Herpes Simplex Superinfection with Hailey-Hailey Disease: Case Report

Hailey-Hailey Hastalığında Herpes Simpleks Süperenfeksiyonu

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ABSTRACT Hailey-Hailey disease (familial benign pemphigus) is an autosomal dominant acantholytic dermatosis. The disease shows painful erosions and vesicles situated on an erythematous background especially in the intertriginous area. Herpes simplex infection associated with Hailey-Hailey disease differs from eczema herpeticum in that it is more localized. A 55-year-old female presented with vesicular lesions on the edge of wide inguinal erosions. A Tzanck smear revealed single hypertrophic nucleated acantholytic round cells with basophilic cytoplasm and one or two marked nucleoli at the periphery of the nucleus, adjacent to the nuclear membrane. Herpes simplex superinfection of Hailey Hailey disease is very rare and may not come to mind in diagnosis. A Tzanck smear, which is faster and easier than other tests for diagnosis, should be undertaken when there is clinical suspicion of herpes infection and antiviral treatment should be administered without delay.

Key Words: Pemphigus, benign familial; Herpes simplex; smear layer

ÖZET Hailey-Hailey hastalığı (benign familial pemfigus) otozomal dominant olarak geçen akantolitik bir dermatozdur. Özellikle intertriginöz alanlarda yerleşen eritematöz zeminde ağrılı erozyonlar ve veziküller mevcuttur. Hailey-Hailey hastalığı ile ilişkili herpes simpleks enfeksiyonu hemen her zaman egzema herpetikum tablosuna benzemeyebilir ya da egzema herpetikum gibi yaygın ve şiddetli vücut dağılımı göstermeyebilir. 55 yaşında kadın olgunun Hailey-Hailey hastalığına bağlı inguinal bölgede ağrılı erozyon ve veziküler lezyonları mevcuttu. Yapılan Tzanck smearda bazofilik sitoplazmalı tek hipertrofik nukleuslu ve nukleus periferinde membrana bitişik, bir ya da iki belirgin nukleolusları olan akantolitik yuvarlak hücreler mevcuttu. Hailey-Hailey hastalığında Herpes simpleks süperenfeksiyonu çok nadirdir ve tanıda akla gelmeyebilir. Tanıda diğer testlerden daha kolay ve daha hızlı olan Tzanck testi, Herpes simpleks enfeksiyonunun klinik şüphesi olduğu zaman yapılmalıdır ve antiviral tedavi tanı gecikmeden başlanmalıdır.

Anahtar Kelimeler: Pemfigus, selim ailesel; Herpes simpleks; smear tabakası

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Hailey-Hailey disease, also known as familial benign chronic pemphigus, is a rare disease with an autosomal dominant inheritance pattern.[1] The disease progresses in the form of recurrent vesicles, eroded plaques and warty papules which involve folds of the skin such as the inguinal region, axilla, neck and perianal region.[1,2]

Heat, friction, maceration, moisture, trauma, infections and UVB exposure are the main factors that trigger the disease. Deterioration of symptoms has been observed in many patients during summer time.[1,2] The epidermal Ca2+ gradient in the skin becomes weaker in patients with Hailey-Hailey disease. This results in a mechanical defect in the tonofilament-desmosome complex or intercellular substance, leading to dissolution of epidermal cells, which is called acantholysis.[3] An infection which is associated with impaired epidermal structure may mimic the lesions of this disease, causing delays in actual diagnosis and leading to unnecessary and wrong treatments. Although there are several studies in the literature which report cases of eczema herpeticum with Hailey-Hailey disease, but there are only a limited number of studies reporting cases of herpes infection localized over the lesions caused by Hailey-Hailey disease. This article presents a case with Herpes simplex infection over the lesions caused by Hailey-Hailey disease in the inguinal region and emphasizes the importance of cytologic findings in diagnosis.

CASE REPORT

A 55-year-old female patient presented to our outpatient clinic with complaints of painful and oozy wounds in her inguinal region. Her dermatologic examination revealed oozy macerated erythematous plaques in both inframammarian regions (Figure 1). The patient had evident vesiculated lesions on an erythematous ground as well as dense maceration and oozy plaques which eroded from place to place in both inguinal areas and pubic regions (Figure 2). The patient's mother and aunt also had Hailey-Hailey disease. Biopsy taken from the patient previously revealed the presence of suprabasal separation and acantholytic dyskeratotic cells in epidermis (Figure 3). No staining appeared in direct immunofluorescence.

A Tzanck smear revealed single hypertrophic nucleated acantholytic round cells with basophilic cytoplasm and one or two marked nucleoli at the periphery of the nucleus, adjacent to the nuclear membrane (Figure 4).

