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Infliximab Treatment in Resistant Pyoderma Gangrenosum: A Case Report

Dirençli Pyoderma Gangrenosumda İnfliksimab Tedavisi: Bir Olgu Sunumu

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Summary

Pyoderma gangrenosum (PG) is an uncommon neutrophilic dermatosis consisting of nodules and pustules that ulcerate. Pyoderma gangrenosum is associated with autoimmune disorders such as inflammatory bowel disease, spondyloarthritis, and rheumatoid arthritis. In mild disease, therapy consists of local wound care and topical or intralesional corticosteroids. For more severe disease, systemic agents are necessary. Herein, we present the case of a patient with steroid resistant pyederma gangrenosum associated with ulcerative colitis and ankylosing spondylitis who responded well to infliximab, a tumor necrosis factor blocker. Biological agents (anti-TNF) may be alternative treatment options in patients with resistant PG. *Turk J Phys Med Rehab 2012;58:332-4.*
Key Words: Pyoderma gangrenosum; infliximab; anti-TNF

Özet

Pyoderma gangrenosum (PG), püstüler ve nodüler ülserlerle seyreden nadir bir nötrofilik dermatozdur. Pyoderma gangrenosum inflamatuvar barsak hastalığı, romatoid artrit, spondiloartrit gibi otoimmün hastalıklarla ilişkili olabilir. Hafif hastalığın tedavisi lokal yara bakımı ve topikal veya intralezyonel kortikosteroidlerden oluşur. Daha şiddetli bir hastalık için sistemik ajanlar gereklidir. Bu sunumda ülseratif kolitle ilişkili ankilozan spondilitli bir vakanın yüksek doz steroide dirençli pyoderma gangrenosum lezyonununun bir tümör nekrozis faktör blokeri olan infliksimab tedavisine yanıtını sunduk. Biyolojik ajanlar dirençli PG tedavi alternatifi olabilirler. *Türk Fiz Tıp Rehab Derg 2012;58:332-4.*
Anahtar Kelimeler: Pyoderma gangrenosum; infliksimab; anti-TNF

Introduction

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis which is seen with pustules and nodules that ulcerate. Seventy percent of cases are associated with systemic diseases such as inflammatory bowel disease (IBD), rheumatoid arthritis (RA) and malignancies (1). The diagnosis of PG is based on the presence of skin lesions. Lesions are mostly located on the lower limbs and are associated with the activation of underlying diseases. Corticosteroids are usually the first treatment option. In resistant cases, immunosuppressive and immunomodulatory agents should be tried. Herein, we present a resistant PG lesion associated with ulcerative colitis and spondylitis which favorably responded to infliximab infusion.

Case

A 31-year-old male attended to our clinic complaining of pain in the front of his left leg, an ulcerative lesion and back pain. He was diagnosed with ulcerative colitis and axial spondilitis 11 years ago. There was a skin lesion with a purulent surface in front of the left foot. Local and steroid (1 mg/kg/day)

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treatments were applied. He had been using sulphasalazine 2 gr daily and acemethazine 120 mg daily for axial spondilitis for 11 years. His uncle was a patient with ankylosing spondylitis and underwent total colectomy and ileostomy for exacerbations of IBD nearly ten years ago.

In physical examination, the measurements were as follows; occiput-to-wall distance: 11 cm, jaw-to-sternum distance: 5 cm, neck rotation to the right: 100^0, neck rotation to the left: 150^0, chest expansion: 2 cm, lomber Schober: 0.8 cm, finger-to-floor distance: 35 cm. An ulcerated lesion measuring 4x5 cm was seen in front of the left tibia and there was also edema on a erythematous swollen base as well as a suppurative skin lesion (Figure 1).

Laboratory values were as follows: hemoglobin: 9.67 g/dl, white blood cell count: 5.97 K/UI, platelet count: 377 K/UI, erythrocyte sedimentation rate (ESR): 91 mm/hour, C-reactive protein (CRP): 62 mg/dl. Direct radiography showed bilateral grade 4 sacroiliitis and spondylitis. A punch biopsy taken from the lesion revealed neutrophilic infiltration of the dermis.

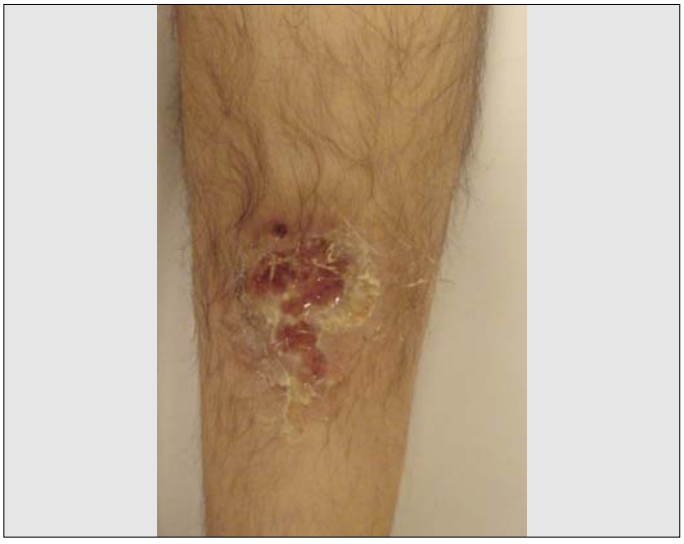

Figure 1. An ulcerated lesion measuring 4x5 cm was seen in front of the left tibia of the patient and there was also edema on a erythematous swollen base as well as a suppurative skin lesion.

