IJHOSCR

Case Report

International Journal of Hematology-Oncology and Stem Cell Research

# When the Skin Speaks for the Bone Marrow: Sweet Syndrome and Pancytopenia as the Initial Manifestation of Occult AML

**Sohrab Aghabeigi[1], Nooshin Ahmadvand[2], Seyedeh Mohadese Mosavi Mirkalaie[3], Azadeh Sedighi Moghadam[4], Arefeh Aref-Eshghi[2]**

[1]Hematologic Malignancies Research Center, Research Institute for Oncology, Hematology and Cell Therapy, Tehran University of Medical Sciences, Tehran, Iran
[2]Shahid Dr. Beheshti Clinical Research Development Unit, Shahid Dr. Beheshti-Anzali Educational and Medical Hospital, Guilan University of Medical Sciences, Rasht, Iran
[3]Student Research Committee, School of Medicine, Anzali International Campus, Guilan University of Medical Sciences, Rasht, Iran
[4]Razi Pathobiology Lab, Rasht, Iran

**Corresponding Author:** Sohrab Aghabeigi, Hematologic Malignancies Research Center, Research Institute for Oncology, Hematology and Cell Therapy, Tehran University of Medical Sciences, Tehran, Iran
**E-mail:** doctorsohrabaghabeigi@gmail.com

Received: 28, Nov, 2025
Accepted: 23, Dec, 2025

**ABSTRACT**

This case report describes the presentation for a 65-year-old patient with Sweet's syndrome (SS) presenting with systemic symptoms of general weakness, fever, and painful skin lesions on the right arm. He reported a history of weight loss with night sweats, while skin lesions manifested as erythematous plaques and painful papules. The diagnosis was confirmed by skin biopsy, which showed features of significant neutrophilic infiltrations on histopathology. Further investigations led to the diagnosis of AML associated with Sweet's syndrome. The study highlights the importance of prompt diagnosis of Sweet's syndrome as a paraneoplastic sign and using multi-disciplinary approach for diagnosis and management of patients with skin lesions and cytopenias.

**Keywords:** Sweet syndrome; Acute myeloid leukemia (AML); Paraneoplastic

## INTRODUCTION

Sweet syndrome is the most frequent febrile neutrophilic dermatosis. It presents with fever, tender erythematous papules, nodules, and plaques that mostly affect the face, neck, and upper limbs, distributing in an asymmetrical manner. The involved areas showed prominent neutrophilic infiltrates in the upper dermis[1]. The exact pathogenesis of Sweet's syndrome remains unclear; however, recent studies have shed light on the role of inflammatory signaling, disease initiation, and its association with malignancies. This includes a better understanding of inflammasome activation, malignant transformation of dermal infiltrating neutrophils, and genetic factors. The cellular and molecular mechanisms highlight the difficulties in diagnosing Sweet's syndrome due to its similarity with other conditions that share clinical features[2]. Diagnosis is primarily clinical, and histologic examination reveals a neutrophilic infiltrate in the lesions, which is needed to confirm the diagnosis. It is important for the clinicians to recognize unusual presentations especially in cases of patients with preexisting diseases like myelodysplastic syndrome, since instead of neutrophils, atypical mononuclear coalescence in the infiltrate may be present[3]. A large-

scale study with a significant population showed that sweet syndrome is a serious dermatological disorder but also stress the importance of its detection for the early diagnoses of neoplastic disorders. Sweet syndrome can present as an early indicator of recurrent malignancy and may facilitate diagnosis before the related neoplasm becomes apparent[4]. Timely recognition and proper treatment may affect the quality of life for the patients. We present a case of Sweet's syndrome in association with AML. The aim of this paper is to emphasize the necessity of early diagnosis of this rare condition as well as to improve the diagnosis and management of such cases.

**Case Presentation**

A 69-year-old man was admitted with generalized weakness, fatigue, heavy sweating, and painful skin lesions on his right upper limb. He had history of poor appetite and lost about 7 kg over the past two months. His weakness and fatigue have gradually worsened in the past month. He has had intermittent fevers. Dyspnea progressed in the past two weeks.

Patient had erythematous plaques and painful papules on his forearm and elbow, which developed in the past two weeks. The presence of lesions along with systemic symptoms suggested the dermatologic condition may have systemic origins. The lesions did not improve after a course of antibiotics.

A thorough review of the patient's history revealed no trauma, livestock exposure, or consumption of local dairy products suggesting zoonotic infection. The patient had no history of tuberculosis, an important differential diagnosis for systemic symptoms with skin lesions.

