Ulcerative Sweet's Syndrome and Aseptic Abscess in Association with Acute Myeloid Leukemia

Areeya Srimuang MD*, Kamonrat Sunantawanich MD*, Purit Pureesrisak MD**.

**Institute of Dermatology, Department of Medical Services, Bangkok, Thailand.*

***Division of Dermatology, Rajavithi Hospital, Bangkok, Thailand.*

ABSTRACT:
Sweet's syndrome (SS) is an uncommon prototype of neutrophilic dermatosis. While the precise pathogenesis remains unclear, it is linked to inflammatory cascade, disease triggers, and an association with many hematologic and visceral malignancy. Ulcerative SS is an uncommon presentation and is often associated with malignancy. Moreover, SS is also related to aseptic neutrophilic abscess in intra-abdominal viscera.
Key words: Acute myeloid leukemia, Intraabdominal abscess, Sweet's syndrome

Introduction

Sweet's syndrome (SS), or acute febrile neutrophilic dermatosis, is marked by acute onset of fever, neutrophilia, and painful erythematous skin lesion. It is classified into 3 types: classical, drug-induced, and malignancy-associated. Although its exact pathogenesis remains unknown, the primary systemic treatments include oral corticosteroids, colchicine, and potassium iodide. This report presents a 43-year-old female who presented with ulcerative Sweet's syndrome on her right cheek, in association with worsening of acute myeloid leukemia.

Case

A 43-year-old female presents with underlying acute myeloid leukemia (AML) had a history of chemotherapy induction one year ago. Following chemotherapy, she developed intra-abdominal abscesses, including bilateral renal abscesses, a psoas abscess, and a liver abscess. She was initially treated with empirical intravenous antibiotics, specifically ceftazidime, meropenem, and vancomycin. The size of the liver abscess decreased in response to this treatment.

Four months later, she developed a small new lesion within the hepatic segments, leading to her readmission for empirical intravenous antibiotic therapy. Subsequently, she developed a fever and an indurated, tender lesion on the right lip commissure during an inpatient admission. Notably, she had never experienced similar lesions on her trunk or extremities. Despite intravenous antibiotic and antiviral treatment, the lesion did not improve; it instead enlarged and developed into an ulcer.

On examination, she presented with a solitary, well-circumscribed, non-blanchable, indurated, ulcerated, erythematous to violaceous plaque on her right cheek. There was no associated lymph node enlargement (Figure 1A, 1B).

Correspondence Author: Kamonrat Sunantawanich MD, Email: kamonrat.sunantawanich@gmail.com

Received: 11 January 2024 Revised: 24 September 2024 Accepted: 16 January 2025

In this case, the patient presents with an ulcerative erythematous plaque on the face. We categorized the differential diagnosis into two groups: 1) infection, such as bacteria (bullous cellulitis), virus (herpes simplex virus infection), or fungus (angioinvasive fungal infection; mucormycosis which may also involve gastrointestinal tract). 2) non-infection, such as SS, pyoderma gangrenosum, leukemia cutis, and lymphoma cutis. However, the lesion cannot differentiate between infection and non-infection, a biopsy must be performed.

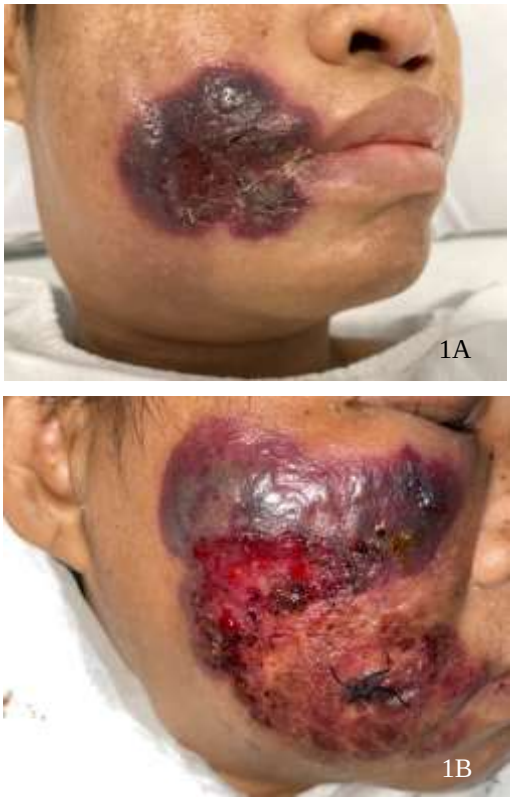

Figure 1A, 1B A solitary well circumscribed non blanchable indurated ulcerated erythematous to violaceous plaque on the right cheek