Laboratory examinations showed the following values for the patient: leukocyte: 11 500/mm^3, neutrophils: 8.98 10^3/µL, sedimentation: 35 mm/hour (8-15) and CRP: 2.3 mg/dL (0-0.8). The remaining CBC results and urine and blood chemistry results were normal.

The patient had been started on systemic methotrexate (15 mg/week) three months ago. Methylprednisolone (40 mg/day) was added, considering this as an exacerbation of her primary disease. On the fifth day of the treatment, Tzanck

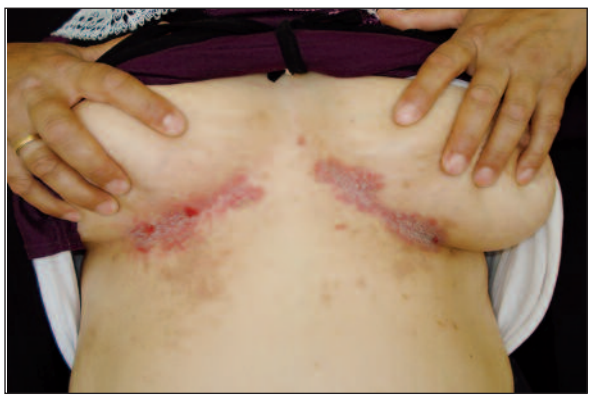

FIGURE 1: Macerated erythematous plaques in both inframammarian regions.
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

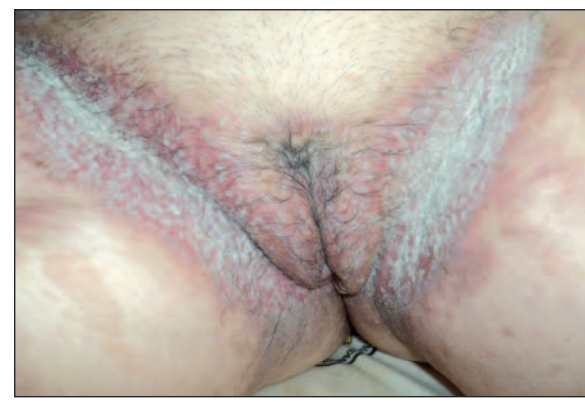

FIGURE 2: Vesicular and eroded plaques in both inguinal areas.
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

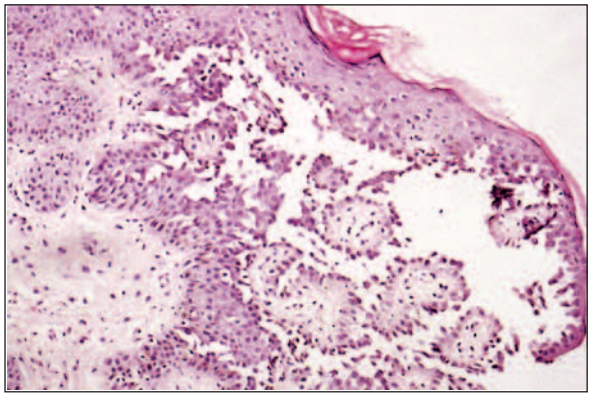

FIGURE 3: Suprabasal separation and acantholytic dyskeratotic cells in epidermis (HEx400).
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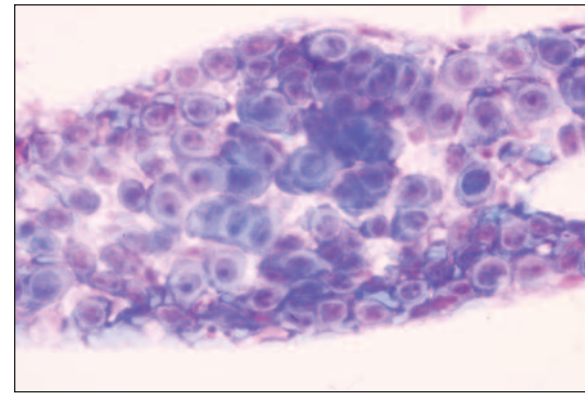

FIGURE 4: Single hypertrophic nucleated acantholytic round cells with basophilic cytoplasm and prominent peripheral nucleoli (Giemsa stainx400).
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

smear was applied on the vesiculated lesions of the patient due to a suspected herpes infection as the lesions did not go into remission and the symptoms did not improve. Giemsa-stained smear revealed massive and multi-nucleated acantholytic keratinocytes (ballooning or pregnant cells) with hazy nucleoli and a hyperbasophilic cytoplasm as well as dense neutrophils (Figure 5). According to serologic examination, VZV antigens, syphilis serology, HSV-1 IgM and HSV-1 IgG antibodies were negative, but HSV-2 IgM and IgG antibodies were positive.

