Sweet’s Syndrome: One Disease, Multiple Faces

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Case Presentations

Case 1

A 48-year-old man with a history of myelodysplastic syndrome (MDS), post-decitabine chemotherapy was admitted with a fever, skin rash, and pancytopenia. Physical examination showed multiple painless, non-itchy, erythematous, maculopapular skin lesions on the dorsum of both hands (figure 1A). Broad spectrum antibiotics, antifungals, and granulocyte colony-stimulating factor (G-CSF) therapy were started. The septic workup came back negative, yet the patient continued having low-grade fever with new skin lesions. Skin biopsy revealed diffuse dermal neutrophilic infiltrate (figure 1B), consistent with Sweet’s syndrome (SS). Prednisone (1mg/kg/day) was started and antibiotics were de-escalated. The skin lesions regressed, and the fever resolved in two days. Triggering factors were thought to be decitabine, MDS, and G-CSF therapy. He was discharged on oral prednisone.

Case 2

A 74-year-old woman with a recent diagnosis of MDS and SS was admitted with acute onset of tongue swelling, painful oral ulcers, fever, and a new skin rash. She was on a tapering dose of prednisone. Physical examination revealed oral ulcers, macroglossia (figure 2A) (with no airway compromise) and an ecchymotic, violaceous skin rash on her trunk. Skin biopsy revealed neutrophilic dermatosis consistent with SS (figure 2B). Bone marrow biopsy revealed MDS transformation to acute myelogenous leukemia. She was started on azacitidine. Control of SS was achieved with a combination of high dose prednisone and supersaturated potassium iodide. Her symptoms resolved, and she was discharged on oral medications.
Discussion

Sweet’s syndrome (SS), or acute febrile neutrophilic dermatosis, is an unusual dermatologic disorder first described in 1964.\textsuperscript{1-3} It is divided into three categories: 1) idiopathic (classical), 2) drug-induced, and 3) malignancy-associated, although the exact cause within any category is not always known. Idiopathic SS predominantly affects middle-aged females (with a recurrence of up to 50%) and could be associated with infections, inflammatory diseases, or pregnancy.

Malignancy-associated SS accounts for approximately 20% of SS cases and is commonly associated with myeloproliferative disorders and, to a lesser extent, solid tumors. Drug-induced SS is an uncommon reaction to medications including G-CSF, non-steroidal anti-inflammatory drugs, and decitabine.\textsuperscript{3-5}

Fever with skin rash involving the face, trunk, and extremities is the usual presentation of SS. In its classic form, the lesions are tender, erythematous plaques or papules with a pseudo-bullous or vesiculous component. Systemic manifestations involve mucosal, renal, cardiac, pulmonary, and central nervous systems. Macroglossia, as seen in our second case, can be a herald for MDS transformation to secondary acute myelogenous leukemia.\textsuperscript{4,6,7} Although the pathogenesis remains unknown, SS is thought to be an immune-mediated hypersensitivity reaction to infectious, inflammatory, drug, or tumor cell antigens. Cytokines, dermal dendrocytes, and auto-antibodies might also have a role.\textsuperscript{2,3,8}

Although the diagnostic criteria have evolved over time to include more clinical aspects;\textsuperscript{9} the original components, as described by Sweets et al,\textsuperscript{1,10} have remained the key to confirming the diagnosis. The original criteria involves fever, peripheral leukocytosis, tender erythematous
plaques, and a diffuse dermal neutrophilic infiltration. Both of our patients did meet these criteria. First line treatment is corticosteroids. Prednisone (1mg/kg/day) can be started and tapered off in two to six weeks according to clinical response. Alternative therapies include supersaturated potassium iodide, rifampin, clofazimine, cyclosporine, dapsone, colchicine, indomethacin, and more recently, tumor necrosis factor antagonists.\textsuperscript{2,4} Treatment of the underlying cause is vital to resolution of this condition. It should also be noted that some cases do resolve spontaneously.

**Conclusion**

Given the diverse associations and manifestations of SS, it should always be considered as a differential diagnosis in patients with an acute febrile illness and skin rash. A timely diagnosis allows the physician to begin appropriate treatment as well as the ability to manage the underlying cause.

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References


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Figure Legends

Figure 1. [Case 1] (A) Examples of multiple non-tender, erythematous papules (less than 1cm), with a pseudo-bullous aspect on the dorsum of one hand. (B) Diffuse dermal neutrophilic infiltrate with papillary edema, consistent with Sweet’s syndrome. Polymorphonuclear cells can also be noted (Hematoxylin & Eosin [H&E] staining, 40x magnification).
Figure 2. [Case 2] (A) Evidence of macroglossia and oral ulcers (arrow). (B) Skin biopsy showing diffuse dermal neutrophilic infiltrate, papillary edema of both the dermis and epidermis, consistent with Sweet’s syndrome (Hematoxylin & Eosin [H&E] staining, 40x magnification).