A biopsy of the lesion on her right cheek revealed a perivascular and diffuse inflammatory-cell infiltrate consisting of neutrophils, lymphocytes, extravasated erythrocytes, and nuclear dust, in conjunction with marked papillary dermal edema in the dermis (Figure 2, 3). Bacterial and fungal cultures showed negative results, and polymerase chain reaction tests ruled out tuberculosis and mycobacterial infection. Blood test showed leukocytosis, with a white blood cell count of 78,570/uL and 75% blast cell, accompanies by anemia, transaminitis and high inflammatory marker (C-reactive protein: 9.28 mg/dL). A computed tomography scan of the entire abdomen identified microabscess at 6th and 8th hepatic segment. The liver biopsy showed hepatoportal infiltration by mixed acute and chronic inflammatory cells, consistent with the edge of liver abscess, there were no evidence of leukemic infiltrate, and neither fungus nor acid fast bacilli were identified. Culture was not found any microbial organisms.

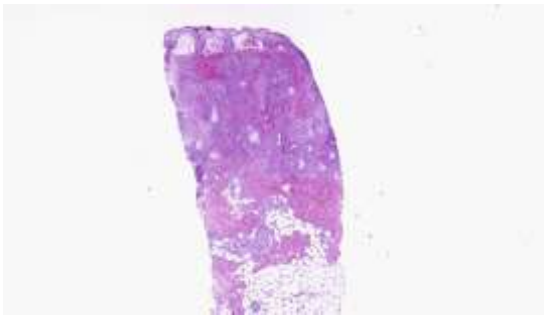

Figure 2 Perivascular and diffuse inflammatory cell infiltrate with marked papillary dermal edema in the dermis (H&E, X40)

Intravenous dexamethasone was given at a dose of 4 mg every 12 hours for treatment. One week later, Blood test indicated leukocytosis, with a white blood cell count of 109,500/uL and 50% blast cells, along with transaminitis. The patient received intravenous cytarabine (130 mg) and intravenous idarubicin (15 mg). Unfortunately, she developed febrile neutropenia with septicemia and passed away three days after receiving chemotherapy.

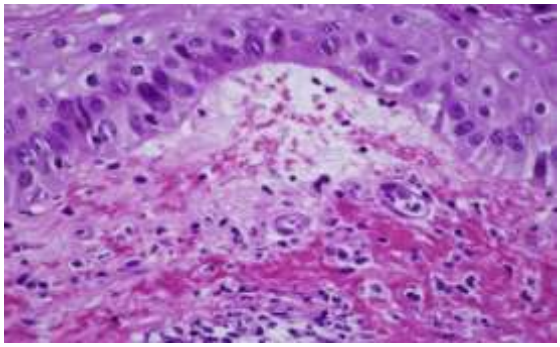

Figure 3 Infiltration of neutrophil, lymphocytes, extravasated red blood cells and nuclear dust with marked papillary dermal edema (H&E, X600)

Discussion

Sweet's syndrome (SS), or acute febrile neutrophilic dermatosis, was initially documented by Dr. Robert Douglas Sweet in 1964. SS can occur throughout lifespan, but it most commonly begins in the 3rd and 6th decade, with a female predominance. The hallmark of SS is the rapid development of tender erythematous papules or plaques. These lesions can appear as singular occurrences or in multiple formations, often distributed asymmetrically affect the upper extremities, neck, and face, while involvement of the oral cavity and mucosa is relatively uncommon[1]. In some instances, these skin lesions are accompanied by fever, arthralgia, generalized malaise, and conjunctivitis[2]. SS is classified into 3 categories: classic SS, drug-induced SS, and malignancy-associated SS[3]. Nonetheless, the clinical presentation can exhibit considerable variation. SS has several variants, including pustular, bullous, cellulitis-like, necrotizing, subcutaneous, and neutrophilic dermatosis of the hand. AML is the malignancy most commonly associated with SS. Among solid tumors, genitourinary, breast, and gastrointestinal cancers are the most frequently linked to SS[4]. Furthermore, SS can present with extracutaneous manifestations affecting various body systems, including the central nervous, cardiopulmonary, gastrointestinal, and musculoskeletal system[2]. Moreover, hepatic involvement is commonly observed in SS, with elevated liver enzyme. Additionally, aseptic neutrophilic abscesses had been reported in the lymph node and intraabdominal organ, including liver[5]. Since the liver septic studied were negative, aseptic neutrophilic abscess could be the possible diagnosis for this patient.

