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A Disease Course of the Oldest Crohn's Disease Patient Reported in Türkiye

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ABSTRACT

Background: Crohn's disease is an inflammatory bowel disease predominantly seen in young people. However, owing to its bimodal age distribution, it reaches its second peak between the ages of 50–70. The treatment of elderly Crohn's disease patients (described as over 60 years of age) remains controversial. Very few studies have described the treatment of elderly patients in our country.

Case Report: We present the management of the oldest patient ever identified with Crohn's disease in our country. In light of recent evidence, the optimal agent for treating fragile patients and those with a history of infections is vedolizumab. However, vedolizumab is not reimbursed as a primary treatment in our country. Therefore, we treated the patient with corticosteroids and azathioprine.

Conclusion: We have determined that the use of corticosteroids for induction of remission and azathioprine for maintenance of remission is safe, on a case-by-case basis, within the framework of conditions in our country.

Keywords: Azathioprine, Crohn's disease, elderly, treatment.

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INTRODUCTION

Typically, the onset of Crohn's disease (CD) symptoms occurs in early maturity during the twenties. Due to the bimodal age distribution of the disease, a second peak can be observed between the ages of 50 and 70 years.[1] Patients over 60 years of age with inflammatory bowel disease (IBD) are considered elderly. In the only study conducted on elderly patients in Türkiye, the oldest patient diagnosed with Crohn's disease was 82 years old.[2] In this case presentation, we describe the management of the oldest CD patient with multiple comorbidities reported in our country to date.

CASE REPORT

An 84-year-old female patient was admitted to the gastroenterology division with bloodless diarrhea, impaired general condition, acute renal failure, and anemia. She had previously been diagnosed with Alzheimer's disease, cerebrovascular disease, and coronary artery disease. The patient had been bedridden for the past four months. Over the last six months, she had been admitted to the internal medicine department four times with complaints of diarrhea, poor general condition, urinary tract infection, and acute kidney injury. Due to diarrhea, the patient's rela-

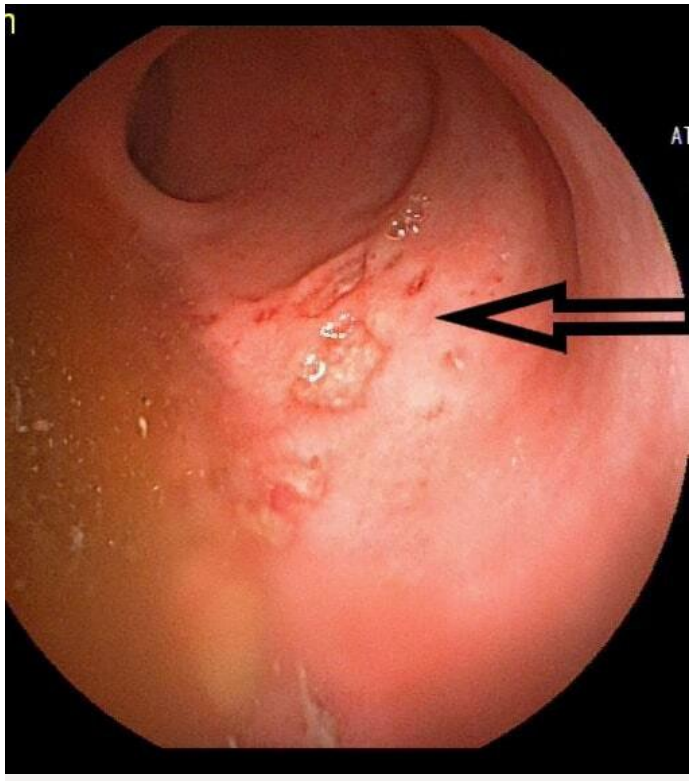

Figure 1. Deep, ovoid, and punch-hole-shaped ulcers in the rectum (as seen in colonoscopy).

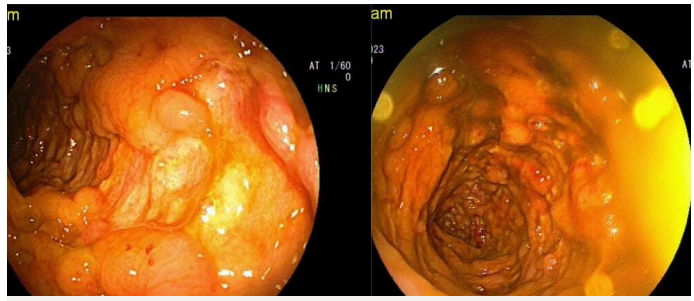

Figure 2. Deep ulcers extending parallel to the lumen (left) and a cobblestone appearance (right).

