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CASE REPORT | INFLAMMATORY BOWEL DISEASE

Sclerosing Mesenteritis Complicated With Mesenteric Lymphoma Responsive to Ustekinumab

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ABSTRACT

A 45-year-old man with a 10-year history of biopsy-proven, steroid-dependent sclerosing mesenteritis failed/was intolerant to tamoxifen, azathioprine, colchicine, cyclophosphamide, and methotrexate. He developed osteoporosis, diabetes, and bilateral cataracts. He responded to infliximab but was diagnosed with mesenteric large B-cell lymphoma 6 months after treatment initiation. He achieved remission from lymphoma after chemotherapy, but the sclerosing mesenteritis remained poorly controlled. He was treated with ustekinumab (520 mg intravenously followed by 90 mg subcutaneously every 8 weeks), leading to complete steroid-free remission. He remains symptom and cancer-free 24 months after starting ustekinumab.

INTRODUCTION

Sclerosing mesenteritis is a rare disease characterized by chronic inflammation and fibrosis of the mesentery. It often presents with abdominal pain, diarrhea, and bowel obstruction. The underlying etiology is unknown.[1,2] There is a lack of consensus on treatment, which is largely anecdotal.[1] Recommended medical therapies include steroids, colchicine, tamoxifen, 6-mercaptopurine, azathioprine, methotrexate, and cyclophosphamide.[2–4] Biologic agents targeting tumor necrosis factor–alpha (TNF-α) and interleukin 12 and 23 (IL-12,23) are used successfully for induction and maintenance of remission of other inflammatory diseases but are not approved for treatment of sclerosing mesenteritis.[5,6] We present a case, complicated by the development of mesenteric lymphoma, where both infliximab and ustekinumab were successfully used.

CASE REPORT

A 45-year-old man with known sclerosing mesenteritis presents as a follow-up to the clinic. He was diagnosed 5 years before this visit after multiple small bowel obstructions requiring open laparotomies. Small bowel enteroscopy at the time of diagnosis was negative. He was diagnosed after finding a 4-cm omental mass on computed tomography, leading to an excisional biopsy with histopathology revealing fat necrosis and foamy histiocytes (Figures 1 and 2).

Over the past several years, the patient was treated with varying doses of steroids. He had frequent flares, often presenting as a partial bowel obstruction. Each time his prednisone dose was lowered below 20 mg, his symptoms returned. He was trialed on tamoxifen, azathioprine, colchicine, methotrexate, and cyclophosphamide without success but significant adverse events. Cyclophosphamide caused severe neutropenia. Methotrexate was discontinued after development of scarring of his liver.

Because of lack of an effective agent, the patient continued prednisone for over 9 years. He developed steroid-induced osteoporosis, nonalcoholic steatohepatitis, bilateral cataracts, and diabetes mellitus. A report by Rothlein et al describing successful treatment of sclerosing mesenteritis with an anti-TNF agent prompted initiation of off-label infliximab therapy. He started at 5-mg/kg dose per infusion given at 0–2–6 weeks' intervals for induction followed by every 8 weeks for maintenance of remission.[7] The patient became asymptomatic and was able to wean his prednisone dose to 12.5 mg daily for the first time since his diagnosis.

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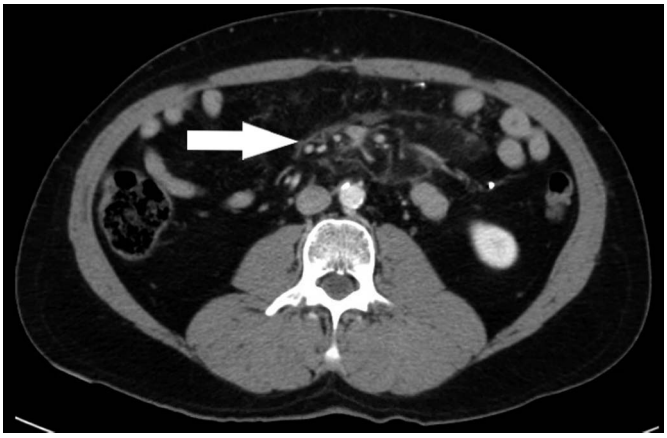

Figure 1. Omental mass (arrow) leading on initial diagnosis of sclerosing mesenteritis.

