



ELDERLY ONSET CROHN'S DISEASE WITH HIGH DISEASE ACTIVITY- A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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ABSTRACT We present a case of an 82-year-old diabetic gentleman who presented with complaints suggestive of subacute intestinal obstruction. He was treated conservatively initially and improved. But, following radiological reports he was diagnosed as Elderly onset Crohn's disease with high disease activity. After proper screening, he was initiated on Anti-TNF alpha inhibitor but due to spontaneous intestinal perforation, it was discontinued. Emergency exploratory laparotomy was done, and he improved gradually post-op. Oral Mesalamine and Budesonide were then initiated, but due to frequent mood swings, worsening TLC, and liver enzymes, they were stopped. Lastly, antibiotic therapy was initiated with Oral ciprofloxacin and metronidazole which improved his abdominal symptoms. He was discharged after optimization of his nutritional status. Hence, we present a case of difficult to manage elderly onset Crohn's disease with high disease activity.

KEYWORDS :

INTRODUCTION

Inflammatory bowel disease (IBD) comprises two major disorders – Ulcerative colitis (UC) and Crohn's disease (CD). CD is characterized by transmural inflammation and may involve any part of luminal gastrointestinal tract, from the oral cavity to the perianal area [1].

CD is usually seen in early adulthood with the initial onset of symptoms in patients usually in their early 20s.

However, due to the bimodal distribution of the disease, there may be another late peak which can occur between 50 and 70 years of age [2,3]. Around 10%-15% of patients diagnosed with IBD are older than 65 years of age [4].

Elderly patients with IBD are classified as those with elderly onset (EO-IBD) who have symptom onset after the age of 60 years [5] and those with non-elderly onset (NEO-IBD) according to the timing of the disease onset and subsequent disease duration.

A cross-sectional study by Gupta et al done in India concluded that the prevalence of elderly onset IBD in the current study was 4.74% and elderly onset IBD is not uncommon in India.

Clinical Course

82-year old gentleman, known diabetic presented with complaints of pain abdomen and constipation for the last 5 days. He had occasional episodes of fever, multiple joint pains, and nausea. He had no history of passing black stools or blood in stools and diarrhea.

At presentation, his vitals were Blood Pressure 100/80mm Hg, Heart rate 100/min. Clinical examination revealed pallor, clubbing, and an irregular mass of around 3 cm diameter, firm in consistency palpable in the epigastric and right lumbar region.

Laboratory workup showed Hemoglobin 9gm/dl, TLC 14000/cu mm, Platelet 1.6lac/cu mm, Creatinine 1.5mg/dl, Albumin 2gm/dl, SGOT 75U/dl, SGPT 86U/dl, ALP 120IU/dl, CRP 12.7mg/dl (<0.5mg/dl), faecal calprotectin 2636.

CT Whole Abdomen demonstrated multiple thick-walled strictured segments with enhancing mucosal lining seen mid to distal ileum and one of the segments between the 2 structured segment appeared ectatic and dilated.

He underwent MR Enterography which showed a long segmental distal loop dilatation with loss of segmentation forming pipe like appearance, deformed ileo-caecal junction with mesenteric thickening, and right iliac lymphadenopathy.