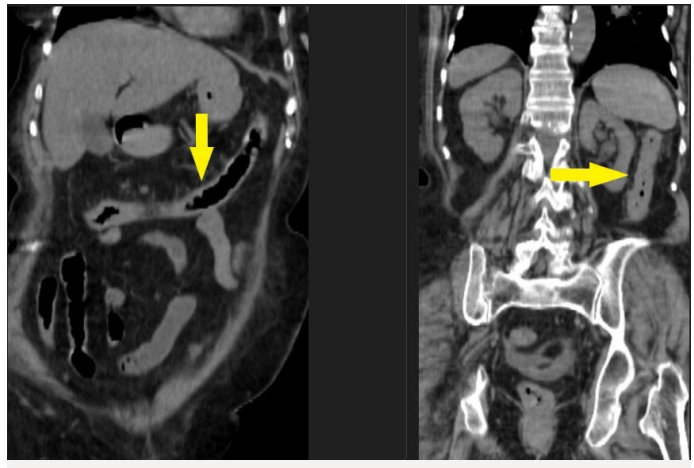

Figure 3. Computerized tomography showing thickening and loosening of the haustra formation of the colonic wall (transverse colon on the left; descending colon on the right).

tives had to change her nappies five to six times per day. On examination, her conjunctiva and skin were pallid, and there was prominent bilateral pretibial edema. Her blood pressure was 110/60 mmHg, heart rate was 95 beats per minute, and respiratory rate was normal. Laboratory values showed urea: 126 mg/dL, creatinine: 3.2 mg/dL, hemoglobin: 9 g/L, white blood cell count: 11.2 x 10^3/uL, platelet count: 278 x 10^3/uL, serum total protein: 3.7 mg/dL, serum albumin: 1.9 mg/dL, C-reactive protein: 148 mg/L, Na: 134 mEq/L, K: 2.7 mEq/L, Cl: 111 mEq/L, and erythrocyte sedimentation rate: 60 mm/hr. No pathogenic bacteria or parasites were detected in the stool culture. Toxin A and B for Clostridium difficile and adhesin antigen for Entamoeba histolytica were negative. Proteinuria was not detected. A colonoscopy was performed, revealing deep, ovoid, and punch-hole shaped ulcers throughout the normal mucosa of the rectum (Fig. 1). Deep ulcers parallel to the lumen and a cobblestone appearance were seen in the sigmoid and descending colon as it moved proximally (Fig. 2). Due to significant involvement and the patient's intolerance, it was not possible to proceed to the proximal level. Histopathological analysis revealed non-necrotizing granulomas. Computed tomography scans showed increased thickness of the colon wall and disappearance of the haustra structures (Fig. 3).

The patient was diagnosed with Crohn's disease based on all findings. The patient was administered low-molecular-weight heparin and antibiotherapy during ward follow-up for thrombophlebitis, and right arm cephalic vein thrombus formation due to vascular access. Percutaneous endoscopic gastrostomy was performed on an Alzheimer's patient who refused to take oral medications. Prior to beginning immunosuppressive treatment, it was determined whether the patient had been exposed to tuberculosis and hepatitis B virus. She had received the hepatitis B vaccination. The Purified Protein Derivative (PPD) test measured 3 millimeters. Additionally, echocardiography demonstrated a decreased ejection fraction (45%) and segmental apical hypokinesis. A cardiology examination revealed New York Heart Association (NYHA) grade 3 cardiac failure. With the diagnosis of non-stricturing, non-penetrating, predominantly colonic, severe luminal CD, 0.75 mg/kg of corticosteroids were administered. Since anti-tumor necrosis factor (TNF) could not be administered as a maintenance treatment

