A Case Report on Giant Cellulitis-like Sweet Syndrome: A Rare Variant

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Received: 10 December 2024

Accepted: 8 April 2025

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DOI 10.5001/omj.2028.20

Abstract

Sweet syndrome, also known as acute febrile neutrophilic dermatosis, encompasses a group of inflammatory skin conditions that are histologically characterized by the presence of neutrophilic infiltrate in the dermis or hypodermis. These conditions are frequently associated with systemic inflammatory and neoplastic disorders. This case report describes a 68-year-old Omani female who presented with recurrent, ill-defined, and diffuse erythema of both breasts, initially suspected to be cellulitis. Despite multiple courses of oral and intravenous antibiotics, the erythema only partially improved. Laboratory results consistently revealed neutrophilic leukocytosis. Extensive laboratory tests and imaging to rule out inflammatory breast cancer did not reveal any significant findings. Skin biopsies consistently showed a dominant neutrophilic infiltrate, consistent with the diagnosis of Sweet syndrome. Based on the clinical presentation, laboratory findings, and skin biopsy results, this case was classified as a "giant cellulitis-like" variant of Sweet syndrome. The patient responded successfully to treatment with prednisolone and topical corticosteroids. Recognition of this atypical variant of Sweet syndrome is essential for proper diagnosis and management.

Keywords: Giant Cellulitis-like Sweet Syndrome, Sweet Syndrome, Rare Variant, Cellulitis, Neutrophilic Dermatosis, Skin Lesions, Case Report, Inflammatory Disorders.

Introduction

Sweet syndrome, also known as acute febrile neutrophilic dermatosis which does not show any racial predilection. However, it demonstrates a notable female predominance, with a ratio of 4:1, and typically affects individuals between the ages of 30 and 60 years.[1,2] The disease is often associated with systemic conditions such as hematologic malignancies, solid tumors, infections, and pregnancy.[2] The pathogenesis of Sweet syndrome remains unclear, and in approximately 50% of cases, the cause remains idiopathic.[1]

In the classic form of Sweet syndrome, patients typically present with fever and sudden appearance of painful erythematous plaques or nodules of various sizes, occurring asymmetrically, most commonly on the face, neck, and upper extremities.[3] Diagnosis is usually made through clinical presentation, supported by histopathological examination that reveals dense neutrophilic infiltration without the presence of vasculitis.[3,4]

Giant Cellulitis-like Sweet Syndrome is a rare and distinctive variant of Sweet syndrome, which is often mistaken for cellulitis due to its clinical resemblance to a localized bacterial infection. However, unlike cellulitis, Giant Cellulitis-like Sweet Syndrome does not show evidence of bacterial infection and instead demonstrates a neutrophilic

dermatosis on biopsy.[5] This variant has been less frequently reported in the literature, making its diagnosis challenging and often delayed. Recognizing this rare variant is essential to avoid unnecessary antibiotic treatment and to ensure appropriate management, which typically involves systemic corticosteroids.

In this case report, we present a 68-year-old male patient who developed Giant Cellulitis-like Sweet Syndrome, providing insight into its clinical features, diagnostic challenges, and management approach. By discussing this case, we aim to increase awareness of this rare variant and highlight the importance of differentiating it from other conditions with similar presentations, such as cellulitis.

Case Report

A 68-year-old woman with a medical history of diabetes mellitus, hypertension, dyslipidemia, and osteoarthritis, on regular medications. Presented with a history of fever, generalized body aches, and noted spreading erythema associated with pain and burning sensation of skin in both breasts. The erythema was more pronounced in the left breast. No prior history of trauma, burn, insect bite, exposure to sun, spillage of fluids or chemicals, etc. There was also no personal nor family history of atopy or psoriasis.

The condition initially appeared 6 months ago, and since then, the patient has experienced recurrent attacks, with the erythema and associated symptoms returning at the same site. The patient has been admitted to the surgical ward four times due to recurrent episodes of the condition. On examination, patient was febrile (temperature 38°C) with stable other vital signs. Localized clinical examination revealed noticeable enlargement in the left breast compared to the right. Well-defined blanchable erythematous plaques were observed in both breasts, more prominently in the left. The affected areas were warm and slightly tender to touch, with an absence of lymphadenopathy, and no areola or nipple changes (Fig. 1). There were no other lesions, nail changes, or significant findings from other systemic examinations.

