A New Patient with Pyoderma Gangrenosum, Acne, and Suppurative Hidradenitis (PASH) Syndrome: Case Report

Piyoderma Gangrenozum, Akne ve Süpüratif Hidradenit (PASH) Sendromlu Yeni Olgu

Sema AYTEKİN,[a]
Derya UÇMAK,[b]
Erhan AYHAN,[b]
Veysi FİDAN[b]

[a]Clinic of Dermatology, Haydarpaşa Numune Training and Research Hospital, İstanbul
[b]Department of Dermatology, Dicle University Faculty of Medicine, Diyarbakır

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Yazışma Adresi/*Correspondence:*
Sema AYTEKİN
Haydarpaşa Numune Training and Research Hospital,
Clinic of Dermatology, İstanbul, TÜRKİYE/TURKEY
semaaytekin@yahoo.com

ABSTRACT PAPA syndrome is a autoinflammatory syndrome clinically characterized by pyogenic arthritis, severe acne, and pyoderma gangrenosum caused by mutations in the PSTPIP1 gene. It is a rare autosomal dominant disease of early onset. Pyoderma gangrenosum, acne and hidradenitis suppurative (PASH) syndrome has been recently identified as nonhereditary and characterized by absence of arthritis different from PAPA syndrome. No mutations have been detected to date in patients with PASH syndrome. Only three patients with PASH syndrome were reported. Herein, we report a new patient with PASH syndrome. He had severe disseminated pyoderma gangrenosum and multiple depressed scars resulting from related acne and hidradenitis suppurative but lacked any episodes of pyogenic arthritis. He was successfully treated with systemic corticosteroids.

Key Words: Pyogenic arthritis, pyoderma gangrenosum and acne; pyoderma gangrenosum

ÖZET PAPA sendromu, PSTPIP1 gen mutasyonun neden olduğu klinik olarak piyojenik artrit, şiddetli akne ve piyoderma gangrenozum ile karakterize otoinflamatuar bir sendromdur. Otozomal dominant erken başlangıçlı nadir görülen bir hastalıktır. Piyoderma gangrenozum, akne ve hidroadenitis süpürative (PASH) sendromu son zamanlarda tanımlanmış PAPA dan artrit yokluğu ile farklı olan herediter olmayan bir sendromdur. PASH sendromunda bugüne kadar mutasyon saptanmamıştır. PASH sendromlu sadece üç olgu bildirilmiştir. Biz burada yaygın piyoderma gangrenozum lezyonları ile akne ve hidradenitis süpürativa ile ilişkili çok sayıda deprese skarları olan, fakat piyojenik artritin bulunmadığı PASH sendromlu yeni bir olguyu sunuyoruz. Hastamız sistemik kortikosteroid ile başarılı bir şekilde tedavi edildi.

Anahtar Kelimeler: Piyojenik artrit, piyoderma gangrenozum ve akne; pyoderma gangrenozum

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Hereditary autoinflammatory syndromes are distinct from infectious, allergic and autoimmune diseases.[1] One of them this is called as autosomal dominantly PAPA syndrome.[1,2] This syndrome consists of the clinical symptom triad of pyogenic sterile arthritis, pyoderma gangrenosum (PG) and acne. This report presents a patient who had clinical for PAPA syndrome except arthritis, that is named PASH syndrome by Braun-Falco et al.[3]

CASE REPORT

A 23-year-old male patient (160cm, 40kg) had severe cystic acne that left behind multiple depressed scars on his face and his back since adolescence. He had clusters of chronic and repeatedly draining sinuses and abscesses in both inguinal areas for 5 years. During the last 2 years, slowly expanding and painful different sized ulcerations with thick crusts developed on his arms, lower legs and pubic area. He denied any episodes of inflammatory arthritis or joint pain. In addition, he had no inflammatory bowel disease. The family history was unremarkable. He had low intelligence and no smoking history.

Physical examination revealed poikilodermia with depressed scars over the patient's face. There were different diameters depressed scars in pubic and inguinal regions. On his back and lower extremities, several painful slough ulcers with thick hemorrhagic crusts and draining purulent, hemorrhagic material up to a size of approximately 3x7 cm were seen (Figure 1, 2).

Laboratory workup revealed a slight increase of leukocytes, C-reactive protein, and sedimentation rate. Serology for hepatitis, HIV disease, VDRL and anticyclic citrullinated protein antibodies revealed negative findings. Results of microbiological analyses of swab samples and wound cultures were negative for bacterial and fungal microorganisms. Mycobacterial infection was ruled out by pulmonary graphy, culture for tuberculosis and tuberculin skin test. Histopathologic examination of biopsy specimen taken from the border of the ulcerated lesion revealed neutrophilic inflammation and focally necroting connecting tissue, consistent with pyoderma gangrenosum (Figure 3). Any genetic study couldn't perform for the patient. He was treated with systemic antibiotics and methyl prednisolone 40 mg/d that was slowly tapered to 5 mg/d during a two-month period. Ten days after the treatment, lesions became

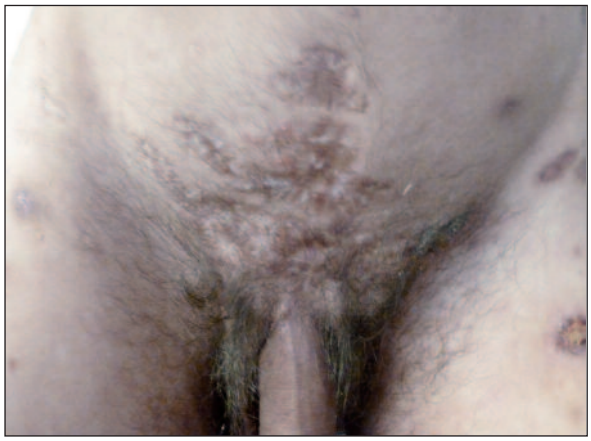

FIGURE 1: Depressed scars in pubic and inguinal regions.
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

