Multiple red plaques on the head and neck

Hussein Hassab El-Naby, MD, Mohamed El-Khalawany, MD

Department of Dermatology, Al-Azhar University, Cairo, Egypt

CLINICAL FINDINGS

A 48-year-old male presented with painful skin lesions on the head and neck since 4 months. The lesions started with a small red lesion on the nape of neck that slowly progressed to form a large lesion. One month later, another lesion appeared on the neck area. The patient was afebrile and reported mild pruritus and edema on the neck. There was no history of other skin disease or systemic illness. On examination, there was a large eroded red plaque on the nape of the neck (Fig. 1) that measured 2.7 x 1.8 cm. The lesion was soft and slightly tender with central erosion and elevated edge. Another red plaque was present in the neck area with smooth glistening surface and skin-colored margins (Fig. 2). General examination was irrelevant and routine examination for malignancy, including complete blood counts and serum protein electrophoresis, and autoimmune disease was negative.

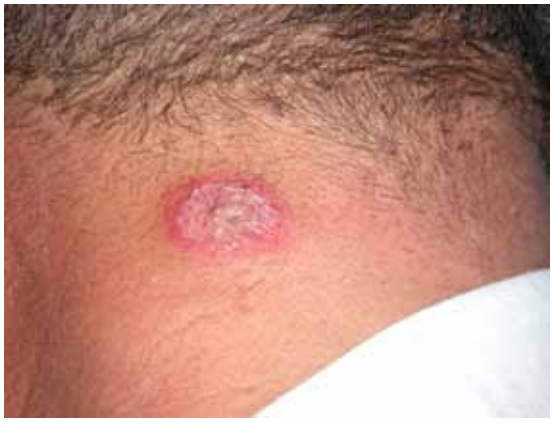

Fig. 1 A large eroded red plaque on the nape of the neck.

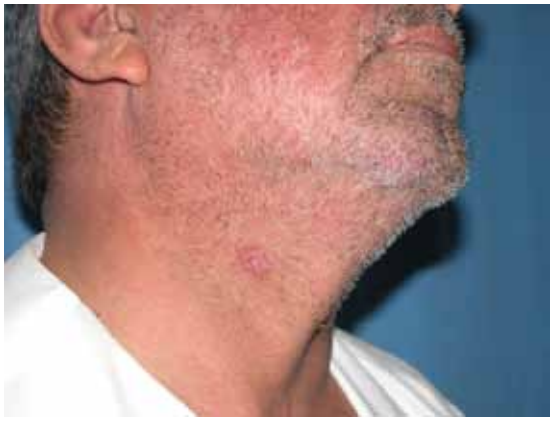

Fig. 2 A red plaque in the neck area with smooth glistening surface and skin-colored margins.

What is your clinical differential diagnosis?

Cutaneous leishmaniasis

Lupus erythematosus

Sweet's syndrome (SS)

Lymphocytoma cutis

Pathological findings

A punch biopsy (6 mm) was performed from the nape of neck lesion. Histological examination showed marked edema of the papillary dermis with dense dermal infiltrate in the upper and mid dermis (Fig. 3). The inflammatory infiltrate was formed mainly of neutrophils and admixed with lymphocytes, histiocytes and few eosinophils (Fig. 4). The blood vessels showed swelling of the endothelial cells with extravasation of RBCs but without signs of vasculitis (Fig. 5). The epidermis showed mild spongiosis with exocytosis of neutrophils and central erosion.

Correspondence: *Dr. Hassab El-Naby H, Department of Dermatology, Al-Azhar University, Cairo, Egypt*

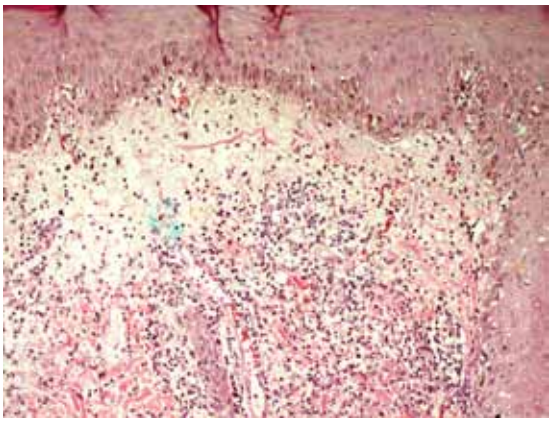

Fig. 3 Marked edema of the papillary dermis with dense dermal infiltrate (HE x200).