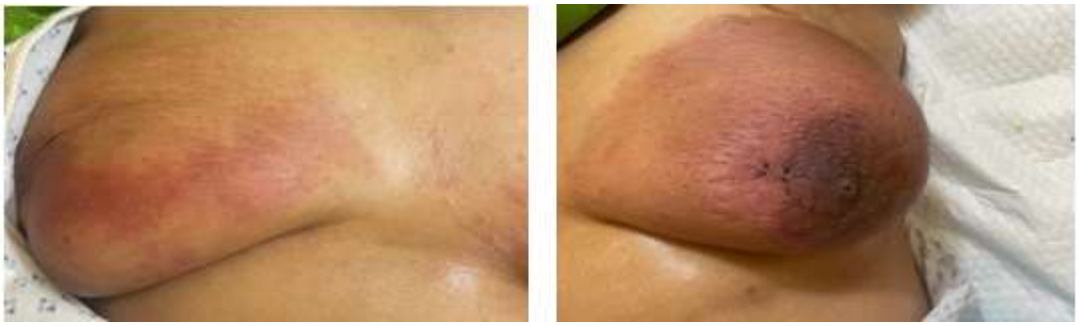

Figure 1: Left breast exhibited enlargement in the left breast compared to the right. Well-defined blanch-able erythematous plaques were observed in both breasts, more prominently in the left. The affected areas were warm and slightly tender to touch, with an absence of lymphadenopathy, and no areola or nipple changes.

The patient was initially diagnosed with cellulitis and treated with multiple courses of intravenous and oral antibiotics; however, there was no significant response to the treatment. Mammography was done twice to rule out underlying infiltrating breast cancer, but results were normal.

Routine laboratory tests showed elevated inflammatory markers with neutrophilic leukocytosis (WBC ranging from 14.27 x 10^3/uL to 10.9 x 10^3/uL, NEU 10.5 x 10^3/uL), CRP 210 mg/L, and ESR 85.00 mm/h. Other serological studies, including ANA, Cyclic Citrullinated Peptide IgG Ab, VDRL, and rheumatoid factors, were negative. Ultrasound of the breast showed an inflammatory process without any fluid collection.

Based on the clinical presentation, laboratory findings, and the lack of response to antibiotics, Sweet syndrome was considered the most likely diagnosis. An excisional biopsy from the left breast was performed, which confirmed the presence of neutrophilic dermatosis, with no evidence of vasculitis or fibrinoid necrosis of the vessel wall (Fig.2).

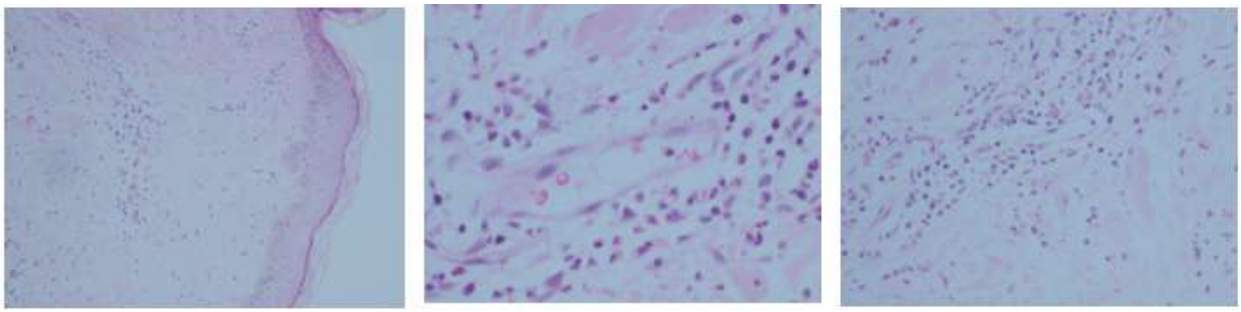

Figure 2: Skin biopsy; shows epidermis with mildly flattened rete ridges and mild neutrophilic exocytosis. The upper, mid, and lower dermisdermis shows mixed, predominantly neutrophilic infiltrate distributed perivascularly, and interstitialy and around eccrine glands. Variable lymphocytes are seen admixed along with rare eosinophils and mast cells. There is upper dermal edema with dilated blood vessels lined by prominent endothelial pulg is seen within one of the capillaries, associated with collection of neutrophils. Special stain (AB-PAS) is negative for dermal mucin.

The patient was diagnosed with a "cellulitis-like" variant of Sweet syndrome and treated with oral prednisolone (30 mg once a day), which was tapered down to 5 mg over 4 weeks, in addition to topical corticosteroids. The skin lesions showed significant improvement (Fig. 3), the fever subsided, and the condition entered a state of remission (Fig. 4).

