Co-Existence of Pyoderma Gangrenosum and Hidradenitis Suppurativa: Case Report

Hidradenitis Süpürativa ve Piyoderma Gangrenosum Birlikteliği

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ABSTRACT Although the cause of pyoderma gangrenosum is not known exactly, abnormal neutrophil chemotaxis is considered to be responsible primarily. Neutrophilic dermatose is described as a multisystemic disease and it is also associated with inflammatory bowel disease, hidradenitis suppurativa, rheumatoid arthritis, hematological malignities and monoclonal immunoglobulin A gammopathies in addition to skin involvement. Hidradenitis suppurativa together with pyoderma gangrenosum was rarely reported and no correlation was determined between severity and association of two diseases in reported cases. High dose oral corticosteroid, cyclosporin, intravenous immunoglobulin and intravenous cyclophosphamide are reported among therapy options in severe cases. Here, 63-years old female patient with pyoderma gangrenosum developing in the hidradenitis suppurativa and responding to cyclosporin and systemic corticosteroid treatment dramatically was presented.

Key Words: Hidradenitis suppurativa; pyoderma gangrenosum

ÖZET Piyoderma gangrenosum nötrofil kemotaksis bozukluğunun sorumlu olduğu, nedeni tam olarak bilinmeyen bir hastalıktır. Nötrofilik dermatozlar multisistemik bir grup hastalık olup, deri tutulumuna ek olarak, inflamatuar barsak hastalığı, hidradenitis süpürativa, romatoid artrit, hematolojik maligniteler ve immunglobulin A gamopatisi ile de birlikte olabilir. Hidradenitis süpürativa ve piyoderma gangrenosum birlikteliği nadir olarak bildirilmiştir ve bildirilen olgularda hastalığın ciddiyeti ile iki hastalık arasında korelasyon saptanmamıştır. Ciddi olgularda yüksek doz sistemik steroidler, siklosporin, intravenöz immünglobulin ve intravenöz siklofosfamid tedavisi verilmektedir. Burada 63 yaşında hidradenitis süpürativa ve piyoderma gangrenosumun beraber olduğu, sistemik steroid ve siklosporine dramatik yanıt alınan kadın hasta sunulmaktadır.

Anahtar Kelimeler: Hidradenit süpüratif; piyoderma gangrenozum

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Pyoderma gangrenosum (PG) is a rarely seen idiopathic neutrophilic dermatosis characterized by destructive cutaneous ulceration and sometimes accompanied by other cutaneous and systemic diseases. It was described for the first time by Brusting et al. in 1930.[1,2] Hidradenitis suppurativa (HS) is a chronic, recurrent, inflammatory skin disorder accompanied by subcutaneous nodules.[3]

In this study, a case of a female patient with pyoderma gangrenosum developing on hidradenitis suppurativa is presented. The patient showed a dramatic response to cyclosporin and systemic corticosteroid treatment.

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CASE REPORT

A sixty-three-year-old female patient presented at our clinic with a complaint of recurrent ulcers not responding to antibiotic treatment in the bilateral axillary and inguinal region for 20 years. In her past history, she had undergone graft operations three times in the inguinal region due to hidradenitis suppurativa, but she had not improved. Cyclosporin 2.5 mg/kg/day was initiated 3 years ago at our clinic following the diagnosis of pyoderma gangrenosum due to the same complaints and she improved after one month of treatment. However, she did not attend follow-up regularly. Systemic examination revealed diabetes mellitus and hidradenitis suppurativa at the bilateral axillar and inguinal region. Dermatological examination showed a brown scar formation that included sinus tracts from place to place in the right and left axillar regions and a purulent ulcer 3x2 cm in size in the right axillar region. Another ulcerated lesion 10x3cm in size, with central purulation and surrounded by granulation tissue, was found beginning from the bilateral inguinal region including the intergluteal region and extending linearly (Figure 1). Laboratory examinations revealed ESR of 73 mm/h, CRP of 5.9 mg/l (<0.5), RF of 35.9 (<20) and Fe, folic acid, TIBC, UIBC, C3-C4 within normal limits. IgG, IgM, IgA, IgE, ANA, Anti Ro, Anti La and Anti Scl-70 were all negative. Incisional biopsy taken from inguinal region was sent for histopathological and microbiological investigations. No growth was determined in tissue culture. Histopathological investigation showed hyperkeratosis and acanthosis, presence of ulceration and leukocytic exuda in some areas in epidermis, granuloma structure composed of proliferated capillary, new connective tissue elements, and acute, chronic inflammatory cell infiltrations in the base of the ulcer in the papillary dermis. In some areas, a fistula tract with its wall lined with squamous epithelium and acute and chronic cell infiltration

