

## Case Report

# Sweet syndrome: a sweet disease with a bitter diagnosis

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### ABSTRACT

Sweet syndrome is an acute febrile neutrophilic dermatosis first described by Robert Douglas Sweet in 1964. Sweet syndrome presents in three clinical settings: classical (or idiopathic), malignancy-associated, and drug-induced. It has been associated with hematopoietic malignancies and myelodysplastic disorders. A-28-years married woman presented to us with chief complaints of Fever and Multiple swellings over the body since 2 months. At presentation she has Pallor; venous hum present. Multiple, tender, erythematous subcutaneous swellings, firm in consistency noted in both forearms. Skin over the swellings is pinchable; superficial skin is normal. Sweet syndrome can occasionally cause an intense systemic response involving the lungs, liver and musculoskeletal system. The skin lesions in Sweet syndrome typically start as erythematous papules, plaques, and nodules. The lesions can take on pseudovesicular or pseudopustular appearance, and sometimes fully formed vesicles or pustules develop. The lesions can be subcutaneous mimicking erythema nodosum which can't be differentiated unless a biopsy is taken. Because the diagnosis of Sweet syndrome can be challenging, particularly when associated with other connective tissue disorders such as SLE, a set of diagnostic criteria were proposed initially by Su and Liu and then revised by Von den Driesch. The diagnosis is based upon the presence of two major and two of the four minor criteria. Concurrent Sweet syndrome and SLE are exceedingly rare. Twelve patients with both Sweet syndrome and systemic lupus erythematosus (SLE) have been previously reported. We report a case of sweet syndrome associated with SLE diagnosed in our hospital. In our patient, diagnostic criteria are satisfied for Sweet syndrome as well as for SLE (ACR criteria-patient had polyarthralgia, anemia, thrombocytopenia, ANA and Ds DNA positive. Four out of 11 are fulfilled for SLE). Patient responded to corticosteroids.

**Keywords:** Febrile neutrophilic dermatosis, Polyarthralgia, Systemic lupus erythematosus, Sweet syndrome

### INTRODUCTION

Sweet syndrome is an acute febrile neutrophilic dermatosis first described by Robert Douglas Sweet in 1964.<sup>1</sup> Whittle et al and Crow et al were the first to use the term "Sweet's syndrome" as titles of their articles.<sup>2</sup>

Sweet syndrome presents in three clinical settings: classical (or idiopathic), malignancy-associated, and drug-induced.

Classical Sweet syndrome (CSS) usually presents in women between the age of 30 to 50 years, it is often preceded by an upper respiratory tract infection and may be associated with inflammatory bowel disease and pregnancy. Approximately one-third of patients with CSS experience recurrence of the dermatosis.

The malignancy-associated Sweet syndrome (MASS) can occur as a paraneoplastic syndrome in patients with an established cancer or individuals whose Sweet

syndrome-related hematologic dyscrasia or solid tumor was previously undiscovered; MASS is most commonly related to acute myelogenous leukemia. The dermatosis can precede, follow, or appear concurrent with the diagnosis of the patient's cancer. Hence, MASS can be the cutaneous harbinger of either an undiagnosed visceral malignancy in a previously cancer-free individual or an unsuspected cancer recurrence in an oncology patient.

Drug-induced Sweet syndrome (DISS)-Su and Liu reported the first patient with drug induced Sweet syndrome in 1986; the associated medication was trimethoprim-sulfamethoxazole.<sup>3</sup> A decade later, criteria for drug-induced Sweet syndrome were established by Walker and Cohen.<sup>4</sup> The most frequently implicated drug is granulocyte-colony stimulating factor. However, several other medications-albiet less often-have been observed to promote the development of Sweet syndrome.

The syndrome often presents in idiopathic fashion. It has been associated with hematopoietic malignancies and myelodysplastic disorders. It has also been observed in association with certain autoimmune disorders such as Sjogren's syndrome, SLE, Rheumatoid arthritis.