In physical exam, the patient looked ill but was not toxic. The patient's vital signs were stable with fever. The spleen was of normal size and there was no evidence of lymphadenopathy.

Dermatological examination revealed three non-itchy erythematous plaques: two on the right arm and one on the right forearm. Additionally, a non-pruritic erythematous papule was observed on the left forearm, presenting two weeks subsequent to the appearance of the plaques. All the lesions were tender and edematous on examination, suggesting an inflammatory process. The plaques on the arm had an annular structure with a central clearing (Figure 1).

The combination of systemic complaints, weight loss, and the specific characteristics of the skin lesions raise a red flag and warrants a multidisciplinary approach. Consultation with infectious diseases specialist, dermatologist, and hematologist for ruling out possibility of malignancies or systemic infections to explain the patient's clinical was requested.

Initial patient evaluation included CBC, LFTs, RFTs, serum electrolytes, and inflammatory markers (Table 1).

An incisional skin biopsy of the plaque on the right forearm was performed. Histopathological examination showed dermal edema and a pronounced neutrophilic infiltrate within the dermis with diffuse distribution. Endothelial cell swelling and RBC extravasation were noted. Mild peri-eccrine lymphocyte infiltration is present, along with moderate epidermal spongiosis (Figure 2).

The microscopic findings confirmed the diagnosis of sweet syndrome. Sweet syndrome is a rare, acute febrile neutrophilic dermatosis often associated with systemic illness, particularly malignancies. Because of pancytopenia and elevated ESR in the context of Sweet's syndrome's known association with malignancies, bone marrow aspiration and biopsy has been done. The peripheral blood smear revealed medium-sized myeloid blasts. Flow cytometry showed 22% myeloid blasts with an immunophenotype positive for CD13, CD33, CD64, and CD117, and negative for CD34 and HLA-DR which is highly suggesting for AML (non m3). Bone marrow aspiration revealed a hypercellular marrow with dysplastic changes and approximately 25% medium-sized myeloid blasts. (Figure 3). These findings confirmed the diagnosis of Sweet's syndrome in association with acute myeloid leukemia (AML). Given the patient's age and performance status, treatment with azacitidine and venetoclax was initiated. This resulted in resolution of the skin lesions and hematologic remission of the AML. Unfortunately, the leukemia subsequently relapsed, and the patient died from the disease.

**Table 1:** Patient's laboratory results

| Variable | Value | Unit |
|---|---|---|
| WBC | 9.8 | ×10⁹/L |
| RBC | 3.58 | ×10⁹/L |
| HB | 10.3 | g/dL |
| MCV | 91.1 | fL |
| Platelets | 118000 | µL |
| ESR | 73 | mm/hr |
| Urea | 25 | mg/dL |
| Cr | 0.9 | mg/dL |
| Uric acid | 2.5 | mg/dL |
| Na | 132 | mEq/L |
| K | 3.9 | mEq/L |
| Bilirubin total | 0.8 | mg/dL |
| Bilirubin direct | 0.2 | mg/dL |
| AST | 32 | U/L |
| ALT | 50 | U/L |
| Alp | 275 | U/L |
| CRP | +1 | mg/dL |
| LDH | 475 | U/L |

WBC: White blood cells, RBC: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, ESR: Erythrocyte sedimentation rate, AST: Aspartate transaminase ALT: Alanine transaminase, ALP: Alkaline phosphatase, CRP: C-reactive protein, LDH: Lactate dehydrogenase