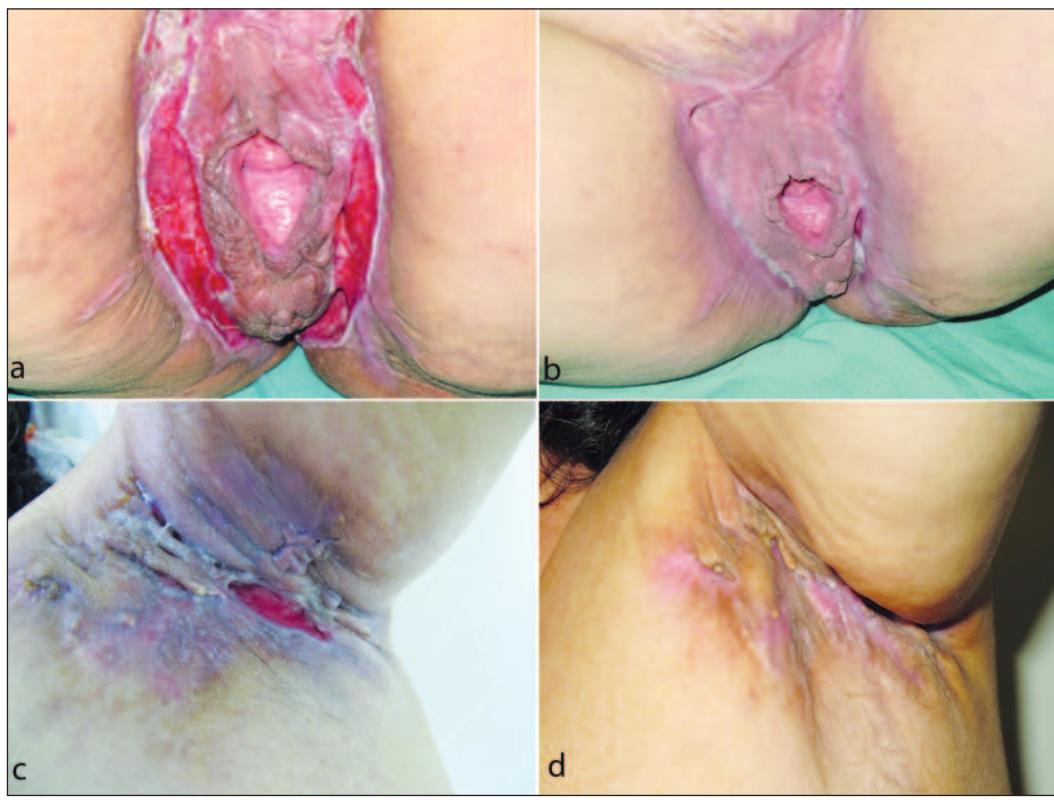

FIGURE 1: a) An ulcerated lesion 10x3cm in size, with central purulation and surrounded by granulation tissue, was found beginning from the bilateral inguinal region including the intergluteal region and extending linearly. **c)** Purulent ulcer 3x2 cm in size in the right axillar region. **b, d)** Cyclosporin and steroid treatment discontinued at the fourth month of the therapy, upon complete healing of the ulcers.