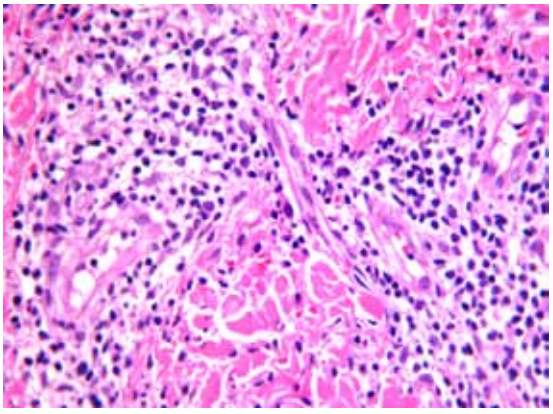

Fig. 4 The inflammatory infiltrate is formed mainly of neutrophils and admixed with lymphocytes, histiocytes and few eosinophils.

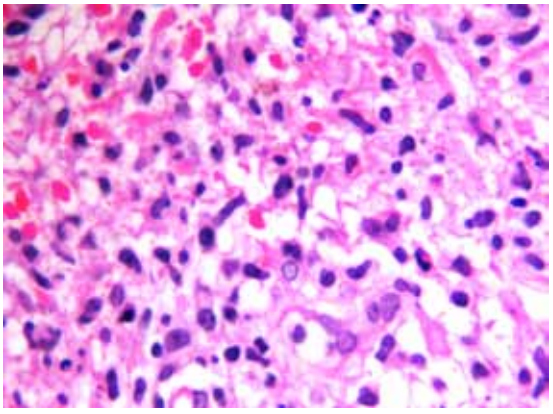

Fig. 5 The blood vessels showed swelling of the endothelial cells with extravasation of RBCs but without signs of vasculitis.

DIAGNOSIS

Acute febrile neutrophilic dermatosis (Sweet's syndrome)

COMMENT

Sweet's syndrome (acute febrile neutrophilic dermatosis) is an uncommon dermatologic eruption characterized by acute onset of painful papules, plaques or nodules on the skin that are red, blue, or violaceous in color. To date, the pathogenesis is largely not understood. Typically the rash is accompanied by fever and elevated inflammatory markers including leukocytosis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and neutrophilia. Though rare, extracutaneous manifestations may include involvement of the eyes, musculoskeletal system or internal organs.

The diagnosis of SS is established by the presence of 2 major and 2 minor criteria.

Major criteria include 1. abrupt onset of painful erythematous plaques or nodules, occasionally with vesicles, pustules, or bullae and 2. a neutrophilic infiltrate in the dermis without leukocytoclastic vasculitis.

Minor criteria include 1. preceding nonspecific respiratory or gastrointestinal tract infection or vaccination or association with inflammatory disease, hemoproliferative disorder, solid malignant tumor, or pregnancy; 2. constitutional symptoms and fever; 3. leukocytosis; and 4. excellent response to treatment with systemic corticosteroids.

The etiology of SS is still unknown but the association with inflammatory autoimmune diseases, infections, malignancies, drugs, and pregnancy suggests a hypersensitivity reaction. Another hypothesis is that a local or systemic dysregulation of cytokine secretion, including interleukin-1, interferon gama, granulocyte colony-stimulating

factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF), contributes to the pathogenesis of SS. SS has been linked with a wide range of infections, including upper respiratory tract infections, due to *streptococcus*, the most common infection associated with SS and gastrointestinal yersiniosis described in the literature.

Women are more frequently affected and seem to be particularly involved by the idiopathic or drug-induced forms. The onset is habitually described as occurring between the ages of 30 and 60 years, being rare in childhood and pediatric patients, the dermatosis is usually preceded by signs and symptoms of infection in the upper respiratory tract, from one to three weeks before the onset of cutaneous lesions. It was suggested that infectious agents might be triggers of reactive skin diseases, either through direct damage or molecular mimicry.