After nearly 6 months of symptom-free remission on infliximab, the patient presented to the emergency department for abdominal pain. Computed tomography revealed a large mesenteric mass around the same location as his initial mass (5 × 6 cm) (Figure 3). Histopathology was consistent with large B-cell lymphoma. Infliximab was discontinued because of his malignancy, and he continued prednisone monotherapy. He underwent 6 cycles of R-CHOP therapy and stem cell transplant. His prednisone dosage ranged from 15 to 30 mg daily during this chemotherapy period. Positron emission tomography scan during treatment showed significant interval decrease in size of the mass and a decrease in fluorodeoxyglucose activity. Follow-up computed tomography scan after completion of treatment showed only scarring of mesentery and no active disease or inflammation (Figure 4). However, he remained symptomatic from his sclerosing mesenteritis on prednisone monotherapy without further immunosuppression.

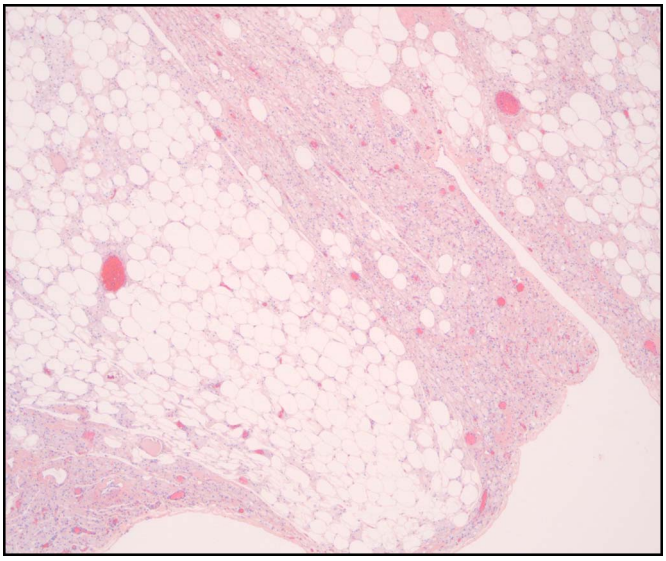

Figure 2. Fat necrosis and foamy histiocytes demonstrating diagnosis of sclerosing mesenteritis.

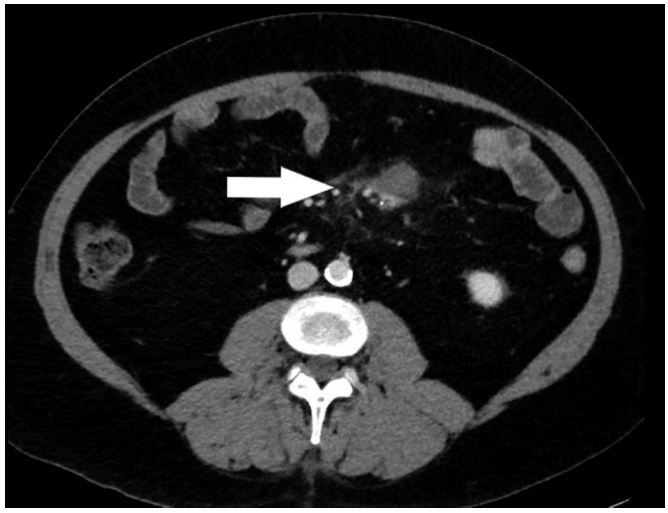

Figure 3. Omental mass (arrow) consistent with B-cell lymphoma.

Multiple attempts to taper prednisone below 15 mg resulted in recurrence of abdominal pain and diarrhea requiring repetitive bursts of prednisone. Two years after remission from cancer and discussions with the patient's oncologist, it was decided to pursue an alternative treatment with a non–TNF-α biologic. An off-label use of ustekinumab was pursued. The patient was induced with a 520-mg dose intravenously and continued on 90-mg dose subcutaneously every 8 weeks, leading to complete resolution of sclerosing mesenteritis symptoms. He was able to taper off prednisone after ustekinumab initiation and has been steroid-free for over 2 years. Cross-sectional imaging after 12 and 24 months of therapy was without any inflammation in his mesentery and only demonstrated scarring.

