

## Ulcerative Type Pyoderma Gangrenosum in Primary Sjogren's Syndrome

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**ABSTRACT** Sjogren's syndrome (SjS) is a systemic chronic autoimmune disorder characterized by lymphocytic infiltrates in exocrine organs. Most patients present with the dryness of mouth, eyes, and other mucous membranes. Extracellular findings such as vasculitis and nonvascular skin findings may also occur in addition to the involvement of exocrine glands in SjS. Rarely, pyoderma gangrenosum (PG) may be present in the skin manifestations of SjS. PG is a rare, ulcerative, neutrophilic dermatosis of unclear etiology. It is associated with systemic inflammatory diseases in at least 50% of patients who are affected. We present a case report of a patient with SjS accompanied by the ulcerative type of PG in the left lower extremity.

**Keywords:** Pyoderma gangrenosum; Sjogren's syndrome; skin ulcer

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis which presents as an inflammatory and ulcerative disorder of the skin. Although the etiology of PG is unknown, the impaired neutrophil chemotaxis plays an important role in the pathophysiology of PG.<sup>1,2</sup>

Sjogren's syndrome (SjS) is a systemic, inflammatory disease characterized by lymphocytic infiltration of the exocrine organs,<sup>3</sup> Dryness of the skin, cutaneous vasculitis and Raynaud's phenomenon can occur in SjS. However, PG is not a common skin finding in SjS. In this case report, a rare association of PG and SjS has been revealed based on a review of the literature.

### CASE REPORT

A 63-year-old female patient with SjS was admitted to rheumatology department because of an ulcer in her left leg (Figure 1). The patient had applied to the rheumatology polyclinic with dry mouth, dry eyes, diffuse joint pain four years ago. She patient's laboratory tests had revealed an increase in acute-phase response with the positivity for antinuclear antibody-indirect immunofluorescence (ANA-IFA) test (1/320 titre, speckled pattern) and anti-Sjogren's syndrome antibody (anti-SSA) (3+, ELISA) test. Schirmer's test had been bilaterally detected less than 5 mm. The minor salivary gland

biopsy had been performed, and Chisholm grade III sialoadenitis had been detected. Subsequently, hydroxychloroquine 200 mg tab 2x1, methylprednisolone 4 mg tab 1x1, and artificial tear drops were started with the diagnosis of SjS according to the 2012 American College of Rheumatology/European League against Rheumatism (ACR/EULAR) classification criteria.<sup>4</sup>

The patient was describing a purplish or violet colored ulcerative lesion on the left leg anterior aspect which had been lasted for 9 months before admission to hospital. Then, viscous yellowish discharge emerged from this lesion. The patient's routine biochemistry panel, hemogram, hepatitis markers and thyroid function tests, activated partial thromboplastin time (aPTT) were within normal limits during the control examination. Serum protein electrophoresis, peripheral smear tests revealed no abnormal findings. Other serum tests including c-ANCA, VDRL, and antiphospholipid antibodies were also negative. Thus, hematologic malignancies, vasculitis, syphilis and antiphospholipid antibody syndrome were ruled out. The doppler ultrasonographic studies of her lower extremities carried out to exclude arterial or venous insufficiency. No apparent vascular pathology was detected in the patient. Erythrocyte sedimentation rate: 42 mm/hr (0-20), C-reactive protein: 10.9 mg/L (0-5), total immunoglobulin G: 27.1 g/L (7-16), C3: 0.713 g/L (0.9-1.8) were found at the last outpatient control. Dermatology consultation was promptly requested for the ulcerative lesion in the anteromedial portion of the left tibia. The diagnosis of PG was established by the gross appearance and clinical findings of the lesion. The confirmatory skin biopsy was performed in the following days, and histopathological examination was reported as secondary vasculitis and edema characterized by marked neutrophil infiltration so that it was considered compatible with the ulcerative form of PG (Figure 2).

Azathioprine (AZA) twice daily at a dose of 50 mg was added to her therapeutic regimen, and the dose of methylprednisolone was increased to 32 mg/day. Because of the risk of secondary infection, swabs were taken from the lesion sites. Wound cul-



FIGURE 1: Skin ulcer on the anterior aspect of the left tibia (black arrow)

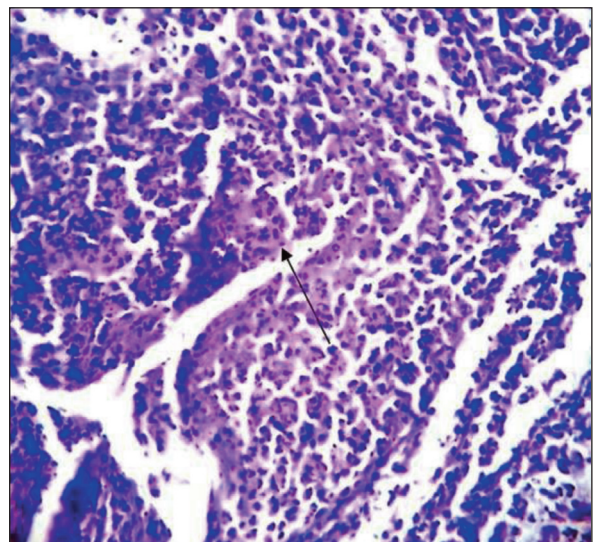


FIGURE 2: Histopathological specimen from the ulcerative lesion (black arrow indicates abundant infiltration of neutrophils, vascular necrosis and edema in dermis). (Hematoxylin and eosin,  $\times 200$ ).