Histiocytoid Sweet's syndrome is a rare variant of SS. Histologically, histiocytoid Sweet's syndrome can present with an infiltrate containing predominantly mononuclear cells with large, slightly eccentric kidney-shaped or elongated nuclei with single indistinct nucleoli and slightly eosinophilic cytoplasm accompanied by numerous mature neutrophils and some mature lymphocytes; these cells may be misinterpreted as histiocytes.

Histopathology shows visible perivascular neutrophilic nodular infiltrates, with necrophiliac cariorrexis. Even though there is no primary vasculitis, blood vessels may be secondarily involved in immunologic response, an infrequent finding. Laboratory alterations include peripheral leukocytosis with neutrophilia and elevated speed of erythrocyte sedimentation or C-reactive protein, particularly in cases where SS associated with malignancy, leukopenia, anemia and thrombocytopenia have been reported.

Sweet's syndrome and erythema nodosum share many similar clinical and histological features. Both have acute onset and occur in association with many of the same systemic conditions, such as upper respiratory infections, medications, hematologic malignancies, and autoimmune disease. The two conditions are responsive to similar therapeutic drugs as systemic glucocortioids or potassium iodide. Nonetheless there are some differences between Sweet's syndrome and erythema nodosum. Sweet's syndrome lesions mainly involve the upper part of the body-head, neck, shoulder and trunk, while erythema nodosum lesions are characteristically seen on the pretibial region. Erythema nodosum lesions reveal deeper inflammatory cell infiltrate in subcutaneous adipose tissue, though this infiltrate is more superficial in dermis in Sweet's syndrome lesions.

In SS associated with hematological diseases such as AML, MDS and MPN, the PMNs in the dermal infiltrate may be clonally derived from either the malignant or non-malignant cells. Occasionally, malignant cells can be found among the PMNs representing concurrent leukemia cutis. Similarly, medications used in management of hematological malignancies such as granulocyte colony stimulation factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), all-trans retinoic acid (ATRA) and hypomethylating agents such as azacytidine and decitabine have been associated with SS, supporting the role of cytokines, maturation defects and epigenetic changes in the pathogenesis of SS.

Various treatments have been proposed for Sweet's

The clinicopathological challenges of Sweet's syndrome

Diagnosis	Clinical	Pathological
Cutaneous leishmaniasis	• The acute lesions are usually single papules, which become nodules, ulcerate and heal, leaving a scar • Chronic lesions are single, or occasionally multiple, raised non-ulcerated plaques • The recidivous (lupoid) form consists of erythematous papules, often circinate, near the scars of previously healed lesions	• In acute lesions there is a massive dermal infiltrate of lymphocytes, parasitized macrophages, epithelioid cells and occasional giant cells, plasma cells, and sometimes a few eosinophils • The epidermis shows hyperkeratosis and acanthosis, but sometimes atrophy, ulceration, or intraepidermal abscesses • The parasites are round to oval basophilic structures, 2-4 µm in size
Lupus erythematosus	• The typical lesions of discoid lupus erythematosus (DLE) are sharply demarcated, erythematous, scaly patches with follicular plugging • They usually involve the skin of the face, often in a butterfly distribution on the cheeks and bridge of the nose • There is a female preponderance	• A lichenoid reaction pattern and a superficial and deep dermal infiltrate of inflammatory cells which have a tendency to accumulate around the pilosebaceous follicles • The dermal infiltrate is composed predominantly of lymphocytes with a few macrophages • Plasma cells are prominent in oral lesions
Lymphocytoma cutis	• The most common sites of involvement include the face (cheeks, nose, and earlobe), chest, and upper extremities • Females are affected more often than males • These lesions usually present as asymptomatic redbrown or violaceous papules or nodules varying in diameter from 3 mm to 5 cm or more	• There is a variably dense infiltrate which may have a perivascular and peri-appendageal distribution or be more diffuse • The epidermis is usually spared but some small lymphocytes may be seen in the epidermis • The infiltrate may extend into the subcutis

syndrome to date and, although it is a self-limiting disease, timely recognition and appropriate treatment may reduce its morbidity. The first-line systemic drugs are corticosteroids, potassium iodide and colchicine, with second-line drugs including indomethacin, clofazimine, cyclosporine and dapsone. Other successful methods, such as biological treatments with tumor necrosis factor antagonists, have been reported. There are several reports on the beneficial effects of the interleukin-1 receptor antagonist anakinra on neutrophilic dermatoses. In addition, limited reports have investigated other biological agents for the treatment of Sweet's syndrome, such as adalimumab, immunoglobulin and infliximab.