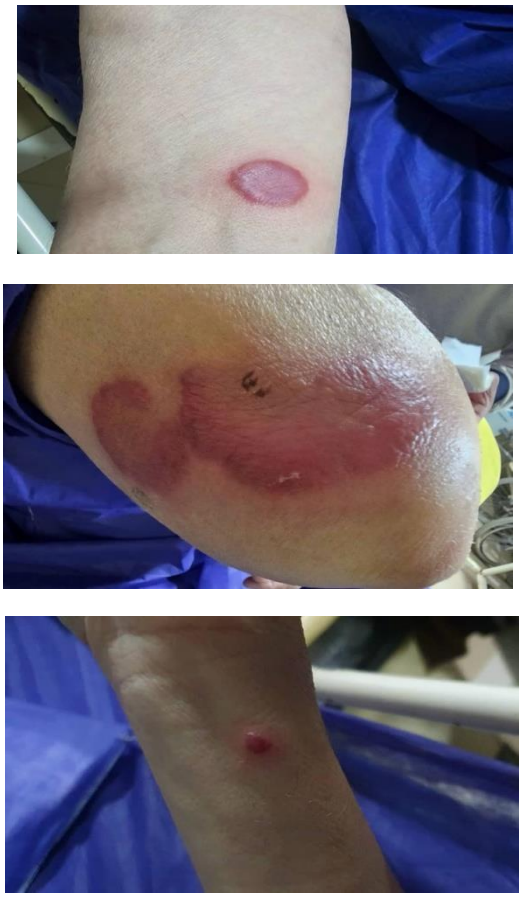
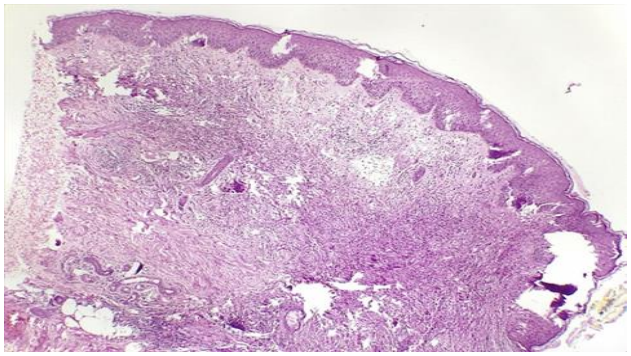
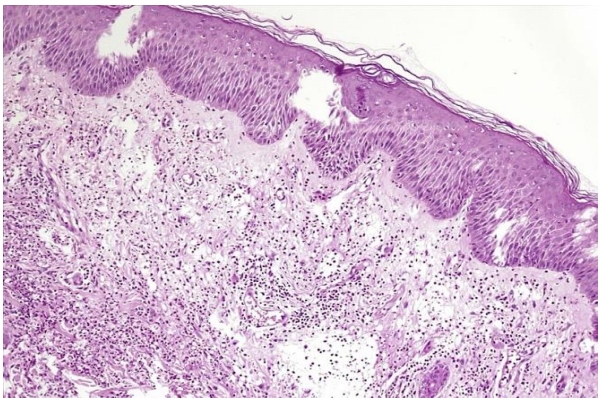


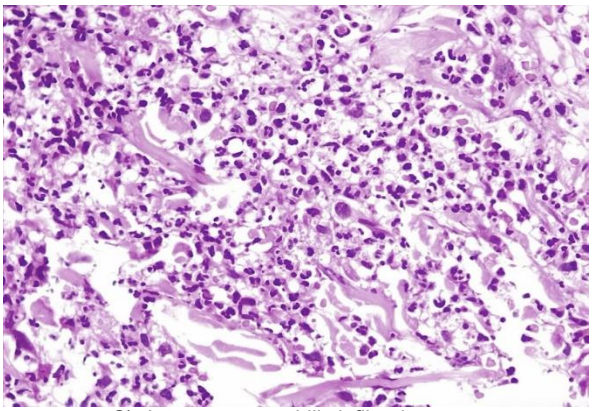
Figure1. Skin lesions: Erythematous and edematous papules and plaques on upper extremities



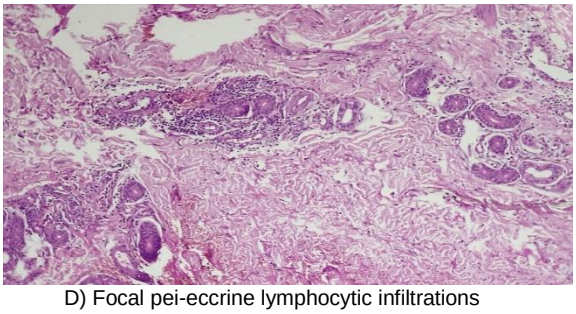
A) Dermal edema with diffuse and intense neutrophilic infiltration



B) Notable dermal edema



C) Intense neutrophilic infiltrations



D) Focal pei-eccrine lymphocytic infiltrations

Figure 2. Skin biopsy

**DISCUSSION**

In 1964, Dr. Robert Douglas Sweet named a condition that had some few but significant identifications in a series of eight women "acute febrile neutrophilic dermatosis." These patients had four major characteristics: fever; the presence of polymorphonuclear leukocytes neutrophils in the blood; the presence of painfully raised plaques in the limbs, face, and neck; and histological evidence for a significant dermal infiltration by mature neutrophil polymorphs. While he acknowledged that the clinical picture resembled that of erythema multiform, Dr. Sweet considered it to be a separate pathological entity not recorded in the medical literature before this time. The condition would later take his name and become widely known as Sweet syndrome[5] .