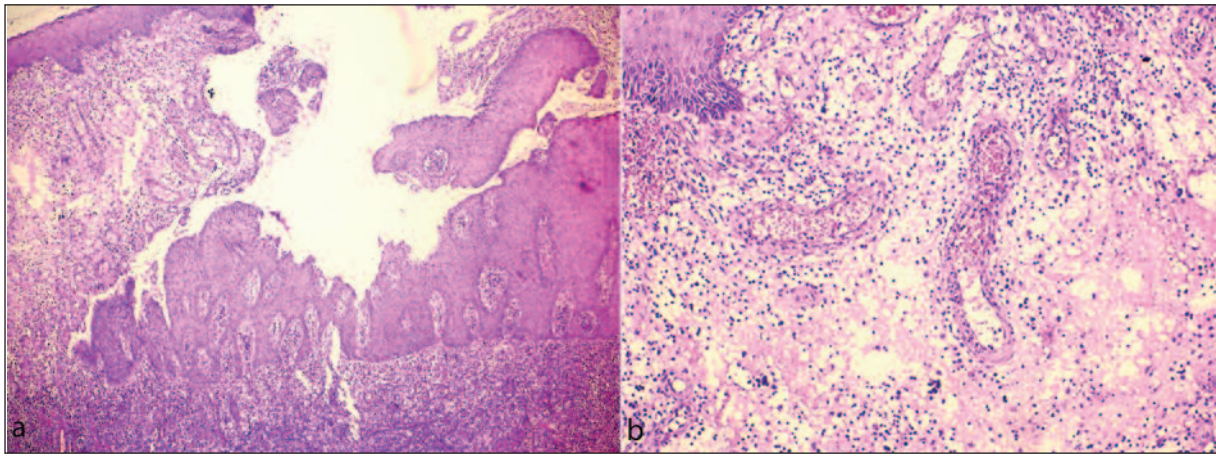

FIGURE 2: a) The center of the lesion shows central necrotizing suppurative inflammation, with fistulization and a dermal neutrophilic infiltrates and vascular reaction comprising perivascular and intramural neutrophilic infiltrates and hemorrhage (HE, x40). **b)** Dermis shows dermolysis of dermal collagen and small vessel vasculitis and intertitial dermal neutrophilia (HE, x200).

around the fistula were seen in the dermis (Figure 2). Pyoderma gangrenosum diagnosis was made based on the clinical characteristics of the patient and after microbiological and histopathological investigation. Cyclosporin 2.5 mg/kg/day and prednisolone 60 mg/day were initiated for treatment. At the first month of treatment, ulcers began to decrease. Cyclosporin and steroid treatment were gradually decreased and discontinued at the fourth month of the therapy, upon complete healing of the ulcers (Figure 1).

DISCUSSION

Pyoderma gangrenosum is a rarely seen skin disorder characterized by large painful ulcers with indistinct borders.[4] It is generally reported between 25-54 years of age and the disease affects females much more than males.[2-5] As reported in the literature, our case was also female and lesions developed at a more advanced age.[4] Classic ulcerative PG can lead to violaceous chronic ulcerations with irregular borders, beginning as one or several nodules or sterile pustules and growing rapidly and show healing with cribriform scarring.[2-6] The lesions in PG are generally localized in a lower extremity as a single lesion.[4] Although rare, cases showing localization at axillar and inguinal regions have also been reported in the literature. Our patient's lesions were located on axilla and gluteal area. The case was considered to show classic PG lesions according to clinical and histopathological characteristics. However, since the base was a cicatricial tissue including sinus tracts and was assessed to be HS by histopathological investigations, this suggested PG development on HS as the diagnosis.