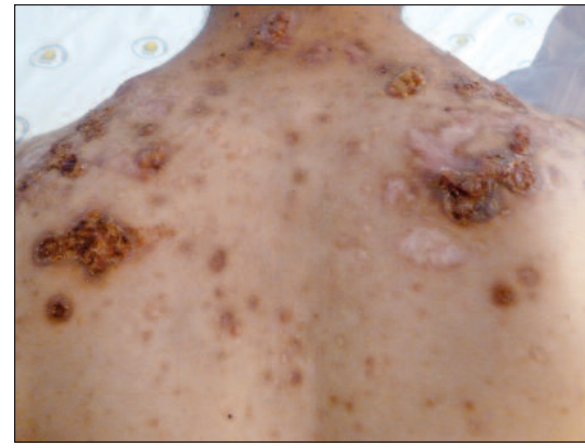

FIGURE 2: Thick hemorrhagic crusts and draining purulent, hemorrhagic material over the back.
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

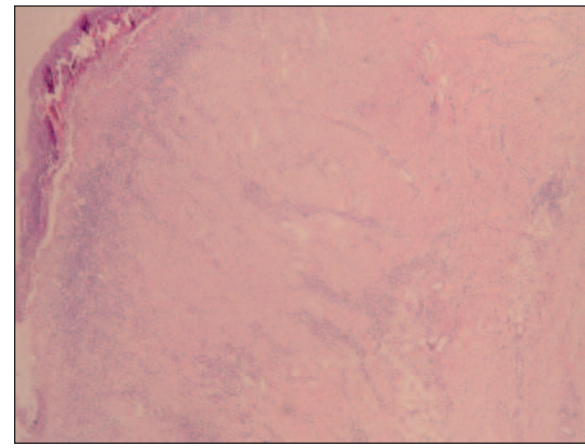

FIGURE 3: Leukocytic exudate and ulceration of the overlying epidermis, abscess formation, intradermal mixed inflammatory cell infiltration with perivascular lymphocyte infiltration (4X10, H&E).
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

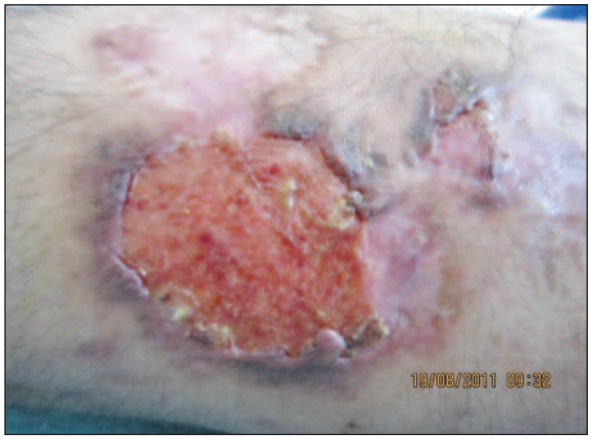

FIGURE 4: Typical pyoderma gangrenosum lesions.
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

irregular and undermined bordered necrotic ulcers and a surrounding rim of erythema for typical PG (Figure 4). The lesions resolved completely within one month.

DISCUSSION

The appearance of hidradenitis suppurative (HS) and PG lesions in the same patient has been rarely reported. HS and PG are both rare inflammatory skin conditions that are characterized by an intense inflammatory response and mediated by neutrophils, and both diseases are commonly seen associated with systemic inflammatory diseases such as IBD[1-5]. In addition, PG and HS are features of the PAPA syndrome, a recognized auto inflammatory disease resulting from over expression of IL-1.[2,4] Auto inflammatory diseases are genetic or acquired clinical entities globally caused by the aberrant release of the proinflammatory cytokine interleukin-1 and mostly characterized by recurrent spontaneous inflammatory events.[1] Other auto inflammatory conditions, such as Behcet disease, are associated with PG, while SAPHO syndrome is associated with HS.[1] In a recent investigation, Ah-Weng et al. reported 6 patients with PG and HS, and three of them had previous severe acne.[6] These associations have also been reported previously. Hsiao et al have identified 11 patients who have an overlap of PG and HS three of them have acne.[7] Nine of the patients in the case series that reported Hsiao et al were obese. Patients with PASH syndrome are also obese. Our patient is not obese. Obesity and smoking may be triggering factors for HS. Therefore, our patient could be recovered only steroid therapy without the need for an additional immunosuppressive agent.

While PASH syndrome shares similar dermatologic signs of PG and acne with PAPA syndrome, it differs from PAPA with low intensive joint inflammation and instead experience severe HS. Two unrelated patients were described with a clinical presentation quite similar. These patients had recovered with systemic steroid and immunosuppressive agent or blockade of interleukin 1. Systemic corticosteroids are still first-line treatment for PG.[3] In a recent report, Marzano at al. reported a new patient with PASH syndrome after bowel bypass surgery.[4] Traditional antineutrophilic agents, such as dapsone and colchicine, have been found as ineffective treatments for HS and PG.[3-7]

PASH syndrome has recently identified and a few cases have been reported until now. But PG, HS, and acne as a distinct clinical association have been reported as unlabeled in previous studies. In the present investigation the focus is on PASH syndrome.

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