Skin manifestations of SS mainly present as erythematous plaques and bumps of different sizes primarily located on the extremities as well as the face and neck. In contrast, further involvement of trunk, back, and mucosal surfaces is rare[6]. Histopathological examination shows a prominent neutrophil infiltration in the dermal layer [7]. This is an unusual condition that manifests as the sudden appearance of very painful, reddish plaques or nodules that may be accompanied by fever, arthralgia, and systemic symptoms like headache. This condition is primarily diagnosed based on clinical findings; however, histological evaluation of the lesions shows unapparent neutrophilic infiltrate, which is important for verification of diagnosis[8]. This case embodies the clinical picture of sweet syndrome. It has a typical febrile pattern, while histological findings describe a marked neutrophilic infiltrate and the acute onset of painful erythematous plaques or nodules.

Sweet's syndrome is seen in three major clinical settings: classical (or idiopathic) Sweet's syndrome, malignancy-associated Sweet's syndrome, and drug-induced Sweet's syndrome. Malignancy-associated Sweet's syndrome (MASS) may present as a paraneoplastic syndrome in patients with established malignancies or those with occult hematologic neoplasms or solid tumors and is most commonly linked to acute myelogenous leukemia. In addition, sweet's syndrome can be a dermatologic marker for an occult malignancy or evidence of cancer recurrence[9, 10].

In the setting of malignancy-associated Sweet's syndrome, the overall hypothesis regarding its pathogenesis centers on dysregulation and overproduction of inflammatory cytokines. Interleukin-1 (IL-1), interleukin-3 (IL-3), interleukin-6 (IL-6), interleukin-8 (IL-8), granulocyte colony-stimulating factor (G-CSF), and granulocyte-macrophage colony-stimulating factor (GM-CSF) are key cytokines involved in this pathogenic process[10].

Around 10 to 15 percent of documented instances of Sweet's syndrome have been reported in individuals diagnosed with cancer[7]. A high percentage, approximately 85%, of malignancy-related Sweet's syndrome has been linked to underlying hematologic neoplasms, and the most frequent among them has been acute myeloid leukemia. Myeloproliferative neoplasms, diffuse large B-cell lymphoma, Hodgkin's lymphoma, myelodysplastic syndrome, and myelofibrosis have also reported. Among solid tumors, carcinomas originating from the genitourinary tract, breast, and gastrointestinal tract are most commonly affected, with adenocarcinoma accounting for 57% of these cases. Recent observations suggest that the incidence of Sweet's syndrome is on the rise, attributed to increased awareness among healthcare professionals[10-14]. Sweet syndrome may occur before, at the same time or after a malignancy is diagnosed. In cancer, it usually occurs in older adults and is associated with cytopenias[8].

In one study among the hematologic malignancies associated with sweet syndrome, AML and myelodysplastic syndromes (MDS) each occurred in 11% of patients, while multiple myeloma (MM) was present in 3%. The overall frequency of AML in this patient population was 4% [12, 15].

The pathogenic mechanisms of sweet syndrome (SS) in acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS) are not yet known. Recent studies have shown the presence of genetic mutations in clonal neutrophilic infiltrates in SS lesions, and these are consistent with the primary hematological diseases. A significant finding was that most patients developed sweet syndrome after their hematologic

malignancy was diagnosed. This temporal relationship suggests that cytopenias, such as thrombocytopenia and anemia, may not only indicate undiagnosed AML/MDS but could also be a consequence of that malignancy's treatment. Additionally, the erythrocyte sedimentation rate (ESR), was observed to be elevated in patients with hematologic malignancies and sweet syndrome. Casarin Costa et al. found an association of malignancy with high ESR levels in patients with sweet syndrome[16-19].

Changes in blood parameters occurred alongside symptom onset, and both rapidly resolved together. This strong association suggested a possible malignancy, prompting further tests to confirm or rule out the diagnosis.

Sweet syndrome secondary to acute myeloid leukemia (AML) often deteriorates rapidly and typically involves subcutaneous tissue. This presentation is often steroid-resistant, necessitating both a prompt diagnostic workup for an underlying malignancy and the early initiation of chemotherapy. While genetic abnormalities may be implicated in the unusual presentation of the disease, more research is needed to establish this[20] .

