Original Study

Characteristics of Sweet Syndrome in Patients With Acute Myeloid Leukemia

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Abstract

Sweet syndrome (SS) is a dermatologic disorder observed in various benign or malignant conditions including acute myeloid leukemia (AML). We reviewed 2178 AML patients treated from 2000 to 2011 and identified 21 patients who developed SS. SS occurred more frequently in the setting of AML with myelodysplasia-related features, −5/del(5q) cytogenetics, and FMS-related tyrosine kinase 3 genetic aberrations.

Introduction: Sweet syndrome (SS) is associated with hematologic malignancies including acute myeloid leukemia (AML). **Patients and Methods:** Records of patients with AML treated at our institution were reviewed to identify those with SS. Patient characteristics, laboratory values, and cytogenetic and molecular abnormalities were retrospectively reviewed. **Results:** We identified 21 of 2178 (1%) AML patients who demonstrated clinical signs and symptoms, and histological features consistent with SS. Eleven patients (52%) were classified as AML with myelodysplasia-related features and 3 patients had therapy-related AML. Three patients had received treatment with granulocyte colony stimulation factor, 1 patient liposomal all-*trans*-retinoic acid, and 2 patients received hypomethylating agents before development of SS. Cytogenetic analysis revealed diploid karyotype in 7 patients (33%); −5/del(5q) in 8 patients (38%): 3 patients had −5/del(5q) as the sole abnormality and 5 patients had −5/del(5q) as part of complex cytogenetics; and complex cytogenetics in 5 patients (24%). Gene mutations in FMS-related tyrosine kinase-3 (*FLT3*) gene were identified in 7 of 18 evaluable patients (39%), including *FLT3*−internal tandem duplication in 4 patients and *FLT3*−D835 tyrosine kinase domain mutation in 3 patients. **Conclusion:** SS occurs in 1% of AML patients; −5/del(5q) karyotype, *FLT3* mutations, and AML with myelodysplasia-related features were more frequent among patients with SS.

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Introduction

Sweet syndrome (SS), or acute febrile neutrophilic dermatosis, is characterized by recurrent fever and presence of a dense papillary or upper reticular dermal infiltrate of normal-appearing mature polymorphonuclear cells (PMNs).[1,2] SS was originally reported by Robert Douglas Sweet in 1964, when he described a case series of 8 women between the ages of 32 and 55 years, who presented with fever, tender erythematous cutaneous plaques, neutrophilia, and a dense neutrophilic infiltrate in the upper dermis on histology. All 8 patients responded promptly to glucocorticoid therapy.[3] Generally, the cutaneous lesions in SS manifest as erythematous plaques and nodules of variable size that mostly involve the extremities or head and neck and less frequently trunk, back, and mucosal surfaces.[4] SS can occasionally cause an intense systemic response

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involving the lungs, liver, and musculoskeletal system, sometimes resulting in shock, multiple organ failure, and death. However, in most instances the manifestations of SS might be reversible with rapid initiation of glucocorticoid therapy.[5-7]

Sweet syndrome is frequently idiopathic; however, in a minority of cases a possible etiologic association can be identified with infections, autoimmune disorders, medications (drug-associated SS; DA-SS) or malignancies (also called malignancy-associated SS; MA-SS). Von den Driesch in 1994 proposed the currently used diagnostic criteria for SS, in turn a modification of diagnostic criteria for SS previously proposed by Su and Liu. These criteria consist of major and minor criteria (see Patients and Methods). Major and at least 2 minor criteria must be fulfilled to confirm a diagnosis of SS.[4,8] Fever, neutrophilia, and increased erythrocyte sedimentation rate (ESR) level remain part of the diagnostic criteria for idiopathic SS and MA-SS, however, these findings can occasionally be absent in MA-SS.[9] For DA-SS, the diagnosis requires establishment of a temporal association between development of SS rash, initiation of therapy with the responsible drug, and improvement when the drug is withheld.[10]

