Insulin-like Growth Factor I Receptor Inhibitor Induced Inflammatory Bowel Disease

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Introduction

Graves' orbitopathy is a debilitating autoimmune disease that develops in approximately 40% of patients with Graves' disease. Insulin-like growth factor I receptor (IGF-IR) is overexpressed in this disease and plays a central role in this ophthalmopathy. Teprotumumab is a monoclonal antibody against IGF-IR used for active Graves' orbitopathy. We report a patient who presented with rectal bleeding and was found to have a reoccurrence of inflammatory bowel disease (IBD) thought to be secondary to recent teprotumumab therapy.

Case Presentation

- 46 year-old female presented with persistent rectal bleeding for more than a week
- Past Medical History: colonic Crohn's disease (documented endoscopic and histologic remission for 2 years), pyoderma gangrenosum, psoriasis, vitiligo and Grave's orbitopathy
- Recently finished teprotumumab infusions
- Labs: Hemoglobin 11.4, CRP 0.4, ESR 28
- Colonoscopy – diffuse continuous severe inflammation extending from dentate line up to 35 cm (sigmoid colon) as well as the presence of a cecal patch
- Biopsy of colonic tissue – active proctocolitis with cryptitis, crypt abscesses and lymphoplasmacytosis
- Treatment – IV solumedrol, then transitioned to oral prednisone
- Follow up – IBD clinic 3 weeks later, achieved clinical remission and therefore tapered prednisone. Offered multiple options for maintenance therapy, however was not interested in biologic immunosuppressive therapy. Started on aminosalicylates with plan for flexible sigmoidoscopy at 6 months

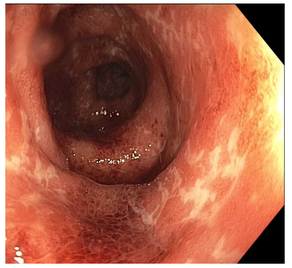

Figure 1. Endoscopic evaluation revealing inflammation in the sigmoid colon.

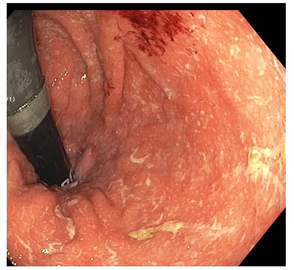

Figure 2. Endoscopic evaluation of rectum with diffuse inflammation and internal hemorrhoids.

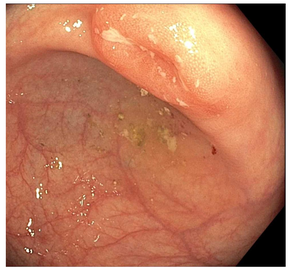

Figure 3. Presence of cecal patch on endoscopic assessment.

Discussion

- IGF-1 induces proliferation of regulatory T cells and pause progression of autoimmune disease in the bowel.
- Patient's with active IBD have reduced IGF-1
- Inferred that use of teprotumumab, a medication whose method of action is to inhibit growth factor receptor, may exacerbate IBD
- Prescribing information caution use in IBD patients. IBD patients were excluded from phase 3 clinical trial of teprotumumab

Conclusion

Unfortunately in this case, teprotumumab was the likely etiology of the patient's reactivation of IBD. This highlights a potentially detrimental side effect and appropriate discussions with patients should be held prior to this medication administration. Ideally the gastroenterologist should be kept abreast of the decision to initiate such therapy to allow for careful monitoring.

References

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