DISCUSSION

Therapy options for sclerosing mesenteritis are limited, largely because of unclear pathophysiology. Because sclerosing mesenteritis is steroid-responsive, a wide range of steroid-sparing

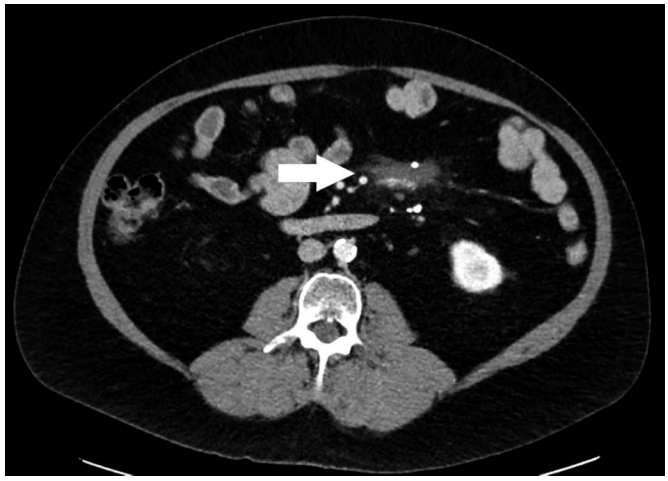

Figure 4. Scarring of mesentery (arrow) with no active disease or inflammation.

immunosuppressive agents were trialed with varying efficacy and tolerability. TNF-α– and IL-12,23–mediated T-cell activation is linked to many chronic inflammatory conditions such as inflammatory bowel disease, rheumatoid arthritis, ankylosing spondylitis, and psoriasis.[8] For these conditions, anti-TNF antagonist infliximab and IL-12,23 antagonist ustekinumab are effective treatment options.[9,10] In 1 open-label pilot study, sclerosing mesenteritis was shown to benefit with treatment from another TNF-α suppressant, thalidomide.[11] These relationships, along with Rothlein's findings, were fundamental for trialing ustekinumab in our patient.

Similar to Rothlein's experience, our patient responded to infliximab. However, its use was hampered by the new diagnosis of mesenteric lymphoma. The likely cause was the patient's 8 years of chronic inflammation. Up to 15% of patients with sclerosing mesenteritis may develop mesenteric lymphoma in their lifetime.[8] It is unlikely infliximab had played a role in the development of lymphoma, given the short period between initiation and the diagnosis. However, there is a known increased malignancy risk with anti-TNF therapies but no head-to-head comparison of ustekinumab vs infliximab.[12] Because of this, the oncology team recommended switching agents. Ustekinumab proved to be effective in inducing steroid-free remission without causing relapse of the mesenteric lymphoma. The successful use of infliximab and ustekinumab in our patient's clinical course may suggest that upregulation of the TNF-α– and IL-12,23–dependent immune pathways may play a role in the pathophysiology of sclerosing mesenteritis.

To the best of our knowledge, this is the first case of steroid-dependent sclerosing mesenteritis where ustekinumab was successfully and safely used to induce and maintain steroid-free remission. This case demonstrates the limitations of currently available treatment options for this disease. Given the rare symptomatic occurrence of the disease, it is unlikely that results from randomized controlled intervention trials will be available to inform treatment decisions. Therefore, case studies setting a precedent for novel effective therapies are important. We hope our experience with infliximab and ustekinumab in the treatment of sclerosing mesenteritis will open an avenue for patients and assist clinicians in obtaining insurance coverage for off-label biologic therapy.

DISCLOSURES

Author contributions: Ben Byriel, DO is the article guarantor. B. Byriel wrote the manuscript and revised the manuscript for intellectual content. M. Walker edited the manuscript. M. Fischer edited the manuscript and revised the manuscript for intellectual content. All authors approved the final manuscript.

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