The exact pathogenesis of SS remains unclear, but it is believed to be multifactorial. Increased number of neutrophils in blood and skin had been proposed as a key role of the disease development[6]. Heath and Ortega-Loayaza reported abnormalities in neutrophilic cycle and localization with treatments such as ATRA, G-CSF, and FLT3 inhibitor[4]. SS is associated with a Th1 predominant response, and many cytokines, including G-CSF, GM-CSF, IFN-gamma, IL-1, IL-3, IL-6, and IL-8, proposed as potential contributors to its pathogenesis[7]. Genetic factors such as HLA-Cw1 or B54 and MEFV gene also play a role in increasing susceptibility to SS. Additionally, epithelium trauma can trigger an inflammatory response, and ultraviolet light stimulates keratinocytes to secrete IL-8 and TNF-alpha. These cytokines, then, attract neutrophils to the trauma site, which may promote the development of SS[8].

In 1994, von den Driesch proposed a revised set of diagnostics consisting of two major criteria: the sudden presence of painful erythematous lesions, plaques or nodules characterized by neutrophilic infiltration, without the evident of vasculitis from skin biopsy. Additionally, there must be 2 of 4 minor criteria, which include body temperature exceeding 38°C, at least 3 of abnormal laboratory tests: erythrocyte sedimentation rate >20 mm/h, high C-reactive protein levels, >70% of neutrophils and >8000/μL leukocytosis, excellent response to systemic corticosteroid therapy, and association with inflammatory disease, pregnancy, infection,

hematologic or visceral malignancy, drug, or vaccination[2,8]. The diagnostic criteria of malignancy-associated SS are similar to those for classic SS with an underlying malignancy in the minor criteria[2].

In 2015, Syed M. Kazmi et al. analyzed 2,178 patients with AML and identified 21 cases of SS, representing 1% of the cohort. The average age of affected patients was 55 years, with a female predominance and the average blast cell at diagnose of SS was 25%. SS was more commonly associated with AML characterized by myelodysplasia-related features, -5/del(5q) cytogenetic abnormalities, and FMS-related tyrosine kinase 3 (FLT3) genetic mutations[9]. Common features frequently observed in malignant-associated Sweet's syndrome are ulcerated skin lesions, bullous lesions, subcutaneous nodules, oral mucosal involvement, anemia, and abnormal platelets counts[4].

In 2017, M. El-Khalawany *et al*. studied 171 cases diagnosed as SS. There were 13 cases (8%) associated with AML. Atypical presentations included ulcerative lesions, indurated masses, and gangrenous masses[10]. Other atypical presentations comprised bullous, subcutaneous, pseudocarcinomatous, giant cellulitis-like, and pustular Sweet's syndrome on photo-distribution area[11-15].

Histopathological findings show marked papillary dermal edema and dermal neutrophilic infiltration without the appearance of vasculitis[2]. In some cases, additional cellular components such as lymphocytes and mononuclear cells resembling histiocytes are observed, which express myeloperoxidase. These variants are referred to as lymphocytic SS or histiocytoid SS, and they are more specifically associated with myelodysplastic syndrome or acute myeloid leukemia[16].

Effective management of any underlying disease or malignancy is crucial. Systemic corticosteroids serve as the first-line treatment with prednisone (0.5-1 mg/kg/day), leading to rapid symptom resolution. This is followed by a gradual tapering over 4–6 weeks. Some other first-line agents include colchicine (1-1.5 mg/day) and potassium iodide (900 mg/day). Alternative options include dapsone, indomethacin, clofazimine, and cyclosporine[17]. For localized disease, topical or intralesional corticosteroids may be considered. Additionally, an IL-1 receptor antagonist (anakinra) demonstrate in treating refractory cases[1].