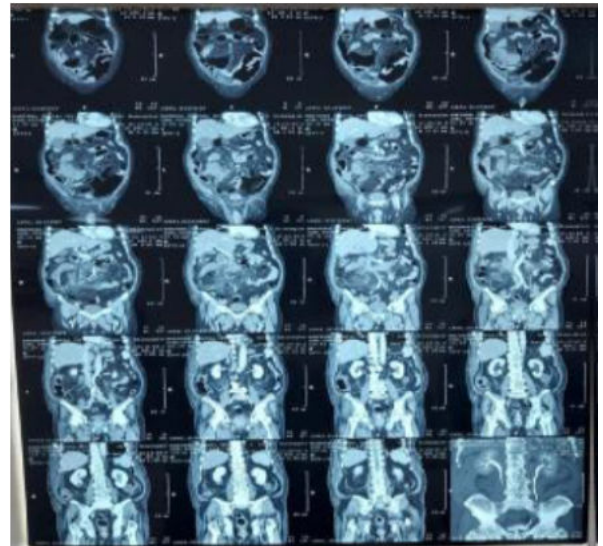


Figure 1

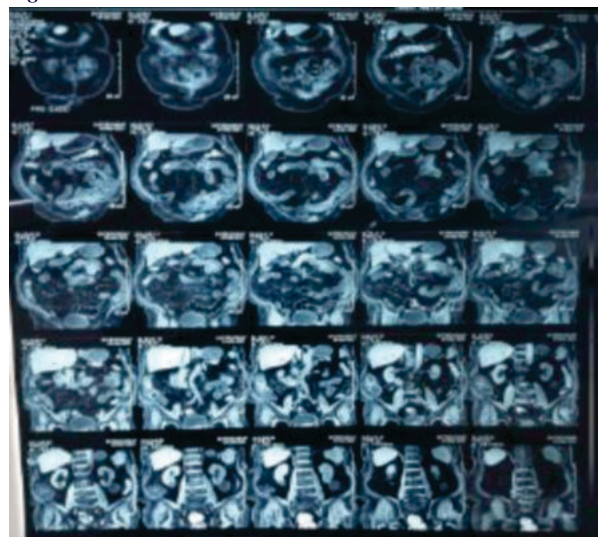


Figure 2

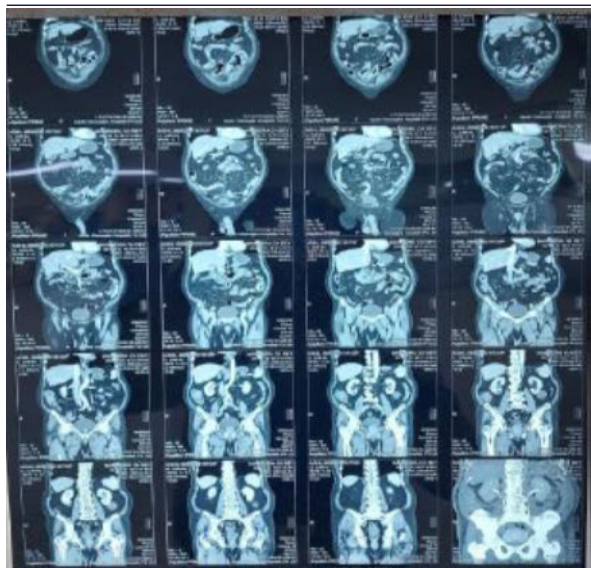


Figure 3
FIGURE 1,2 & 3: Radiological Images Showing Multiple Constrictions In Small Bowel

He was then diagnosed as elderly onset Crohn's disease with subacute intestinal obstruction. He was treated conservatively initially with IV Fluids and IV Antibiotics with Ceftriaxone and Metronidazole. He improved symptomatically in the next 3 days. Colonoscopy revealed terminal ileitis with partial stricture. Colonoscopic biopsy showed non-specific ileitis with mild chronic inflammation. He was planned for immunosuppressive therapy. HBV DNA, Anti Hep C, HIV antibody, IGRA, TB Gene Xpert all came were negative.

He was started on anti-TNF alpha inhibitor Adalimumab-40mg on Day 1 and Day 2. But on Day 2 of receiving it, he developed fever, pain abdomen, bloating of the abdomen, obstipation with increasing total count, CRP with guarding of the abdomen, and sluggish IPS.

Repeat CECT whole abdomen revealed terminal ileum perforation with abscess formation in the right iliac fossa. He underwent exploratory laparotomy and Adhesiolysis with ileal resection and end ileostomy. He made recovery from the complications of surgery conservatively.

