature of OM described in the literature, resumption and continued use of antimetabolites may be necessary, along with routine monitoring for adverse effects. Due to the fact that our patient was a young woman of childbearing age and had underlying non-alcoholic steatohepatitis, we chose to add a thiopurine over MTX to vedolizumab, to avoid the risk of progression of liver disease, or potential teratogenicity associated with MTX use.

To the best of our knowledge, this is the first case of OM in a patient with CD that has developed while on vedolizumab therapy and that was treated successfully with 6-MP as an adjunctive agent. Given its chronic and recurrent nature, long-term therapy of OM can be challenging. An individualized approach to treatment is necessary, with consideration of previous biologic exposure and safety data of available therapies.

DISCLOSURES

Author contributions: S. Sandhu reviewed the literature, wrote the manuscript, revised it for intellectual content, was involved in the final approval of the version to be published, and is the article guarantor. T. Wang revised the manuscript for intellectual content and was involved in the final approval of the version to be published. J. Donet revised the manuscript for important intellectual content and was involved in the final approval of the version to be published.

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