Patients with Behçet's disease may develop multiple mucocutaneous manifestations, several of which are mediated by neutrophils. These include aphthous ulcers, pseudofolliculitis, acneform lesions, and pathergy. We report another neutrophil-mediated disorder, neutrophilic eccrine hidradenitis (NEH), in a patient with Behçet's disease. NEH should be added to the list of mucocutaneous lesions that may be seen in patients with Behçet's disease.

GOAL
To discuss a case of neutrophilic eccrine hidradenitis (NEH) in a patient with Behçet's disease

OBJECTIVES
Upon completion of this activity, dermatologists and general practitioners should be able to:
1. Describe NEH and its associated medical conditions.
2. Identify the histologic appearance of NEH.
3. Delineate the pathogenesis of skin lesions in Behçet's disease.

CME Test on page 119.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: July 2001.

This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Albert Einstein College of Medicine and Quadrant HealthCom, Inc. The Albert Einstein College of Medicine is accredited by the ACCME to provide continuing medical education for physicians. Albert Einstein College of Medicine designates this educational activity for a maximum of 1.0 hour in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

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Behçet's disease is a complex, multisystem, inflammatory disorder of unknown etiology. The diagnosis is made on the basis of the clinical criteria proposed by the International Study Group for Behçet's Disease in 1990. According to the criteria, recurrent oral ulceration must be present, as well as at least two of the following: recurrent genital ulceration, eye lesions, skin lesions, and a positive pathergy test result. Cutaneous manifestations include pseudofolliculitis, acneform lesions, erythema nodosum, and pathergy. Behçet's disease also may affect the gastrointestinal tract, central nervous system, and peripheral joints.

Neutrophilic eccrine hidradenitis (NEH) is a self-limited inflammatory dermatosis seen primarily in patients with hematologic malignancies who are receiving chemotherapy. Harrist et al first described
this condition in a man with acute myelogenous leukemia undergoing induction chemotherapy. NEH also has been reported with many other clinical conditions and drug intake. An eruption of NEH commonly presents as solitary or grouped erythematous edematous papulopustules and plaques that are variably tender. The lesions are usually located on the proximal extremities, trunk, and periorbital region. The histopathology of NEH is characteristic and reveals a neutrophilic infiltrate around the eccrine secretory coils and ducts, with focal epithelial cell necrosis and vacuolar degeneration. Diffuse dermal edema with perivascular infiltrate consisting of lymphocytes, neutrophils, macrophages, and eosinophils also may be seen. Skin lesions spontaneously resolve in 1 to 2 weeks without scarring.

The etiology of NEH is unclear; however, there are 2 theories regarding its pathogenesis. The first suggests that NEH belongs to the spectrum of neutrophilic dermatoses, with primary involvement of the eccrine glands. The other theory postulates that the infiltrate in NEH is secondary to drug-induced eccrine gland changes. We report a case of NEH in a patient with Behçet’s disease and suggest that NEH is related to the group of neutrophilic dermatoses.

**Case Report**

A 17-year-old white man presented with a 2-year history of lesions on the face, oral mucosa, penis, scrotum, and anterior thighs. His medical history was significant for relapsing joint pain with effusions and recurrent iritis. Antinuclear antibody test and rheumatoid factor results were negative. On physical examination, the patient had punched-out ulcers on his tongue, scrotum, and penile shaft. He had pustules and erythematous papules on his face consistent with an acneform eruption. In addition, he had several vesiculopustular lesions on the anterior thighs. Results of a biopsy of a pustule from the thigh revealed a mixed infiltrate rich in neutrophils within the superficial and deep reticular dermis. These findings are consistent with the cutaneous lesions of systemic disorders associated with...
pathergy. Direct immunofluorescence test results of perilesional skin were negative. A diagnosis of Behçet’s disease was made, and the patient was treated with multiple systemic agents, including prednisone, dapsone, colchicine, and azathioprine, with variable success.

Sixteen months later, the patient presented with a 1-week history of a pruritic, burning eruption on his arms (Figure 1A), hands, and face. Examination revealed multiple discrete and confluent erythematous papules and plaques, with a few minute vesicopustules on the upper extremities (Figure 1B) and crusted erosions on the face. Histopathologic examination of an upper extremity lesion revealed an unremarkable epidermis. There was an infiltrate around the eccrine glands and blood vessels, consisting of neutrophils and lymphocytes characteristic of NEH (Figure 2). The lesions resolved after 2 weeks of prednisone therapy. Similar lesions recurred 2 years later. A biopsy specimen revealed similar findings. Treatment with thalidomide was initiated. The skin lesions and oral and genital ulcers resolved and remained clear during 18 months of thalidomide therapy.

