

Strictures Following Ustekinumab Treatment in Patient with Crohn's Disease

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1. Abstract

Crohn's disease is a chronic inflammatory entity that affects the gastrointestinal tract transmurally in variable pattern. It is classified according to age of presentation, location, behavior and severity. This case illustrates a patient with severe Crohn's disease with poor prognostic characteristics that was treated with two biologics infliximab and Ustekinumab. Ustekinumab resulted in anorectal and colonic strictures and this is the first case to report this complication in Ustekinumab. The colonic stricture responded to dilatation but the anorectal stricture showed partial response to dilatation.

2. Introduction

Crohn's disease is a chronic idiopathic inflammatory condition that can affect the gastrointestinal tract from mouth to anus and can also has extraintestinal manifestations, so it is considered a systemic illness that can affect any organ of the body [1]. It is characterized with transmural involvement and skip lesions [2].

There are several treatment options for Crohn's disease including immunomodulators, steroids and biologics that induce and maintain remission [3].

Ustekinumab is an IL12/23 inhibitor that it is used for treatment of moderate to severe Crohn's disease, ulcerative colitis, psoriasis and rheumatological diseases [4].

3. Case Report

The patient is a 22 year old male patient who was diagnosed to have Crohn's disease (Montreal classification A1, L3, B3P and CDAI 400) in 2014. He was initially started on Infliximab 5mg/kg at week zero, two and six and then every eight weeks along with Azathioprine 2mg/kg daily. He responded very well on treatment until June 2020 when he got a flare of his disease and active peri-

anal disease. Inflammatory markers such as ESR (90), CRP (150) and calprotectin (1000) were high. Stool tests did not reveal any infectious agent. Clonoscopy showed perianal fistulae with active colonic and ileal disease. Biopsies showed active disease but no evidence of CMV infection. Therefore, Infliximab was increased to 10mg/kg every 8 weeks but with no response over the following 12 weeks despite increasing the frequency of Infliximab to become every 4 weeks and increasing the azathioprine to 2.5mg/kg daily. Then, the decision was to start Ustekinumab 390 mg intravenous induction dose followed by 90 mg subcutaneously every 8 weeks. His diarrhea stopped and the inflammatory markers decreased substantially but he developed constipation in March 2021. Colonoscopy was planned but on per rectal exam the anus was stenosed that per rectal exam could not be done and the old fistulae were closed and scarred, so a pediatric gastroscopy was used to evaluate the anorectal area and the rest of colon and small bowel. This showed severe anorectal stricture with relatively normal rectal segment proximal to the stricture and then two segmental stenosis at of around 3 cm at 25 cm and 35 cm from anal verge. Biopsies were taken from the strictures and were benign. Pelvic MRI and examination under anesthesia revealed no collection and no fistulae but the short segment stenoses. Colonoscopy and balloon dilatation were planned and done with satisfactory results of the sigmoid strictures but the anorectal stricture still tight, so a joint decision was taken to be dilated with Hegars self-dilators and not to use larger balloon dilators because of the risk of incontinence secondary to the anal sphincter injury from balloons.

4. Discussion

Crohn's disease is a chronic inflammatory bowel disease of unknown etiology that causes transmural inflammation of the gut from mouth to anus. Treatment of Crohn's disease depends on sev-

eral factors: location of the disease, severity, activity, extraintestinal involvement, presence of poor prognostic factors and previous treatment [1, 3].

Biological agents are indicated for moderate to severe Crohn's disease. There are several classes of these agents like anti-tumor necrosis factor, anti-integrin $\alpha 4$, $\beta 7$, anti IL12/23.

Patients with Crohn's disease are prone to develop colonic strictures that can be due to the disease itself, surgeries and anastomosis, and medications. There is conflicting evidence of whether anti-TNF can exacerbate fibrostenotic lesions in patients with Crohn's disease or not [4, 5].

This case showed the development of multiple strictures following the commencing of Ustekinumab treatment which is the first case reported in medical literature. There are documented cases of acute intestinal obstruction following the initiation of anti TNF agents [6]. The cause of stricture in this case could be due to rapid aberrant healing which results in scarring and stenosis.

This patient was treated with balloon dilatation which was effective in colonic strictures but not the anorectal stricture indicating the need to adopt another approach for dilatation such as self-dilatation or stricturotomy using needle knife.

In conclusion, the anorectal stricture and colonic strictures could be a complication of Ustekinumab treatment but this needs further studies to confirm it.

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