Conclusion

Sweet's syndrome can manifest in various clinical conditions. This case reports ulcerative SS co-occurring with AML. Ulcerative SS is uncommon presentation and often associated with malignancy. The presence of SS with a prior history of malignancy may suggest a potential relapse or progression of the associated cancer. However, it's important to note that SS can affect multiple organs. Therefore, we recommend considering multidisciplinary treatments and finding extracutaneous manifestations as well as work up malignancy in patients presenting with SS.

References

1. Weiss EH, Ko CJ, Leung TH, Micheletti RG, et al. Neutrophilic Dermatoses: a Clinical Update. Curr Dermatol Rep 2022;11:89-102.
2. Ferea CR, Mihai SN, Balan G, Badescu MC, Tutunaru D, Tatu AL. Sweet Syndrome Associated with Myelodysplastic Syndrome-A Review of a Multidisciplinary Approach. Life (Basel) 2023;13:809.
3. Heath MS, Ortega-Loayza AG. Insights Into the Pathogenesis of Sweet's Syndrome. Front Immunol 2019;10:414.
4. Jung EH, Park JH, Hwan Kim K, et al. Characteristics of Sweet syndrome in patients with or without malignancy. Ann Hematol 2022;101:1499-508.
5. Vignon-Pennamen. The Extracutaneous Involvement in the Neutrophilic Dermatoses. Clinics in Dermatology 2000;18:339-47.

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. Philip RC, Razelle K. Sweet Syndrome. In: Kang S, Amagai M, Bruckner AL, editors. Fitzpatrick's dermatology in general medicine. 9th ed. New York: Mcgraw-Hill 2012:587-602.
8. Joshi TP, Friske SK, Hsiou DA, Duvic M. New Practical Aspects of Sweet Syndrome. Am J Clin Dermatol 2022;23:301-18.
9. Kazmi SM, Pemmaraju N, Patel KP, et al. Characteristics of Sweet Syndrome in Patients with Acute Myeloid Leukemia. Clinical Lymphoma, Myeloma & Leukemia 2015;15: 358-63.
10. El-Khalawany M, Aboeldahab S, Mosbeh AS, et al. Clinicopathologic, immunophenotyping and cytogenetic analysis of Sweet syndrome in Egyptian patients with acute myeloid leukemia. Pathology-Research and Practice 2017;213:143-53.
11. Chiewchanvit S, Jamjanya S, Rattanathammethee T, Mahanupab P, Tovanabutra N, Chuamanochan M. Bullous Sweet syndrome in a patient with acute myeloid leukemia treated with midostaurin: Rapid response to acitretin and colchicine-A case report. Dermatologic Therapy 2021;34:e15171.
12. Ting S, Zhao C, Cook DK. Subcutaneous Sweet syndrome leading to the diagnosis of acute myeloidleukemia. Aust J Gen Pract 2022;51:391-3.
13. Lukach AJ, Han J, Gardeen SJ, et al. Pseudocarcinomatous Sweet syndrome. JAAD Case Report 2022;26:73-5.
14. Li W, Mian A, Zaidi K, Mahmud T. Giant Cellulitis-Like Sweet Syndrome Masquerading As Cellulitis and Shingles: A Case Report and Literature Review. Cureus 2023;15:e36232.
15. Saad S, Korbi M, Ben Abdeljelil N, et al. Photodistributed pustular acute febrile neutrophilic dermatosis revealing an acute myeloid leukemia. Clin Case Rep. 2022;10:e05702.
16. Ghoufi L, Ortonne N, Ingen-Housz-Oro S, et al. Histiocytoid Sweet Syndrome Is More Frequently Associated With Myelodysplastic Syndromes Than the Classic Neutrophilic Variant. Medicine, Balt 2016;95:e3033.
17. Maller B, Bigness A, Moiño D, Greene J. Sweet's syndrome associated with hematological malignancies. Leukemia Research. 2020;99: 106461.