Figure 3: skin lesion improvement after one week of starting prednisolone

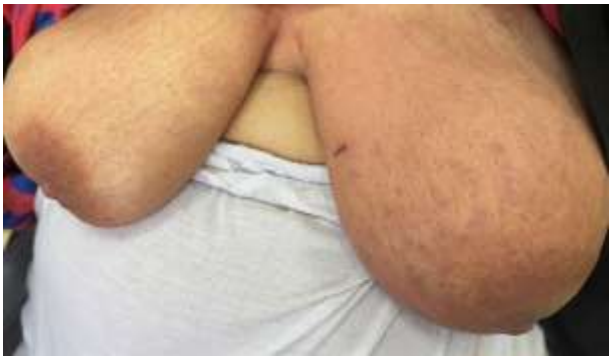

Figure 4: skin lesion improvement after 4 weeks of starting prednisolone

The patient was referred to a hematologist for further evaluation of potential hematological causes. The hematologist conducted a thorough evaluation, including blood tests such as inflammatory markers, LDH, ANA, and a blood film, as well as imaging studies, which ruled out any underlying hematologic malignancies or related conditions. The patient's condition appeared to be isolated and unrelated to hematologic disorders. Additionally, mammography results revealed the following: Left breast features were consistent with dermatitis mastitis, with histopathological evidence of dermatitis, likely an acute exacerbation, requiring clinical correlation. The findings were

categorized as BI-RADS 3. The right breast showed benign calcifications and oil cysts, categorized as BI-RADS 2. The patient is currently undergoing regular follow-up appointments with the specialist in surgery and dermatology.

Discussion

Sweet syndrome (SS), first defined by Robert Douglas Sweet in 1964, is an acute febrile neutrophilic dermatosis characterized by erythematous, painful lesions associated with systemic symptoms such as fever and leukocytosis.[6,7] While the condition is most commonly idiopathic, it can occur in association with malignancy, as a drug reaction, during pregnancy, and in some infectious and inflammatory diseases.[8]

Skin manifestations of acute febrile neutrophilic dermatosis can vary in number, ranging from a few to numerous lesions. The face, neck, chest, and extremities are commonly affected, though other areas of the skin and mucosa may also be involved. Sweet syndrome lesions can exhibit diverse appearances, such as small papules or vesicles, larger thickened or edematous plaques, nodules, a pseudovesicular appearance resembling blistering, annular lesions, and erosions or ulcers resembling atypical pyoderma gangrenosum.[7,9,10]

Histologically, Sweet syndrome is characterized by a substantial dermal infiltrate of mature neutrophils, significant edema in the upper dermis, and the absence of leukocytoclastic vasculitis, which is typically seen in other conditions, such as vasculitis or pyoderma gangrenosum.[6,9] There may also be fragmented nuclear 'dust' from neutrophils, arranged in a 'top-heavy' manner, indicative of cellular degeneration or inflammation.[9] Neutrophilic spongiosis or intraepidermal abscess formation may also be present.[9] The histologic features observed in our patient were consistent with this, further supporting the diagnosis of Sweet syndrome (SS) following a thorough evaluation. A similar case by Muche et al. (2024) also highlighted the characteristic histological features of SS, including parakeratotic and moderately acanthotic epidermis overlying significant edema of the papillary dermis.[11] The pattern of nodular and diffuse dermatitis was observed, with an inflammatory infiltrate composed of numerous neutrophils, leukocytoclastic debris, lymphocytes, a few eosinophils, and plasma cells, in the absence of vasculitis. The infiltrates also extended into the subcutaneous fat, consistent with Sweet syndrome.[11]

The diagnosis of Sweet syndrome is based on the criteria established by Su and Liu in 1986 and later revised by Von den Driesch in 1994. The diagnostic criteria require the fulfillment of two major criteria and at least two of the four minor criteria listed in Table 1.[8,9] Our patient met both major criteria and 3 of the minor criteria.

Table 1: Criteria for Diagnosis of Sweet Syndrome.[8,9]

Von Den Driesch Criteria for Diagnosis of Sweet Syndrome
Major Criteria
1. Abrupt onset of painful erythematous plaques or nodules
2. Histopathologic evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis
Minor Criteria
1. Pyrexia >38 °C
2. Association with an underlying hematological or visceral malignancy, inflammatory disease, or pregnancy, or preceded by an upper respiratory or gastrointestinal tract infection or vaccination
3. Excellent response to systemic corticosteroids or potassium iodide
4. Elevation of three of the four laboratory values: (i) erythrocyte sedimentation rate >20 mm/h (ii) positive C-reactive protein (iii) leukocyte count >8000 (iv) neutrophils >70%

In recent years, a broader spectrum of Sweet syndrome presentations has been recognized, with several reports highlighting novel clinical and histological variants **(Table 2)**.[8] These variants have expanded the understanding of Sweet syndrome (SS) beyond its classical form, each presenting with unique challenges in diagnosis and management. For instance, **cellulitis-like Sweet syndrome (clSS)** often mimics cellulitis with erythema and swelling, but

histopathology typically reveals features distinct from those seen in common infections. Another important variant, Cryptococcoid Sweet syndrome (cSS), was described by Volonté et al. (2024), who published a case highlighting the atypical histological features of Cryptococcoid Sweet syndrome, including capsular and yeast-like structures resembling *Cryptococcus* species.[12] However, despite these features, fungal staining and cultures were negative, while myeloperoxidase (MPO) staining was positive. This case emphasizes the diagnostic challenge of cellulitis-like Sweet syndrome (cSS) and the importance of recognizing this variant to avoid misdiagnosis.[12]

