Sweet’s syndrome associated with cellulitis - a challenging diagnosis*

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Abstract: Sweet’s syndrome is a neutrophilic dermatosis with worldwide distribution that has been associated with inflammatory autoimmune diseases, infections, malignancies, drugs, and pregnancy. The disease is idiopathic in up to 50% of patients. A 64-year-old woman, diagnosed with right limb cellulitis (4 days of evolution), was seen at our department, due to persistent cellulitis and progressive appearance of painful nodules and plaques in both shins and the right forearm (2 days of evolution). Taken together, clinical, laboratory and pathological data suggested the diagnosis of Sweet’s syndrome, probably secondary to cellulitis of the right inferior limb. We suggest that cellulitis may be associated with Sweet’s syndrome, a rare association in the literature.

Keywords: Cellulitis; Infection; Sweet syndrome

INTRODUCTION

Sweet’s syndrome (SS) has worldwide distribution, without racial predilection but with a female predominance of 4 to 1 and an average onset age of 30-60 years.¹,²,³ It has been associated with inflammatory autoimmune diseases, infections, malignancies, especially acute myelogenous leukemia, drugs, and pregnancy.⁴,⁵ The disease is idiopathic in up to 50% of patients.¹,⁶

Initial cutaneous lesions are tender, non-pruritic, erythematous papules and plaques, with a pseudovesicular appearance.¹,² Patients may present with constitutional signs and symptoms, such as fever and malaise.⁷ Lesions predominantly favor the head, neck and upper extremities, though they can occur anywhere.¹,⁵ Typical histological features include a dense, perivascular, neutrophilic infiltrate, edema and leukocytoclasia without evidence of vasculitis.¹,⁵ Leukocytosis and increased erythrocyte sedimentation arises in the majority of SS patients.⁵,⁶

CASE REPORT

A 64-year-old woman, diagnosed with cellulitis of the right inferior limb (4 days of evolution) was seen at our department due to persistent cellulitis and progressive appearance of painful nodules and plaques in both shins (2 days of evolution). She had previously been treated with ceftriaxone 500mg 4 times daily, without any improvement. The patient reported that the lesions appeared about 4 days later, following a trauma caused by a metal object. Physical examination revealed erythema, edema, heat and pain in the right inferior limb. The redness had a well-demarcated but irregular border and spared portions of skin in an unpredictable pattern. The inflamed area was edematous, creating a plaque that pitted under pressure. Moreover, the patient had multiple, infiltrated, painful, erythematous, violaceous nodules and plaques of variable sizes, measuring 1-7cm in diameter, with a vesicular or bullous appearance, localized in both shins (Figure 1). In addition, she had painful, reddened eyes.
Her medical history was unremarkable and there was no family history of cutaneous diseases. She was not taking any medication prior to the diagnosis of cellulitis in the right inferior limb. She denied fever and she was afebrile at our observation.

Laboratory examination revealed leukocytosis (white blood cells 11700/uL, with a high absolute neutrophils count (78%) and an increased C-reactive protein level of 159 mg/L.

Histopathologic examination of an incisional biopsy on a lesion taken from the left leg revealed edema in the papillary dermis with dense inflammatory infiltrate in the upper dermis, consisting mainly of mature neutrophils without fibrinoid necrosis (Figure 2).

The patient underwent extensive investigation, including a CT of the chest, abdomen and pelvis, esophagogastroscopey, colonoscopy and mammography. This extensive workup revealed no focus of infection or malignancy.

Taken together, clinical, laboratory and pathological data suggested the diagnosis of SS, probably secondary to cellulitis of the right inferior limb.

The medication was changed from cefatrizine to penicillin G 20 million units, divided into 4 daily doses over 14 days. Moreover, she was given prednisone 0.5mg/kg/daily, tapered by 5mg every 4 days, resulting in significant improvement of the skin lesions within 2 weeks, without residual scarring.

During the 18 months of follow-up, the patient did not experience recurrence of skin lesions.

DISCUSSION

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.

In our case, we suggested that SS was probably secondary to cellulitis of the right inferior limb.

Furthermore, SS has reportedly been caused by a wide variety of drugs, including granulocyte colony-stimulating factor, antibacterials, retinoids, antiepileptics, antihypertensives, oral contraceptives and vaccines. Drug-induced SS is rare and affects predominantly middle-aged women, with skin lesions usually appearing 5-7 days after the first administration of the drug. The most common localization of drug-induced SS was the arms, followed by the legs, face, neck and trunk.

Figure 1: Erythema, edema of the right inferior limb and multiple, infiltrated, painful erythematous, violaceous nodules and plaques, of variable sizes, measuring 1-7cm in diameter, with a vesicular or bullous appearance, localized in both shins.

Figure 2: Edema of the papillary dermis with dense inflammatory infiltrate in the upper dermis, consisting mainly of mature neutrophils without fibrinoid necrosis (haematoxylin and eosin, magnification 400x).
Our patient was not on any medication before the diagnosis of cellulitis in the right inferior limb but she was medicated with ceftriaxone 500mg, two days prior to the onset of SS lesions. Consequently, another, less likely, hypothesis, is that our patient had drug-induced SS caused by ceftriaxone. It is less probable because the temporal relationship between drug ingestion and the clinical presentation of SS was only two days after the onset of antibiotic therapy. Furthermore, the patient saw significant improvement in skin lesions within 2 weeks, after our first observation. In addition to discontinuing ceftriaxone, penicillin G and prednisone were administered to the patient, which could explain the rapid improvement in the lesions.

Our patient also underwent an extensive investigation to exclude other causes of SS, which revealed no specific findings.

The presence of neutrophilia, common in most SS patients, including our patient, was observed in a few patients with drug-induced SS, described in the literature. Ocular involvement, also observed in our patient, is more frequent in classic SS than in drug-induced SS.

To our knowledge, Dinh H. et al. reported the first-ever published case of SS that was likely secondary to cellulitis, involving a 38-year-old woman, who developed SS following cellulitis in her left leg. Our patient also developed cellulitis in the lower limb; two days later, she developed SS in the shins and forearms. We identified precisely the simultaneous presence of both diseases. The cellulitis in her right limb improved quickly within a few days, while the SS improved following the institution of antibiotic therapy with penicillin and systemic corticotherapy.

We suggest that cellulitis, a frequent cutaneous infection, may be associated with SS, an unusual association in the literature. However, we cannot exclude the hypothesis that SS is a mimicker of cellulitis called “giant cellulitis-like SS”, recently described in the literature as a possible new variant of neutrophilic dermatosis.

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