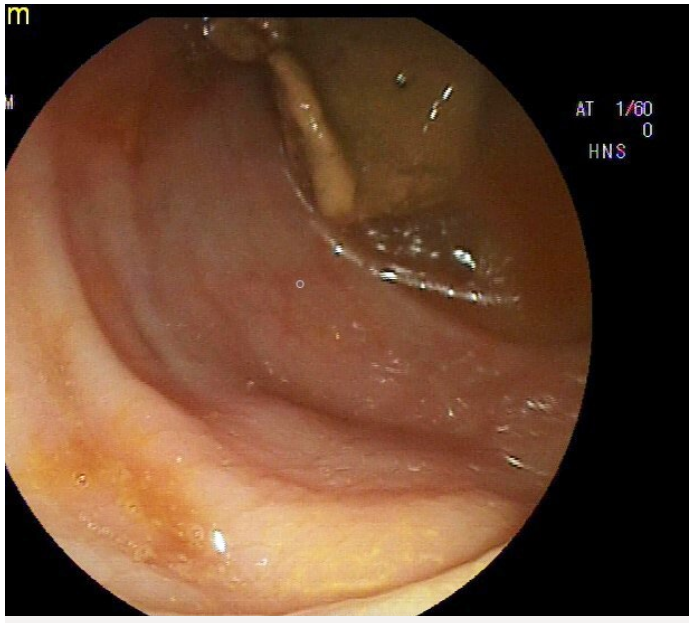

Figure 4. Control colonoscopy reveals normal mucosa in the sigmoid colon.

due to heart failure, vedolizumab was considered, primarily due to the patient's age, multiple comorbidities, and history of infections. However, we were unable to obtain the vedolizumab we needed due to the healthcare policies in our nation (the cost of vedolizumab was not covered by our insurance for first-line treatment). Therefore, azathioprine at a dosage of 2.5 mg/kg was administered as a standalone treatment to maintain remission. The patient's observation in the hospital ward continued for 3.5 months. The patient's symptoms of diarrhea disappeared entirely, and test readings returned to normal. Rectosigmoidoscopy, conducted 24 weeks after the initial therapy was started, showed that the mucosal appearance of both the rectum and sigmoid colon was normal (Fig. 4).

DISCUSSION

According to the findings of large-scale investigations carried out in our nation, Crohn's disease is most prevalent in young adults. These findings are consistent with those of previous studies. Researchers Tozun et al.[3] examined 877 IBD patients between 2001 and 2003 and found that the average age of CD patients (n=216) was 37.4±12.8 years. In the only study conducted in our country on elderly patients with Crohn's disease, ages ranged from 60 to 82 years (median 66 years).2 Hugh J. Freeman presented data on 43 patients over 60 years of age, with the oldest female patient being 82 years and the oldest male 86 years. However, the oldest reported CD patient worldwide was 92 years of age.[4] Our patient is the eldest with Crohn's disease described in our country to date.

In addition to Crohn's disease in elderly patients, infectious, ischemic, and segmental colitis due to diverticular disease, as well as drug-related colitis (associated with nonsteroidal anti-inflammatory medications, digitalis, sodium phosphate enema), should be considered.[5] The long duration of diarrhea in our patient (approximately six months), absence of infectious causes in stool samples, no diverticula observed in tomography and colonoscopy, no new medications in the anamnesis, lack of sudden pain typical in ischemic colitis, absence of hematochezia, involvement of the rectum, and all colonic segments affected in tomography led us to diagnose Crohn's disease, confirmed by the presence of non-caseating granulomas in the biopsy. Corticosteroid therapy was administered to induce remission.

The risks of infection and cancer are heightened in the treatment of older adults, making these issues particularly challenging. These factors should be considered when developing treatment plans. To consider less detrimental therapy for elderly IBD patients, less effective aminosalicylates and long-term low-dose steroids are commonly administered.[6]

Corticosteroids and aminosalicylates are not recommended by the European Crohn's and Colitis Organisation (ECCO) guidelines for the maintenance of remission in CD. Thiopurines, anti-TNF agents, vedolizumab, and ustekinumab are recommended agents.[7]

Anti-TNF agents are contraindicated in heart failure, particularly in stages 3 and 4, according to the NYHA classification. Therefore, this option was not applicable for our patient.[8]

As vedolizumab is a gut-selective agent that produces less systemic immunosuppression, fewer or comparable adverse events were observed compared to other agents. Despite having less available data, ustekinumab is among the recommended agents.[9] Although vedolizumab was the treatment of choice for an elderly and frail patient with a history of infection, it could not be administered in our country as it was not permitted as a first-line medication.

It has been noted that the use of thiopurines is associated with an increased risk of long-term malignancy (including non-melanoma skin cancer and lymphoproliferative disease), as well as increased acute-term hepatotoxicity in older IBD patients. However, thiopurines might be favored in many individuals due to their oral form and convenience of administration. Avoiding or discontinuing these medications solely on the basis of the patient's chronological age is not an acceptable practice. A decision should be made after conducting a case-by-case analysis.[10]

CONCLUSION

In our case, all the hazards associated with azathioprine administration were discussed with the patient's family. Clinical and endoscopic remission were achieved after 24 weeks of treatment.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Conflict of Interest: The author have no conflict of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

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