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SHORT COMMUNICATION

# Clonal neutrophil infiltrates in concurrent Sweet's syndrome and acute myeloid leukemia: A case report and literature review

Wenbin Mo, Xiaoxue Wang, Yue Wang, Yan Li, Rui Zhang*

*Department of Hematology, The First Affiliated Hospital of China Medical University, No.155, Nanjing North Street, Shenyang, Liaoning 110001, PR China*

**Abstract**

Sweet's syndrome (SS), also known as acute febrile neutrophilic dermatosis is often associated with a hematological malignancy, especially acute myeloid leukemia (AML) and myeloid dysplasia syndrome. Histopathologically, SS is characterized by diffuse infiltrates in the upper dermis, predominantly consisting of mature neutrophils. The origin of neutrophils invading the skin remains unknown. Herein, we report a patient with concurrent acute monoblastic leukemia and SS who initially presented with discrete erythematous papules and nodules on the neck. Single nucleotide polymorphism (SNP) array and next generation sequencing (NGS) revealed a concordant fms-related tyrosine kinase-3 (FLT-3) gene mutation in the bone marrow and skin lesion, indicating that the neutrophilic infiltrates were clonally related to the underlying myeloid neoplasm. This is the first case report of concurrent SS and AML, in which SNP array and NGS analysis were applied to confirm the clonality of the neutrophilic infiltrates.

**Keywords** Sweet's syndrome, Hematological malignancy, Clonality, SNP array, Sequencing.


## Introduction

Sweet's syndrome (SS), also known as acute febrile neutrophilic dermatosis, is a rare clinical condition characterized by fever, painful erythematous papules or plaques and leukocytosis. Histologically, dense dermal infiltrations of mature neutrophils with nuclear fragmentation and absence of signs of vasculitis are seen in the plaques. Both major and at least two minor criteria must be fulfilled to confirm a diagnosis of SS according to Von den Driesch modified criteria for SS [1]. The major criteria include abrupt onset of tender erythematous papules and nodules, and dense neutrophilic infiltrates in the dermis without leukocytoclastic vasculitis. The minor criteria include presence of fever $>38\,^{\circ}C$, increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), and an excellent response to glucocorticoid treatment.

According to its etiology or clinical setting, SS can be classified as classical (or idiopathic), drug-associated and malignancy-associated (MA-SS). MA-SS accounts for 15–20% of all SS cases, and is mainly associated with hematological neoplasms such as myeloid dysplasia syndrome (MDS) and acute myeloid leukemia (AML) [2]. MA-SS related to hematological disorders may present prior to or concurrently with the diagnosis of hematological neoplasms, namely paraneoplastic SS, or as drug-associated SS due to the medication used during treatment like granulocyte-colony stimulating factor (G-CSF) [3]. The pathogenesis of SS in AML or MDS remains unclear. Genetic mutations of clonal neutrophilic infiltrates in SS lesions, which are concordant with the underlying hematological disorders, have been recently reported [4,5].

Herein, we reported a patient with AML who initially had typical presentations of SS involving the face and extremities. Evaluation of the underlying cutaneous infiltrates using single nucleotide polymorphism (SNP) array and gene sequencing analysis showed fms-related tyrosine kinase 3 (FLT-3) gene mutations, which was concordant with changes in the bone marrow. This study was approved by the Ethics Committee of the First Affiliated Hospital of China Medical University

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* Correspondence author.
*E-mail address:* hemozerro2008@hotmail.com

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(No. AF-SOP-07-1.0-01). Written informed consent was obtained from the patient.

## Material and methods

### Cytogenetics

Short-term cultures of unstimulated bone marrow samples were prepared and fixed according to standard laboratory protocols. Karyotype analysis was performed by the R-banding technique. The cytogenetic abnormalities were described according to the International System for Human Cytogenetic Nomenclature.