Systemic corticosteroids (prednisone) produce rapid improvement and are considered the "gold standard" for treatment of Sweet's syndrome. The skin lesions usually clear within 3 to 9 days. Topical and/or intralesional corticosteroids may be effective as either monotherapy or adjuvant therapy. Oral potassium iodide or colchicine may induce

rapid resolution. Individuals who have a potential systemic infection or in whom corticosteroids are contraindicated can use the above agents as first-line therapy. Other alternatives to corticosteroid treatment include dapsone, doxycycline, clofazimine, and cyclosporine. All of these agents influence neutrophil migration and function.

REFERENCES

1. Sweet RD. An acute febrile neutrophilic dermatosis. Br J Dermatol. 1964; 76:349-56.
2. Cohen PR, Kurzrock R. Sweet's syndrome: a review of current treatment options. Am J Clin Dermatol. 2002; 3:117-31.
3. Cohen PR, Kurzrock R. Sweet's syndrome and malignancy. Am J Med. 1987; 82:1220-26.
4. Spector JI, Zimbler H, Levine R, Ross JS, Valigorsky JM, Cole LM. Sweet's syndrome. Association with acute leukemia. JAMA. 1980; 244:1131-32.
5. Klock JC, Oken RL. Febrile neutrophilic dermatosis in acute myelogenous leukemia. Cancer. 1976; 37:922-27.
6. Cohen PR, Talpaz M, Kurzrock R. Malignancy-associated Sweet's syndrome: review of the world literature. J Clin Oncol. 1988; 6:1887-97.
7. Cooper PH, Innes DJ, Jr, Greer KE. Acute febrile neutrophilic dermatosis (Sweet's syndrome) and myeloproliferative disorders. Cancer. 1983; 51:1518-26.
8. Soppi E, Nousiainen T, Seppa A, Lahtinen R. Acute febrile neutrophilic dermatosis (Sweet's syndrome) in association with myelodysplastic syndromes: a report of three cases and a review of the literature. Br J Haematol. 1989; 73:43-47.
9. Glaspy JA, Baldwin GC, Robertson PA, Souza L, Vincent M, Ambersley J, Golde DW. Therapy for neutropenia in hairy cell leukemia with recombinant human granulocyte colony-stimulating factor. Ann Intern Med. 1988; 109:789-95.
10. Park JW, Mehrotra B, Barnett BO, Baron AD, Venook AP. The Sweet syndrome during therapy with granulocyte colony-stimulating factor. Ann Intern Med. 1992; 116:996-98.
11. Suehisa S, Tagami H, Inoue F, Matsumoto K, Yoshikuni K. Colchicine in the treatment of acute febrile neutrophilic dermatosis (Sweet's syndrome) Br J Dermatol. 1983; 108:99-101.
12. Bonamigo RR, Razera F, Olm GS. Neutrophilic dermatoses: part I. An Bras Dermatol. 2011; 86 (1):11-25.
13. Thompson DF, Montarella KE. Drug-induced Sweet's syndrome. Ann Pharmacother. 2007; 41:802-11.
14. Roujeau JC. Neutrophilic drug eruptions. Clin Dermatol. 2000; 18:331-37.
15. Saez M, Garcia-Bustinduy M, Noda A, Dorta S, Escoda M, Fagundo E, et al. Drug-induced Sweet's syndrome. J Eur Acad Derm Venereol. 2004; 18:233.
16. Walker DC, Cohen PR. Trimethoprim-sulfamethoxazole-associated acute febrile neutrophilic dermatosis: case report and review of drug-induced Sweet's syndrome. J Am Acad Dermatol. 1996; 34:918-23.
17. Gyorfy A, Kovács T, Szegedi I, Oláh E, Kiss C. Sweet syndrome associated with 13-cis-retinoic acid (isotretinoin) therapy. Med Pediatr Oncol. 2003; 40:135-36.