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CASE REPORT

Ustekinumab or vedolizumab for refractory metastatic Crohn's disease?

Refrakter metastatik Crohn hastalığında ustekinumab veya vedolizumab?

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Metastatic Crohn's disease is a rare skin manifestation of Crohn's disease. A variety of treatment options are available for this condition. But there is a lack of clarity regarding the treatment of resistant cases. There is ongoing debate as to which agent should be selected (vedolizumab or ustekinumab) in patients that are not responding to anti-tumor necrosis factor agents. This study identifies a unique patient who has developed a disease (metastatic Crohn's disease) under treatment with vedolizumab. Following treatment with ustekinumab, the patient regressed completely. Therefore, we recommend ustekinumab primarily in metastatic Crohn's disease.

Key words: Metastatic Crohn's disease, ustekinumab, vedolizumab

Metastatik Crohn hastalığı, Crohn hastalığının nadir görülen deri tutulumudur. Bu tutulum için çeşitli tedavi seçenekleri mevcuttur. Ancak dirençli vakaların tedavisi konusunda netlik yoktur. Anti-tümör nekrozis faktör ajanlara yanıt vermeyen hastalarda hangi ajanın (vedolizumab veya ustekinumab) seçilmesi konusunda tartışmalar devam etmektedir. Bu çalışmada, vedolizumab tedavisi altında iken hastalık (metastatik Crohn hastalığı) gelişen benzersiz bir hasta tarif etmekteyiz. Ustekinumab tedavisi sonrası hastalık tamamen geriledi. Bu nedenle metastatik Crohn hastalığında öncelikle ustekinumab tedavisini önermekteyiz.

Anahtar kelimeler: Metastatik Crohn hastalığı, ustekinumab, vedolizumab

INTRODUCTION

Between 18 and 44% of Crohn's patients have been reported to have skin involvement (1). The rarest cutaneous form, metastatic Crohn's disease (MCD) was described by Park et al. in 1965 (1,2). Although its treatment remains controversial, topical treatments and systemic immunosuppressants are employed (3). In this study, we sought to demonstrate the successful treatment of peristomal metastatic Crohn's disease with ustekinmab in a patient who had undergone total proctocolectomy, was unresponsive to anti-tumor necrosis factor agents (Anti-TNF), and was in endoscopic remission while receiving vedolizumab.

CASE REPORT

A 55-year-old female patient has been followed for 10 years with Crohn's disease. In 2012, she received a diagnosis of colonic and perianal fistulizing disease in accordance with the Montreal classification A3, L2, B3, p (A - age, L - location, B - behaviour, p – perianal disease). Infliximab and azathiopurine were started. The use of adalimumab was initiated after an allergic reaction to infliximab had occurred. In 2016, loop ileostomy was performed for refractory perianal disease and rectovaginal fistula. Consequently, a total proctocolectomy and end-ileostomy were performed due to the progression of the disease. Stoma revision

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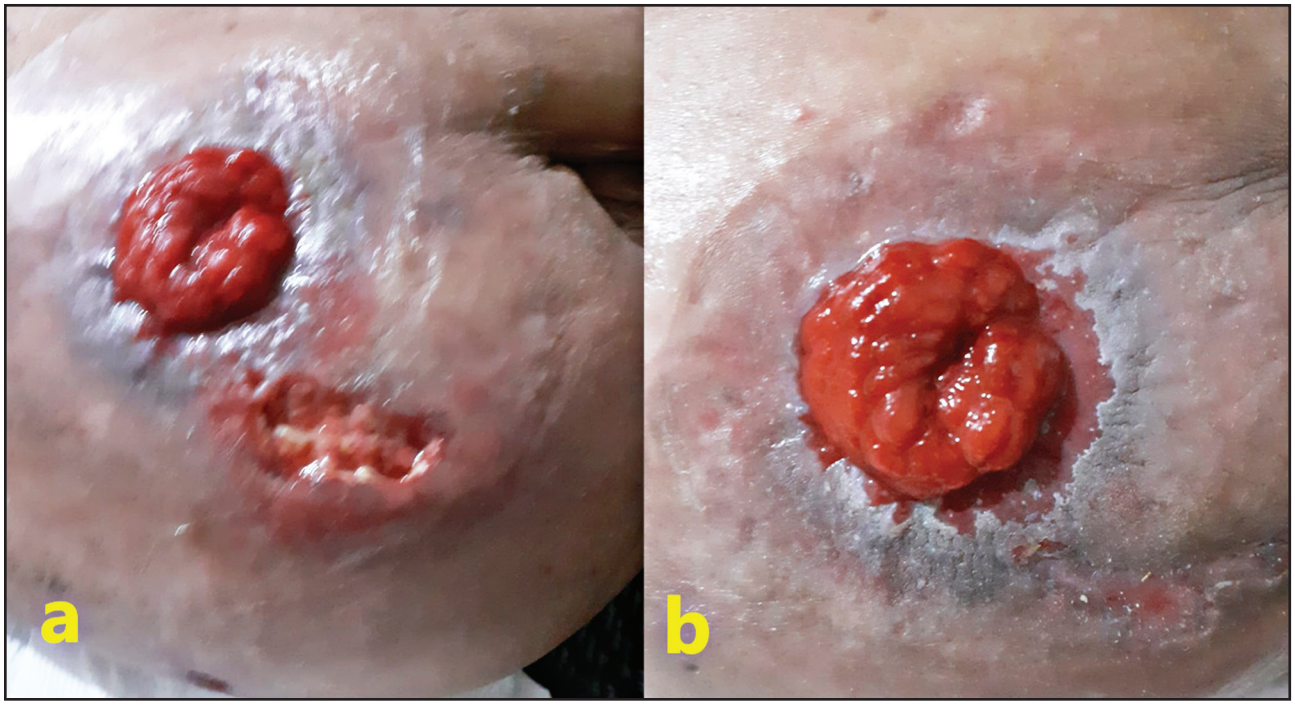