tures of the ulcer for bacteria, fungi, atypical mycobacteria were negative. After 4 weeks, ulcer was prominently improved. And then, the dose of methylprednisolone was reduced as 4 mg each week. At the 3<sup>rd</sup> month, methylprednisolone was stopped but AZA treatment was going on. At that control, ulcer was completely healed (Figure 3).

## DISCUSSION

Typical manifestation of PG is an inflammatory papule or pustule that progresses to a necrotic and



**FIGURE 3:** Healed skin ulcer after combined immunosuppressive treatment (black arrow).

painful ulcer with violaceous undermined edge. There are several variants of PG; however, classic ulcerative type occurs most frequently. Classic ulcerative form usually develops on the legs as present in our patient, and a more superficial variant known as atypical PG tends to occur on the hands. PG is diagnosed by excluding other causes of similar appearing cutaneous ulcers including infection, collagen tissue diseases, vasculitis, malignancy, trauma, and diabetes. PG may lead to the phenomenon of pathergy, so the skin biopsy should be done carefully. In the histopathological evaluation of PG, intense neutrophilic infiltration, abscess formation and necrotic areas are observed. Although not specific to PG, these pathologic findings are significant in the differential diagnosis. Apart from neutrophilic infiltration, sometimes it may be also accompanied by leukocytoclastic vasculitis.<sup>1</sup>

PG is also an inflammatory and reactive skin disease frequently associated with the other underlying disorders. Infection and malignancy are not included in the etiopathogenesis of PG; however, systemic lupus erythematosus, antiphospholipid antibody syndrome and inflammatory bowel disease may lead to PG.<sup>1,2</sup> Additionally, the association of PG and SjS has been reported in the literature rarely.<sup>5-7</sup> Furthermore, PG may be the first clinical sign in patients with rheumatoid arthritis and SjS who having resistant leg ulcers on their

lower extremities.<sup>8,9</sup> Although the etiopathogenesis of both diseases is quite different and poorly understood, a common unknown triggering factor may lead to dysregulation in the autoimmune system involving the activation of two distinct inflammatory pathways in the same patient. Besides, it might develop a cutaneous vasculitis characterized by palpable purpura, especially in some patients with SjS in which detected the hypergammaglobulinemia or cryoglobulinemia. In this regard, secondary vasculitis may cause skin ulcers. Aside from numerous extraglandular features such as vasculitis, approximately 50% of patients with SjS have cutaneous findings, such as xeroderma, palpable and nonpalpable purpura, and urticaria.<sup>10</sup> Non-vasculitic cutaneous manifestations such as eyelid dermatitis, erythema annulare may also occur in SjS.<sup>11</sup>

The treatment of SjS is actually symptomatic. In the same way, no specific treatment is equivalently effective for patients with PG. The effective therapy in patients with PG for the underlying disease or associated condition might be linked to the control of skin diseases as well. Systemic therapies including glucocorticosteroids (GCs), AZA can be used for any type of PG in addition to topical therapy.<sup>2,12,13</sup> Therapy with GCs is often primarily prescribed as used in our case effectively. An immunosuppressive agent is also sometimes started, either simultaneously or later for as a GC-sparing agent. Recently, topical anti-tumor necrosis factor (anti-TNF) drug such as etanercept has been reported to be successful in treating persistent PG in patients with primary SjS.<sup>14</sup>

As a result, various skin manifestations with atypical features in SjS can be detected. If an ulcerative lesion develops in a patient with SjS, especially in the lower extremities, PG should be considered in differential diagnosis. It should not be forgotten that this kind of dermatologic complication in SjS may be rarely seen. Although there is no standard and effective treatment option in all cases, combined immunosuppressive drugs may be effective in the treatment of PG in SjS.

#### **Informed Consent**

*Informed consent was obtained from the patient.*

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### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or

members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** Barış Gündoğdu; **Design:** Barış Gündoğdu; **Control/Supervision:** Süleyman Serdar Koca; **Data Collection and/or Processing:** Barış Gündoğdu; **Analysis and/or Interpretation:** Barış Gündoğdu; **Literature Review:** Barış Gündoğdu; **Writing the Article:** Barış Gündoğdu; **Critical Review:** Demet Cicek, Süleyman Serdar Koca.

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