### DNA samples

DNA was extracted from the cells of bone marrow mononuclear and buccal swab mucosa using the QiaAmp DNA Blood Mini kit (Qiagen, Hilden, Germany). QIAamp_FFPE_DNA_kit was used to extract DNA from formalin-fixed paraffin-embedded (FFPE) skin tissue sections.

### SNP array

The DNA copy number and SNP analyses were performed with CytoScan® Array from Affymetrix® at KingMed Clinical Laboratory (Guangzhou, China), as per the manufacturer's protocols. The Affymetrix® 450 fluidics station and GeneChip® Scanner 3000 7G were used to wash, stain and scan the arrays.

### DNA sequencing analysis

PCR-based mutational analysis of FLT-3 and the next generation sequencing (NGS) based assay using a panel designed to detect diagnostic, prognostic, and therapeutic markers across a spectrum of AML were performed at Yuanqi Biomedical technology co. LTD (Shanghai, China). The panel covers 21 AML-associated genes including FLT-3, DMNT3A, NPM1, CEBPA, TET2, IDH1/2, C-KIT, AML1, RUNX1, SRSF2, SF3B1, U2AF1, NRAS, JAK2, ASXL1, PHF6, CBL, EZH2, TP53, and SETBP1.

## Case presentation

A 53-year-old woman was admitted to our hospital with a one-month history of fever up to 39 °C, and painful erythematous papules and nodules (with a maximum size of $4 \times 4$ cm) on the extremities and face. Laboratory tests revealed leukocytosis with a WBC count of $12.66 \times 10^9$/L, and elevated levels of ESR and CRP. Subsequently, a skin biopsy from her face showed dense neutrophilic infiltration in the dermis, without vasculitis (Fig. 1). Mature neutrophils were evidenced by the positive expression of myeloperoxidase and negative expression of CD34 using immunohistochemical staining. Oral prednisone was prescribed at a dosage of 1 mg/kg/d based on the diagnosis of SS. The skin lesion resolved quickly but the leukocyte count of the patient continued to increase. Two

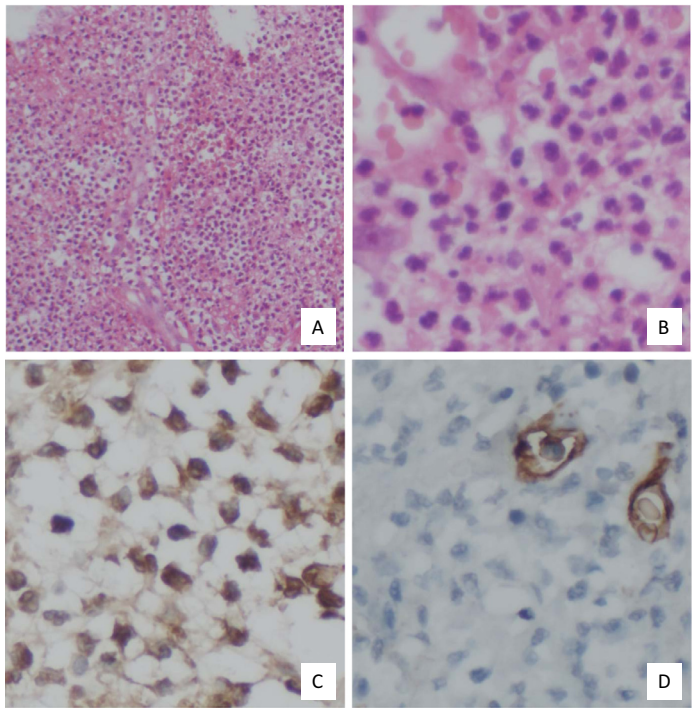


**Fig. 1** Histopathological changes of the skin biopsy sample of the patient. Infiltration of mature neutrophils in the upper dermis and the epidermis at low power view (A) and high power view (B). Positive expression of myeloperoxidase (C) and negative stain of CD34 (D) were demonstrated by immunohistochemical staining.