Figure 1 Peristomally located metastatic Crohn's disease; before (A) and after (B) ustekinumab treatment.

was performed in 2021 due to peristomal abscess, fistulas, and endoluminal active disease. The treatment was switched to vedolizumab. An ulcerated lesion appeared around the stoma of a patient who was in clinical and endoscopic remission after seven doses of vedolizumab (Figure 1-A). Swab cultures and biopsies were obtained by department of dermatology. The patient received topical therapy with moist gauze dressings and cream containing zinc oxide and Hamamelis virginiana distillate. No infective pathogen was detected in the cultures. Polymerase chain reaction for tuberculosis in sampled tissue was negative. Histopathology revealed a nonnecrotizing granulomatous reaction within the lymphocyte infiltration with abundant plasma cells in the papillary dermis (Figure 2). Findings were consistent with metastatic Crohn's disease. As a result of a lack of response to topical therapy (additionally with corticosteroid content), ustekinumab was administered. The lesion regressed following an intravenous loading dose of 390 mg. And fully resolved within a week following a subcutaneous dosage of 90 mg (Figure 1-B). Informed consent was obtained from the patient.

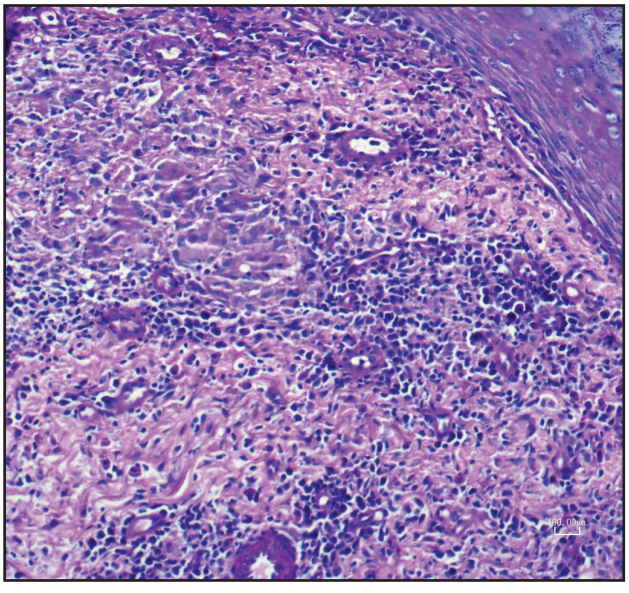

Figure 2 Periodic acid schiff stain x400; nonnecrotizing granulomatous reaction and plasma cell enriched, abundant lymphocyte infiltration in papillary dermis.

DISCUSSION

In a sizable population study, up to 43% of individuals with Crohn's disease exhibited extraintestinal manifestations. Metastatic Crohn's disease is among them (4).

On a histopathological level, it is distinguished from Crohn's disease by the presence of a non-caseating granulomatous response in an organ or focus that is not part of the gastrointestinal tract (5).

Its etiology has not been fully elucidated. The first hypothesis is that the antigen from the gastrointestinal tract accumulates under the epidermis via the bloodstream, causing a granulomatous reaction involving monocytes and epithelioid cells in the perivascular region. The second theory proposes that T lymphocytes that have been sensitized by circulating antigens create a type IV hypersensitivity reaction. Diverse lymphokines released by lymphocytes also activate monocytes, resulting in vessel wall inflammation and granulomatous reaction (6).

While MCD management is still controversial, topical treatments, systemic immunosuppressive drugs, and biological agents are commonly used (3).

In resistant MCD, vedolizumab and ustekinumab are being considered as biological agents other than anti-TNFs. Phillips, Frank M et al. conducted the most comprehensive study comparing vedolizumba with ustekinumab, although the number of healed cases with vedolizumab is low (7). Based on a case series involving 28 patients from 14 centers, 10 patients were diagnosed with MCD. Nine of these patients responded to ustekinumab (5 remissions, 4 partial responses), and one responded to vedolizumab. A total of three patients were administered vedolizumab, and two of them did not respond to the drug. Remissions were achieved after either the first or second dose of ustekinumab, with a median duration of five months. Similarly, the lesion in our patient healed after the second dose.

It has also been reported that another case has responded to vedolizumab (8).

Ustekinumab, however, results in a much higher number of cases with a response, which is in accordance with the previous study (9-14). Furthermore, it has been shown that increasing the dosage can result in achieving a complete response when the expected response cannot be attained with the standard dosage (90 mg subcutaneously in 4 weeks) (13). In the case study conducted by Zullow, Samantha, and colleagues all patients underwent an ileostomy operation, while two of them underwent a complete proctocolectomy, which is similar to our circumstances (14).

Based on these pieces of evidence, we suggest utilizing ustekinumab for managing refractory MCD. Moreover, adequately planned and randomized trials are required.

Conflict of Interest: *There is no conflict of interest with any institution or person.*

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