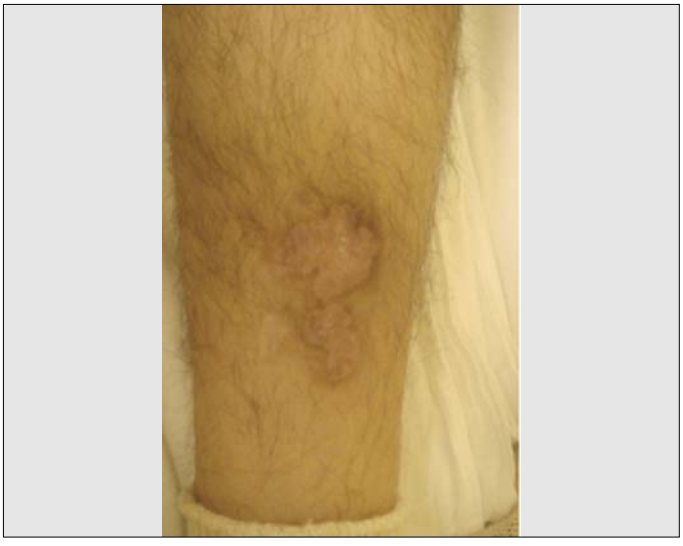

Figure 2. The residual scar after 4 months of treatment.

For the resistant PG and high disease activity for spondylitis (BASDAI >8.1), 5mg/kg infliximab treatment was planned for the baseline, 2nd and 6th weeks and in every following six weeks. At follow-up, the clinical and laboratory findings had improved dramatically. After the third infusion of infliximab, the patient's BASDAI score reduced to 3.1 and the exudation was over. ESR was 20 mm/hour and (CRP) level was 3 mg/dl (normal values: 0-5 mg/dl). The skin lesion was completely healed with a slight scar after the 5th infusion (Figure 2). After a follow-up of 12 months no recurrence was noted.

Discussion

PG is an important extraintestinal complication of IBDs. It has been reported to occur in 2-12% of patients. Lesions are often located in the lower limps (70%) and closely related to the underlying disease activity. The treatment of the underlying disease is also effective for the treatment of the skin lesion as well (2).

Diagnosis is based on the presence of the characteristic skin lesions since skin histopathology and laboratory investigations are not specific for PG diagnosis. The major and minor diagnostic criteria have been defined in the studies of recent years (3) (Table 1). According to this, 2 major and 2 minor criteria are sufficient for a diagnosis of PG.

The pathophysiology of PG is not completely understood. Neutrophile chemotaxis defect mediated by TNF which is proinflammatory cytokine, neutrophil hyperactivity, over-oscillation of some cytokines; and adhesion molecules can take part in the pathogenesis. Besides, the disorganization of T cell response in pathogenesis and the abnormality of the production of TNF-alpha can take part (4). In diseases such as RA, Crohn related to PG, TNF-alpha levels are increased (1), thus, TNF-alpha inhibitors can be a good treatment option in resistant cases of PG. Here, we present a case of ulcerative colitis associated with PG which did not respond to other immunosuppressive drugs, however, improved after treatment with infliximab.

Table 1. Diagnostic criteria for pyoderm gangrenosum.

Major criteria
• Violet edges of the inflammatory lesion
• Exclusion of relevant differential diagnoses (venous and arterial ulcers, vasculitis)
Minor criteria
• Histological examination showing neutrophilic infiltration of the dermis
• Immunoglobulin or complement or both of the storage
• The presence of an associated disease
• Partial response or no response to conventional therapy
• Response to immunosuppressive treatment

Brooklyn et al. (5) reported 30 patients with PG who were treated with either infliximab (5 mg/kg) (n=13) or placebo (n=17). At the end of the second week, there was 46% decrease in ulcer diameter and intensity in the first group whereas they found this rate as 6% in the second group. They switched to infliximab treatment in the placebo group at the end of the second week. At the end of six-week-observation, 63% of patients had clinically important improvement. In our case, low back pain improved after the 3rd dose of infliximab infusion. The skin lesion healed with a scar after the 5th infusion.

Ljung et al. (6) started infliximab treatment in 8 patients with PG and Crohn's disease, and 3 patients got completely well after the 3rd infusion. One of these patients stopped the treatment because of a skin disease. One of them completely improved after the sixth month but the disease flared up again. One of these patients recovered almost entirely after the 3rd infusion but an infection occurred and the treatment was discontinued. Two of them had partial response but one never responded. In our case, we did not observe any side effects during one year of infliximab infusion.

In the literature, there are several studies showing the effectiveness of the adalimumab and etanercept in patients with PG.

Michael et al. (1) started adalimumab treatment for a 47-year-old female patient who had PG and did not respond to topical treatments. Adalimumab 8 mg was administered twice a week for the first two weeks, and 40 mg subcutaneously in a week during the following weeks. At the 8th week of the treatment, the patient responded well to anti-TNF treatment. PG completely resolved by the 22-week follow-up examination.

Fabrice et al. (8) applied 50 mg etanercept (subcutaneously) treatment once a week for a 56-year-old male patient who had PG but did not respond to steroid treatment. He described a significant improvement with resolution of skin lesion at the and of the 2nd application. There was no recurrence at the end of 7-week-observation.

Our case and similar reports in the literature show that anti-TNF agents can be used in the treatment of PG lesions with inadequate response to previous local and systemic treatments. Since PG lesions associate with other diseases, the use of anti-TNF agents can be a good alternative for the treatment of both underlying diseases and skin lesions. Despite the effectiveness of the administration of infliximab in our patient, prospective clinical trials are needed to evaluate its efficacy to treat resistant cases of PG.

Conflict of Interest:

Authors reported no conflicts of interest.

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