This report underscores the overriding significance of clinicians suspecting sweet syndrome as a potential paraneoplastic syndrome in patients presenting with cytopenias. Prompt identification and treatment of SS not only may decrease patient discomfort but can also result in earlier diagnosis of underlying malignancies. Future research into the genetic and immunologic aspects of sweet syndrome in blood cancers will help clarify its pathophysiology and enhance patient care.

This case illustrates the complex interplay between dermatologic manifestations and systemic disease, highlighting the critical role of a multidisciplinary approach in diagnosing and managing patients with atypical cutaneous presentations.

**REFERENCES**

1. Villarreal-Villarreal CD, Ocampo-Candiani J, Villarreal-Martínez A. Sweet Syndrome: A Review and Update. Actas Dermosifiliogr. 2016;107(5):369-78

2. Heath MS, Ortega-Loayza AG. Insights Into the Pathogenesis of Sweet's Syndrome. Front Immunol. 2019;10:414.

3. Vashisht P, Goyal A, Hearth Holmes MP. Sweet Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-[Updated 2023 Aug 8]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK431050/

4. Corazza M, Lauriola MM, Borghi A, et al. Sweet's syndrome: a retrospective clinical, histopathological and immunohistochemical analysis of 11 cases. Acta Derm Venereol. 2008;88(6):601-6.

5. Sweet R. An acute neutrophilic dermatosis. Br J Dermatol.1964; 76:349-56.

6. Von Den Driesch P. Sweet's syndrome (acute febrile neutrophilic dermatosis). J Am Acad Dermatol. 1994;31(4):535-56; quiz 557-60.

7. Cohen PR, Kurzrock R. Sweet's syndrome and malignancy. Am J Med. 1987;82(6):1220-6.

8. Vashisht P, Goyal A, Hearth Holmes MP. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Available from: https://pubmed.ncbi.nlm.nih.gov/28613704/

9. Cohen PR. Sweet's syndrome--a comprehensive review of an acute febrile neutrophilic dermatosis. Orphanet J Rare Dis. 2007;2:34.

10. Paydas S. Sweet's syndrome: a revisit for hematologists and oncologists. Crit Rev Oncol Hematol. 2013;86(1):85-95.

11. Cohen PR, Kurzrock R. Sweet's syndrome and cancer and cancer. Clin Dermatol. 1993;11(1):149-57.

12. Cohen PR, Talpaz M, Kurzrock R. Malignancy-associated Sweet's syndrome: review of the world literature. J Clin Oncol. 1988;6(12):1887-97.

13. Haverstock C, Libecco JF, Sadeghi P, et al. Tender Erythematous Plaques in a Woman With Acute Myelogenous Leukemia—Quiz Case. Arch Dermatol. 2006;142(2):235-40.

14. Disel U, Paydas S, Yavuz S, et al. Bilateral ear Sweet's syndrome in a case with relapse acute myeloblastic leukemia. Leuk Res. 2006;30(3):364.

15. Rochet NM, Chavan RN, Cappel MA, et al. Sweet syndrome: clinical presentation, associations, and response to treatment in 77 patients. J Am Acad Dermatol. 2013;69(4):557-64.

16. Casarin Costa JR, Virgens AR, de Oliveira Mestre L, et al. Sweet syndrome: clinical features, histopathology, and

associations of 83 cases. J Cutan Med Surg. 2017;21(3):211-6.
17. Zheng S, Li S, Tang S, et al. Insights Into the Characteristics of Sweet Syndrome in Patients With and Without Hematologic Malignancy. Front Med (Lausanne). 2020:7:20.
18. Kazmi SM, Pemmaraju N, Patel KP, et al. Characteristics of Sweet Syndrome in patients with acute myeloid leukemia. Clin Lymphoma Myeloma Leuk. 2015;15(6):358-63.
19. Alegría-Landa V, Rodríguez-Pinilla SM, Santos-Briz A, et al. Clinicopathologic, Immunohistochemical, and Molecular Features of Histiocytoid Sweet Syndrome. JAMA Dermatol. 2017;153(7):651-9.
20. El-Khalawany M, Aboeldahab S, Mosbeh AS, et al. Clinicopathologic, immunophenotyping and cytogenetic analysis of Sweet syndrome in Egyptian patients with acute myeloid leukemia. Pathol Res Pract. 2017;213(2):143-53.