Exclusion of cutaneous ulcerative diseases with biopsy and culture and clinical diagnosis play a key role in diagnosis of PG. Diagnosis is made clinically because its histopathology is not pathognomonic.[4]

Neutrophilic dermatoses like PG are described as multisystemic diseases and are also associated with inflammatory bowel disease, HS, systemic lupus erythematosus, rheumatoid arthritis, hematological malignancies, and monoclonal immunoglobulin A gammopathies, in addition to skin involvement.[4-7]

Hidradenitis suppurativa is a chronic, recurrent inflammatory skin disorder involving skin folds including dense terminal hair and apocrine glands. In its pathogenesis, follicle rupture and abscess formation occurs following occlusion of the follicular infindibulum.[8] While the cause of the chronic suppuration in HS is not known, cellular immunity and neutrophil function of some patients have been found to be normal in the studies performed.[9] However, reduction in numbers of T lymphocytes, increases in numbers of suppressor

T lymphocytes, decreases in intracellular cyclic GMP responsible for bacterial phagocytosis in polymorphonuclear leukocytes has been reported.[3] Bacterial infection, comedonal occlusion of the follicles, relative estrogen increases or lack of androgen, impaired glucose tolerance and genetic factors have been reported as other responsible factors.[3-9]

Our patient has also diabetes mellitus. Cellular immun system and phagocytosis may decrease in diabetes mellitus. This factor could be contribute to coexistence of PG and HS.

Although the pathogenesis of PG is as yet unidentified, neutrophilic dysfunction and increases in IL-8 release have been suggested. In both HS and PG, pathogenesis is not actually clear and there is a similar dysfunction in humoral and cellular immunity. Association of HS with PG is rarely reported in the literature. Ah-Weng et al. reported a series of 6 cases; however, similar to our case, PG was determined to have developed in the hidradenitis suppurativa in one of 6 cases.[7] Garcia-Rabasco et al. also reported a male case that developed PG after 20 years of HS, with independent disease activities from each other.[10] Hsiao et al. reported 11 cases of PG lesions presenting in patients with HS. All patients received multiple therapeutic agents because of ineffective to standard therapies.[11] Reddick et al. reported a patient with severe PG associated with HS was respond to adalimumab.[12]

In the treatment of PG, the size, depth, growth rate of the lesion, emergence of new lesions, accompanying diseases (inflammatory bowel diseases, arthritis, etc.), and the general health condition of the patient should be taken into consideration.[4] First-line treatment is high dose systemic corticosteroids. In mild cases, topical and intralesional corticosteroids can be used. Immunosuppressant drugs, intravenous immunoglobulin, and biological agents are used in recalcitrant patients.[4,13,14] Cyclosporine, alone or as combined therapy, is the preferred treatment in recalcitrant patients not responding to corticosteroid treatment.[4] PG treatment with cyclosporine has been used successfully since 1985. The mechanism of action of cyclosporine is to suppress the lymphokine production and T cell activation.[1] In the study performed by Vidal et al., complete recovery was reported in 22 patients with 4.9 mg/kg/day cyclosporine treatment over an average 3.2 month follow-up.[1] In the study performed by Reichrath et al., prednisolone 0.3-1 mg/kg/day and cyclosporine 5 mg/kg/day treatments were used together.[15] In our case, we obtained dramatic response to systemic corticosteroid and cyclosporine treatments, as the size of the ulcer decreased rapidly in the first month and the ulcer epithelialized completely by the fourth month. Similar to the literature reports, the response to cyclosporine treatment in our case was good and rapid since HS was a chronic disease.

Although surgical treatments are performed successfully, its place in PG treatment is controversial. Even though our case had undergone graft operations three times, surgery was not successful due to PG development in HS; in fact, the graft operations aggravated the PG lesions.[16]

In conclusion, PG should be taken into consideration in cases of ulcer development that does not heal and does not respond to treatment in chronic, inflammatory conditions with chemotactic defect, like HS. In such cases, unnecessary surgical intervention should be avoided, histopathological investigation should be performed, and the efficacy of the treatment should be increased by addition of an immunosuppressive agent like cyclosporine to the standard corticosteroid treatment.

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