The pathogenesis of Sweet syndrome may be multifactorial and still remains to be definitively established. Clinical and laboratory evidence suggests that cytokines have an etiologic role. Systemic corticosteroids are the therapeutic gold standard for Sweet syndrome. After initiation of treatment with systemic corticosteroids, there is a prompt response consisting of dramatic improvement of both the dermatosis-related symptoms and skin lesions. Topical application of high potency corticosteroids or intralesional corticosteroids may be efficacious for treating localized lesions. Other first-line oral systemic agents are potassium iodide and colchicine. Second-line oral systemic agents include indomethacin, clofazimine, cyclosporine, and dapsone.

Twelve patients with both Sweet syndrome and systemic lupus erythematosus (SLE) have been previously reported.<sup>5,6</sup> We report a case of sweet syndrome associated with SLE diagnosed in our hospital.

### CASE REPORT

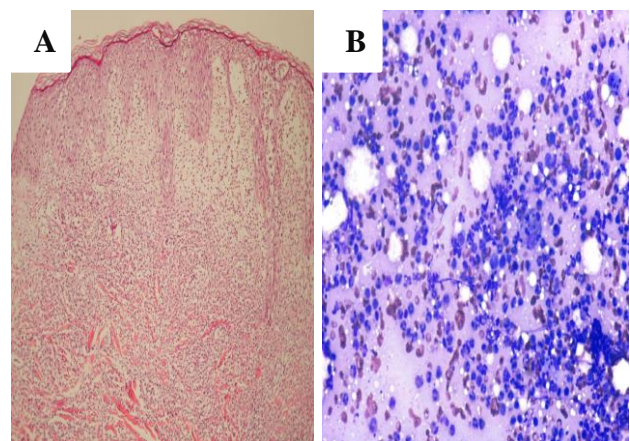
A-28-years married woman presented with chief complaints of Fever and Multiple swellings over the body since 2 months. Fever is high grade, intermittent associated with chills, multiple erythematous papules which are painful present bilaterally in both upper and lower limbs, abdomen, neck. She also complaints of polyarthralgia. She denied illicit or prescribed drug use, drug allergies, alcohol, or tobacco. History of similar complaint from the past 3 years; every year the patient suffers for few months with the similar complaint and the nodules had no ulceration or residual scarring. Patient

was treated outside and was started on anti-rheumatoid drugs (using since 7 months), she had multiple blood transfusions in the past, had 2 uneventful pregnancies.

At presentation she has Pallor; venous hum present. Multiple, tender, erythematous subcutaneous swellings, firm in consistency noted in both forearms as shown in Figure 1. Skin over the swellings is pinchable; superficial skin is normal. Her vitals showed temperature-100 F; pulse rate-120/min, regular; blood pressure-110/60mmHg; respiratory rate-19/min. On systemic examination; cardiovascular system showed apex beat present in 5<sup>th</sup> IC space, parasternal pulsations/parasternal heave present, palpable 2<sup>nd</sup> sound in pulmonary area, pulmonary area-loud S2 present and per-abdomen showed splenomegaly. Her respiratory and neurological examination is normal.



**Figure 1: Multiple tender erythematous swellings over both forearms.**



**Figure 2: (A) Low magnification showing a diffuse dermal infiltration by neutrophils. (B) High magnification showing plenty of polymorphs, tingible body macrophages and lymphocytes with background showing RBC without leucocytoclasia.**

Investigations- Hb-6.1gm%; WBC-3600cells/cumm; N76 L18 E4 M2; platelet count-60000cells/cumm; peripheral smear-microcytic, hypochromic with thrombocytopenia;

ESR-150mm/1<sup>st</sup>hr; RBS-103mg%; complete urine examination-albumin 2+; 24 urine protein-1200mg/dl; urea-25mg%; Sr. creatinine-0.9mg%; Na-135; k-5.0meq/l; viral markers HIV, HbsAg are negative; CRP-positive; RA Factor-negative ASO-negative; ECG-WNL; LFT'S are within normal limits; thyroid profile is normal; skeletal survey- normal; anti-nuclear Ab's-139U/ml (normal <25 ); Anti ds DNA-90IU/ml (normal <20). Aspirate culture from the swellings were sterile. 2D Echo: global hypokinesia with EF = 35%, RVSP of 57mmHg; mild MR BIOPSY from swellings (forearm).