He was initiated on oral Mesalamine and Budesonide on Day 7 post-op, after ruling out any active infection. But on day 5 of initiation, he had a gradual worsening of SGOT, SGPT, ALP, and WBC counts along with frequent mood swings and nausea. Mesalazine and Budesonide were discontinued. The mentioned symptoms and blood parameters improved after stopping them. He was then started on Antibiotic therapy for Crohn's disease with ciprofloxacin and metronidazole. He improved on the abdominal symptoms of Crohn's disease and was discharged after optimizing his nutritional status.

DISCUSSION

EOCD (elderly onset Crohn's disease) is more severe than compared to young individuals and has less extraintestinal manifestations and very few have a family history of CD. EOCD usually manifests with colonic involvement [6].

EOCD is difficult to diagnose and often gets missed and confused with other differential diagnoses commonly seen in the elderly like Diverticulosis, NSAID-induced colitis, radiation colitis and ischaemic colitis, infectious colitis. The disease course is inflammatory, and the patient can present with atypical manifestations rather than common presenting symptoms of abdominal pain, diarrhoea, and bleeding per rectum as seen in younger individuals [7]. EOCD can lead to a multitude of complications, including abdominal abscesses, entero-enteric or perianal fistulas, and bowel obstruction, localized peritonitis, and these complications increase with the duration of the disease [8].

Our patient had high faecal calprotectin with multiple strictured segments which were suggestive of Crohn's disease, and a score of 324

as per Crohn's disease activity index- suggestive of moderate to severely active Crohn's disease [9].

Treatment of Crohn's disease includes induction and maintenance therapy. Our patient with the said disease activity required immunosuppression which was done as per protocol with TNF-alpha inhibitor adalimumab after appropriate screening [10].

However, he had a spontaneous gut perforation with abscess formation following the initiation of immunosuppressive therapy and required emergency surgery. Resection of the diseased portions of the gut was done. Surgery as a treatment option for Crohn's disease is well-documented in cases of primary treatment failure or complications [11].

Following his recovery from the surgery, he was initiated on maintenance therapy with oral steroid Budesonide and 5-aminosalicylic acid Mesalazine. Budesonide is recommended to induce remission in mild-to-moderate distal small bowel and right-sided colonic CD and affects bone metabolism less than conventional corticosteroids [12]. However, side effects include altered mental state, depression, and fluid retention which are more seen in the elderly, as was seen in our patient [13]. Mesalazine is a widely used current therapeutic strategy for maintaining remission in Crohn's disease, having better effects in surgically induced remission and or limited small bowel disease [14]. Side effects include rising liver enzymes, blood dyscrasias which were seen in our case, which forced us to stop them [15].

Failure of steroids and 5-ASA led us to go on to the next phase of treatment for the disease. A full dose of ciprofloxacin and metronidazole combination for a mean duration of 10 weeks has shown good results in achieving and maintaining remission in patients of Crohn's disease with more than 75% efficacy. The most probable mechanism is due to the suppression of intestinal bacteria causing inflammation leading to the disease [16]. Our patient tolerated the antibiotics well and has been now on regular follow-up.

CONCLUSION

Hence, we present a case of Elderly onset Crohn's disease with moderate to severe disease activity where great challenges were faced in the diagnostic and treatment phase requiring every little detail of literature present regarding the subject.

Since the introduction of tumor necrosis factor (TNF)-alpha inhibitors, other drugs have become available that are highly effective in patients with Crohn's disease, including ustekinumab, which is a monoclonal antibody that binds to the p40 subunit of interleukin (IL)-12 and IL-23, and vedolizumab, which is an antagonist that binds to alpha-4-beta-7 integrin. Since the introduction of tumor necrosis factor (TNF)-alpha inhibitors, other drugs have become available that are highly effective in patients with Crohn's disease, including ustekinumab, which is a monoclonal antibody that binds to the p40 subunit of interleukin (IL)-12 and IL-23, and vedolizumab, which is an antagonist that binds to alpha-4-beta-7 integrin. Since the introduction of tumor necrosis factor (TNF)-alpha inhibitors, other drugs have become available that are highly effective in patients with Crohn's disease, including ustekinumab, which is a monoclonal antibody that binds to the p40 subunit of interleukin (IL)-12 and IL-23, and vedolizumab, which is an antagonist that binds to alpha-4-beta-7 integrin.