Table 2: Clinical and histological variants of Sweet syndrome.[8]

Clinical Variant	**Description**
Prototypic clinical presentation	Tender, erythematous nodules/papules/plaques located on the upper extremities, face, and neck
Bullous SS	Flaccid or tense blisters on the acral surfaces, extremities, the trunk, and face
Cellulitis-like SS	Tender, erythematous, edematous lesions that are indistinguishable from bacterial cellulitis; cultures do not reveal bacteria
Necrotizing SS	Rapidly progressive erythematous, edematous cutaneous lesions with necrotic involvement of underlying soft tissues; must rule out necrotizing fasciitis
Neutrophilic dermatosis of the dorsal hands	Indurated, painful, erythematous plaques admixed with possible ulcers and pustules involving the dorsal hands
HISTOLOGICAL VARIANT	**Description**
Prototypic histological presentation	Diffuse neutrophilic invasion into the upper dermis; infiltrated neutrophils may display karyorrhexis; IHC reveals IL-17E and iNOS expression in the epidermis
Cryptococcoid	Vacuolated mononuclear cells with the presence of basophilic yeast-like bodies. PAS stain fails to reveal fungal elements
Eosinophilic	Dense eosinophilic infiltrate into the dermis; must rule out eosinophilic dermatosis of hematologic malignancy
Histiocytoid	Dermal infiltrate of immature neutrophils that resemble histiocytes; IHC is positive for CD68 and MPO
Lymphocytic	Exuberant dermal lymphocytic infiltrate
Normolipemic xanthomized	CD163-positive foam cells accompany dense neutrophilic infiltrate extending into the deep dermis

In our patient, the presentation was initially misdiagnosed as cellulitis, which is not uncommon. Cellulitis-like Sweet Syndrome (SS), a rare variant of SS, presents with erythematous, edematous lesions resembling cellulitis, particularly on the breasts in our case. However, unlike cellulitis, these lesions do not exhibit any bacterial growth on cultures, and the condition does not resolve with antibiotic therapy, as seen in our patient. This variant has been reported in several other cases, emphasizing the diagnostic challenge it presents. For instance, a case by Muche et al. (2024) reported a patient with giant cellulitis-like Sweet syndrome who, despite multiple antibiotic treatments, did not show improvement until corticosteroids were introduced.[11]

Sweet syndrome is known for its rapid response to systemic corticosteroids, often leading to a dramatic resolution of symptoms. However, it is important to note that relapse occurs in approximately 25% of cases, often after discontinuation of corticosteroid therapy.[7] In some instances, SS can present as recurrent or chronic, complicating the

management and treatment strategies. Chronic Sweet Syndrome (cSS) is characterized by persistent or recurrent skin lesions, which often return upon attempts to taper corticosteroids. This was illustrated in a study by Gowda et al. (2016), which discussed two women with SS who experienced a longer-than-expected disease course.[13] Neither case had any factors such as malignancy or SS-inducing medications identified as the cause. Both women responded well to treatment with prednisone; however, skin lesions returned immediately when attempts were made to taper the medication. The authors concluded that these cases represented a chronic variant of classical SS, suggesting that clinicians consider chronic SS in patients with persistent SS-characteristic skin lesions lasting over four months.[13] This is consistent with our patient's experience, where careful steroid tapering is being considered to prevent relapse.

It is recommended to administer 0.5 to 1.0 mg/kg/day of oral prednisone for a duration of 4 to 6 weeks. For localized lesions or when the number of lesions is limited, topical corticosteroids and calcineurin inhibitors may be considered. Colchicine, dapsone, and potassium iodide are all effective first-line therapy options. Additional treatments include cyclosporine, indomethacin, and clofazimine.[9]

Conclusion

Sweet syndrome remains a challenging diagnosis due to its clinical overlap with other inflammatory dermatoses, particularly cellulitis. The case described here adds to the growing body of literature on cellulitis-like Sweet Syndrome, a rare but clinically significant variant. The timely recognition of SS, supported by appropriate histological examination and response to corticosteroid therapy, is crucial for effective management. Cellulitis-like Sweet syndrome is difficult to diagnose, and therefore, when a clinical presentation resembling cellulitis is present with negative bacterial cultures and shows no improvement with antibiotic therapy, clinicians should maintain a high index of suspicion for Sweet syndrome. Further studies and case reports are needed to explore the full spectrum of Sweet syndrome presentations and treatment strategies, particularly in cases resistant to initial antibiotic therapy.

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