**DISCUSSION**

Concurrent Sweet disease and SLE are exceedingly rare. Only three other papers reported Sweet syndrome as an initial presentation in adult SLE.<sup>7-9</sup>

Sweet syndrome is an acute febrile neutrophilic dermatosis which often presents in idiopathic fashion can also be drug induced, associated with malignancy, or connective tissue diseases.<sup>10</sup> It is shown in Table 1. Our case is the fourth.

**Table 1: Diseases and drugs reported in association with sweet syndrome.**

Malignancies	Autoimmune Diseases	IBD*	Others
AML	Rheumatoid Arthritis	Crohn's	Post-infection (bacterial, fungal, parasitic)
Myelodysplasia	SLE	Ulcerative colitis	Behcet's
CML*	Thyroid disease (Grave's, Hashimoto's)		Sarcoidosis
Multiple myeloma	-	-	Pregnancy
Solid tumors (Genito-urinary, Gastro-intestinal and breast)	-	-	Drugs (G-CSF*, Cotrimoxazole, OCP's*, Carbamazepine)

IBD\*- Inflammatory bowel disease, CML\* - Chronic myelogenous leukaemia, G-CSF\*-Granulocyte colony stimulating factor, OCP's\*-Oral contraceptive pills

**Table 2: Diagnostic criteria by von den Driesch (1992).**

Major criteria
Clinical criterium: abrupt onset of tender or painful erythematous plaques or nodules occasionally with vesicles, pustules or bullae.
Histopathological criterium: predominantly neutrophilic infiltration in the dermis without leukocytoclastic vasculitis.
Minor criteria
<b>Preceded by a nonspecific respiratory or gastrointestinal tract infection or vaccination or associated with</b>
Inflammatory diseases such as chronic autoimmune disorders, infections
Hemoproliferative disorders or solid malignant tumors
Pregnancy
Accompanied by periods of general malaise and fever (>38°C)
<b>Three of four of the following laboratory values during onset</b>
ESR > 20 mm
C-reactive protein positive
Segmented-nuclear neutrophils and stabs > 70% in peripheral blood smear
Leukocytosis >800
Excellent response to treatment with systemic corticosteroids or potassium iodide
Diagnosis-2 major and 2 minor criteria required

The skin lesions in Sweet syndrome typically start as erythematous papules, plaques, and nodules. The lesions can take on pseudovesicular or pseudopustular appearance, and sometimes fully formed vesicles or pustules develop.

The lesions can be subcutaneous mimicking erythema nodosum which can't be differentiated unless a biopsy is taken. The lesions are usually painful, and typical sites include the head, neck, and upper extremities, although

lesions can be found anywhere. Lesions usually develop abruptly, resolve over 1-3 months without any residual scarring, and can recur in 30% of patients.<sup>11</sup>

Histopathologically, older studies reported that leukocytoclastic vasculitis is not seen which is as in our case.<sup>12</sup> However, more recent reports have convincingly demonstrated that leukocytoclastic vasculitis can occasionally be found.<sup>13</sup>

Because the diagnosis of Sweet syndrome can be challenging, particularly when associated with other connective tissue disorders such as SLE, a set of diagnostic criteria were proposed initially by Su and Liu.<sup>14</sup> It was then revised by Von den Driesch. The diagnosis is based upon the presence of two major and two of the four minor criteria which is shown in table-2. In our patient, diagnostic criteria are satisfied for Sweet syndrome as well as for SLE (ACR criteria-patient had polyarthralgia, anemia, thrombocytopenia, ANA and Ds DNA positive 4 out of 11 are fulfilled for SLE.)

Like other cases in the literature, our patient responded dramatically to corticosteroids, which are the mainstay of therapy for Sweet syndrome.

## CONCLUSION

In summary, Sweet syndrome is a neutrophilic dermatosis that may be more commonly associated with SLE than previously suspected because of the role of cytokine dysregulation in the pathogenesis of both conditions. Sweet disease observed in the setting of lupus may also be classified as “neutrophilic dermatosis of LE” and may be the first manifestation of SLE. Further research is needed to define the exact relationship between the two conditions.

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