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ustekinumab in a case of EOAD who was diagnosed with CD at the age of 65 years and had loss of responsiveness to two TNF alpha inhibitors

Patient Consent: TAKEN

Conflict Of Interest: NONE

REFERENCES

- [1] UPTODATE
- [2] Loftus EV Jr, Silverstein MD, Sandborn WJ, Tremaine WJ, Harmsen WS, Zinsmeister AR. Ulcerative colitis in Olmsted County, Minnesota, 1940-1993: incidence, prevalence, and survival. *Gut*. 2000;46:336-343.
- [3] Rose JD, Roberts GM, Williams G, Mayberry JF, Rhodes J. Cardiff. Crohn's disease jubilee: the incidence over 50 years. *Gut*. 1988;29:346-351.
- [4] Charpentier C, Salleron J, Savoye G, et al. Natural history of elderly-onset inflammatory bowel disease: a population-based cohort study. *Gut*. 2014;63:423-432
- [5] Saygili F, Saygili SM, Tenlik I, Yuksel M, Kilic ZMY, Ozin YO, Kayacetin E. Crohn's disease in the elderly: clinical presentation and manifestations from a tertiary referral center in Turkey. *North Clin Istanb*. 2017;3:183-186.
- [6] Desai A, et al. Older age is associated with higher rate of discontinuation of anti-TNF therapy in patients with inflammatory bowel disease. *Inflamm. Bowel Dis*. 19, 309-315. doi: 10.1002/ibd.23026.
- [7] Kappelman MD, Horvath Puho E, Sandler RS et al. Thromboembolic risk among Danish children and adults with inflammatory bowel disease patients. *Am J Gastroenterol* 2008; 103 :2272.
- [8] Iwamoto M, Kato K, Moriyama M. Elderly-onset Crohn's disease remarkably responsive to ustekinumab: a case report. *Int J Colorectal Dis*. 2020 Feb; 35(2):355-359. doi: 10.1007/s00384-019-03476-y.
- [9] Freeman HJ. Use of the Crohn's disease activity index in clinical trials of biological agents. *World J Gastroenterol*. 2008 Jul 14; 14(26):4127-30. doi: 10.3748/wjg.14.4127.
- [10] Cushing K, Higgins PDR. Management of Crohn Disease: A Review. *JAMA*. 2021 Jan 5; 325(1):69-80. doi: 10.1001/jama.2020.18936.
- [11] Scott A Strong. *Surgical Management in Crohn's Disease*. National Library of Medicine. 2001.
- [12] Everhov AH, Halfvarson J, Myreliid P, Sachs MC, Nordenvall C, Söderling J, Ekbohm A, Neovius M, Ludvigsson JF, Askling J, Olén O. Incidence and Treatment of Patients Diagnosed with Inflammatory Bowel Diseases at 60 Years or Older in Sweden. *Gastroenterology*. 2018; 154:518-528.e15.
- [13] Akerkar GA, Peppercorn MA, Hamel MB, Parker RA. Corticosteroid-associated complications in elderly Crohn's disease patients. *Am J Gastroenterol*. 1997; 92:461-464.
- [14] Brookes MJ, Green JR. Maintenance of remission in Crohn's disease: current and emerging therapeutic options. *Drugs*. 2004; 64(10):1069-89. doi: 10.2165/00003495-200464100-00004.
- [15] Ransford RA, Langman MJ. Sulphasalazine and mesalazine: serious adverse reactions re-evaluated on the basis of suspected adverse reaction reports to the Committee on Safety of Medicines. *Gut*. 2002 Oct; 51(4):536-9. doi: 10.1136/gut.51.4.536.
- [16] Greenbloom SL, Steinhart AH, Greenberg GR. Combination ciprofloxacin and metronidazole for active Crohn's disease. *Can J Gastroenterol*. 1998 Jan-Feb; 12(1):53-6. doi: 10.1155/1998/349460.