In the light of clinical and cytologic findings, the patient was diagnosed as having HSV-2 infection over Hailey-Hailey lesions. Upon diagnosis, systemic steroid treatment was withdrawn and the patient was administered 1 gram of oral acyclovir daily. A marked improvement was observed in her subjective complaints and skin lesions in one week following the initiation of the antiviral treatment. The antiviral treatment was completed and stopped in ten days. No exacerbation has occurred in the patient who has been visiting the clinic at certain intervals in the last 8 months for follow-up purposes.

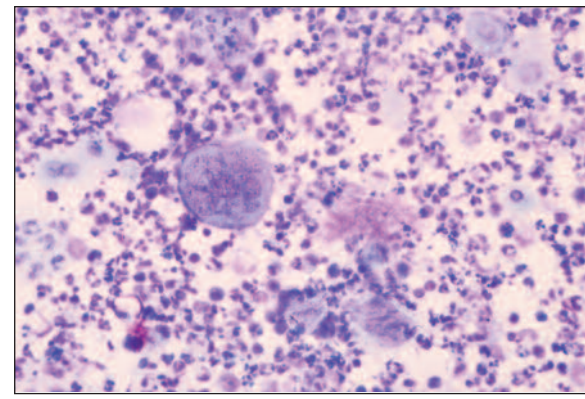

FIGURE 5: Multi-nucleated acantholytic keratinocytes with hazy nucleoli and a hyperbasophilic cytoplasm surrounded by dense neutrophils (Giemsa stainx400).
(See color figure at http://www.turkiyeklinikleri.com/journal/dermatoloji-dergisi/1300-0330/)

DISCUSSION

Hailey-Hailey disease is an autosomal dominant disease characterised by adhesion-related disorders in suprabasal keratinocytes. Although it usually develops after puberty, especially in the third and fourth decade of life, it may develop anytime in life. Almost two thirds of the patients have a family history. The disease is shows painful erosion and vesicles situated on an erythematous ground especially in the intertriginous area.[1,2]

Severe lesions cause pain and lead to restrictions in physical activity.[2] In our case, lesions increased in number and severe pain occurred after development of herpes virus infection.

A characteristic histopathologic finding of Hailey-Hailey disease is suprabasal acantholysis. Severe acantholysis may develop in some cases. Histologically, 'dilapidated brick wall appearance' is characteristic of Hailey-Hailey disease.[2,3] Hailey-Hailey disease is accepted as a non-immunologic acantholytic dermatosis. Unlike pemphigus, Hailey-Hailey gives negative immunofluorescence results.[4] Our patient's direct immunoflorescent examination was negative.

Human Herpes simplex virus infections are widely recognized complications of various dermatoses. They have been reported in both hereditary and acquired acantholytic diseases such as dyskeratosis follicularis (Darier's disease), Hailey-Hailey disease and pemphigus vulgaris, respectively.[5] In these diseases, the most common appearance is widespread lesions associated with impaired integrity of epidermis.[2]

In the cytodiagnosis of Hailey-Hailey disease; the pattern is characterized by numerous acantholytic (or Tzanck) cells, which usually demonstrate round, uniform and larger than normal keratinocytes with a hypertrophic, nucleolated, single nucleus and an abundant basophilic cytoplasm. The basophilic staining is darker at the periphery on the cellular membrane (''mourning-edged'' cells).[6]

Tzanck smear provides a fast and reliable diagnosis of herpes virus infections. Multi-nucleated massive acantholytic keratinocytes showing in the smear of the vesicular ground (Tzanck smear) ensures establishment of a quick diagnosis. Cells look swollen (''ballooning degeneration''); they may even reach 60-80 μm in diameter at times. As cellular diameter increases, chromatin pattern of the nucleus blurs and the stain fades. There are numerous multi-nucleated cells in various diameters and sizes. Intranuclear inclusion bodies are surrounded by an unclear perinuclear halo, which is not an easy finding to obtain from smear.[6]

Similar to the pathway followed in eczema herpeticum, visualization of infected cells by direct fluorescent antibody in viral culture taken from fresh vesicular lesions and swap sample taken from ulcerative lesions is the most reliable and useful method in diagnosis of herpes simplex infection.[7] Diagnosis should be verified by biopsy and polymerase chain reaction in suspected cases with old and atypical lesions. However, in the presence of significant clinical suspicion or positive Tzanck test results, treatment should be administered without delay.[2]

In conclusion, Herpes simplex infection associated with Hailey-Hailey disease may not always look the same as eczema herpeticum or may not spread over a wide region in the body. Therefore, it may not come to mind in diagnosis. However, even if it is localized, HSV infection should be suspected in Hailey-Hailey disease which is accompanied by rapid onset severe pain and burning sensation. Tzanck test should be done, which is faster and easier than the other tests and biopsy for diagnosis, and antiviral treatment should be administered without delay.

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