Comment
NEH is associated with numerous conditions. Bachmeyer and Aractingi reviewed 51 reports of NEH and found that 90% of cases developed in patients with malignancies. Furthermore, 84% of patients had recently received antineoplastic chemotherapy before the onset of skin lesions. The main cytotoxic agents used were cytarabine and anthracyclines. Acute myelogenous leukemia was the most frequently associated malignancy. Chronic lymphocytic leukemia, Hodgkin’s disease, and non-Hodgkin’s lymphoma also have been reported. Occasional cases with solid tumors, including testicular carcinoma, Wilms’ tumor, osteosarcoma, breast cancer, and lung cancer, have been described. Attempts to link a specific cytotoxic drug to NEH have been unsuccessful.
because most patients receiving chemotherapy for the treatment of cancer receive multiple drugs. Several studies have suggested that NEH belongs to the spectrum of drug-induced eccrine gland changes that include syringosquamous metaplasia and eccrine necrosis. There are several reports of chemotherapy-related eruptions in which histologic examination showed isolated necrosis or syringometaplasia of the eccrine coils without neutrophilic infiltration.\textsuperscript{11,13,16} In 1997, Brehler et al.\textsuperscript{17} reported a case of a patient with acute myelogenous leukemia receiving cytarabine, daunorubicin, and thioguanine who developed NEH on the third day of treatment. The lesions healed spontaneously and reappeared with the administration of chemotherapy. Histologic examination and immunohistochemical staining revealed necrosis of the eccrine and apocrine glands with a mixed infiltrate of neutrophils, histiocytes, and lymphocytes (T- and B-cell types). Based on these findings, they suggested that NEH occurs secondary to the cytotoxic effect of chemotherapeutic agents on eccrine glands.\textsuperscript{17} The theory that NEH is a drug side effect is supported by a study that demonstrates the presence of NEH after intradermal injections of bleomycin into normal human skin.\textsuperscript{18} NEH also has been observed in HIV-infected patients, two of whom were treated with zidovudine\textsuperscript{19} and one with stavudine.\textsuperscript{20}

To our knowledge, there are 2 reported cases of NEH heralding the onset of acute myelogenous leukemia.\textsuperscript{21,22} In addition, NEH has been reported in 2 patients receiving granulocyte colony-stimulating factor\textsuperscript{3-24} and in a healthy adult taking acetaminophen.\textsuperscript{25} Furthermore, there are rare case reports of NEH attributed to bacterial infections including \textit{Serratia marcescens}, \textit{Enterobacter cloacae}, and \textit{Staphylococcus aureus}.\textsuperscript{26-29} The diversity of the presentations suggests that there are various etiologies of NEH, including drug toxicity, paraneoplastic, infectious, and idiopathic. As such, NEH represents a cutaneous reaction pattern to a broad spectrum of clinical conditions.

The identification of NEH in a patient with Behçet’s disease supports the theory that it belongs to the spectrum of neutrophilic dermatoses including Sweet’s syndrome. Sweet’s syndrome and NEH have similar clinical findings, such as erythematous edematous plaques, and are differentiated on the basis of histology. Sweet’s syndrome demonstrates a neutrophilic infiltrate of the dermis sparing the glandular apparatus. In NEH, the neutrophilic infiltrate is concentrated around the eccrine coils and ducts. Both disease processes may be paraneoplastic to hematologic malignancies, pathergy, a feature seen in Behçet’s disease and Sweet’s syndrome, also is present in NEH.\textsuperscript{30}

The pathogenesis of skin lesions in Behçet’s disease, including those of NEH, is unclear. Previous studies have demonstrated that active lesions in Behçet’s disease, including those induced by the pathergy test, are infiltrated by neutrophils.\textsuperscript{3} Neutrophilic vasculitis is believed to contribute to various organ pathology in Behçet’s disease. To our knowledge, this is the first case that documents a neutrophilic infiltrate involving the eccrine glands in a patient with Behçet’s disease. The predominance of neutrophils in spontaneous and induced lesions of Behçet’s disease is interesting. Neutrophils from patients with Behçet’s disease have increased superoxide production, enhanced chemotaxis, and excessive production of lysosomal enzymes that are believed to result in tissue injury.\textsuperscript{31-33} Levels of circulating tumor necrosis factor \(\alpha\), interleukin 1\(\beta\), and interleukin 8 are elevated; these cytokines may be involved in the activation of neutrophils.\textsuperscript{34} Neutrophil hyperfunction is only one aspect of the complex immunopathology of Behçet’s disease. Antibodies, endothelial cells, autoreactive T cells, and circulating immune complexes also have been implicated in the pathogenesis of Behçet’s disease.\textsuperscript{2,13,34}

**Conclusion**

We report a case of Behçet’s disease with an unusual eruption that revealed the histologic findings of NEH. NEH should be added to the list of skin lesions that may be seen in Behçet’s disease.

**REFERENCES**


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