Malignancy-associated SS, constituting only 15% to 20% of cases of SS, has been reported in association with hematological and visceral malignancies, with acute myeloid leukemia (AML) being the most common malignancy associated with MA-SS.[11-14] SS might also occur as a paraneoplastic condition in other hematological conditions such as myelodysplastic syndrome (MDS), B and T cell non-Hodgkin lymphoma, chronic lymphocytic leukemia, multiple myeloma, myeloproliferative neoplasms (MPN), or in the setting of visceral malignancies such as genitourinary, breast, or colorectal cancer. In MA-SS, the cutaneous manifestations of SS can occur before, during, or after the diagnosis of the malignancy and thus its onset might herald the diagnosis of malignancy in individuals with no previous malignancy or might indicate a recurrence in patients with a previous history of cancer.[2,15] In SS associated with hematological diseases such as AML, MDS, and MPN, the PMNs in the dermal infiltrate might be clonally derived from either the malignant or nonmalignant cells.[16-18] Occasionally, malignant cells can be found among the PMNs (representing concurrent leukemia cutis).[18] Similarly, medications used in management of hematological malignancies such as granulocyte colony stimulation factor (G-CSF), granulocyte-macrophage colony stimulating factor, all-*trans*-retinoic acid (ATRA), and hypomethylating agents such as azacytidine and decitabine have been associated with SS, supporting the role of cytokines, maturation defects, and epigenetic changes in the pathogenesis of SS.[15,19-24]

Although AML is the most common hematological malignancy associated with SS, the exact incidence and molecular characteristics of AML patients who develop SS remains undefined. In this study, we sought to identify specific disease features and cytogenetic or molecular aberrations that occur in patients with AML and SS.

Patients and Methods

The charts of all patients with AML who had been diagnosed, received treatment, and had follow-up at M.D. Anderson Cancer Center between January 2000 and December 2011 were retrospectively reviewed after receiving approval from our institutional review board (IRB; protocol PA11-0878). Patients who had a skin biopsy during the management of AML were identified and only patients with skin biopsy consistent with neutrophilic dermatosis (SS) were included. To identify the patients who met von den Driesch-modified Su and Liu diagnostic criteria for SS, the clinical characteristics were reviewed. This diagnostic criteria consists of major criteria (ie, abrupt onset of tender erythematous papules and nodules, and dense neutrophilic infiltrate in the dermis without leukocytoclastic vasculitis) and minor criteria including presence of fever $\geq 38^{\circ}C$, at least 2 of 4 abnormal laboratory values (White blood cell count [WBC] > 8000, neutrophils $> 70\%$, ESR > 20 mm/h and positive C-reactive protein), a disease condition associated with SS (eg, infection, malignancy, inflammatory disorder, etc) and an excellent response to treatment with glucocorticoids. To diagnose SS, both major criteria and at least 2 minor criteria had to be fulfilled. Patients who fulfilled the von den Driesch diagnostic criteria were included in our analysis. Patients were excluded from this analysis if the clinical signs and symptoms were consistent with skin infection, abscess, or if infectious organisms were isolated from skin culture. Similarly, patients were excluded if the signs and symptoms or skin biopsy were more consistent with other causes of neutrophilic dermatosis (such as pyoderma gangrenosum) or if there was histological evidence of vasculitis. In addition, patient characteristics, and AML characteristics at initial diagnosis and at the time of diagnosis of SS were reviewed. The latter included cytogenetics and molecular aberrations by banding karyotype, fluorescence in situ hybridization (FISH) analysis, and reverse transcriptase polymerase chain reaction (RT-PCR).

Additionally, after obtaining separate IRB protocol approval from our institution (PA13-0840), FMS-related tyrosine kinase-3 (*FLT3*) mutational analysis (codon 835 and internal tandem duplication [ITD]) was performed on DNA extracted from formalin-fixed paraffin embedded (FFPE) tissue sections of the skin lesions from patients who were found to have *FLT3* mutations, using previously described methods.[25]

Descriptive statistics including median and range for continuous variables such as age and laboratory measurements, and time to improvement of SS signs and symptoms are provided. Frequency counts and percentages for categorical variables such as sex, classification of AML, and cytogenetic and genetic mutations expression are also described. The Kaplan–Meier method was used for analysis of overall survival from diagnosis of AML and reported as median months with a 95% confidence interval. Statistical software IBM SPSS Statistics 19.0 (IBM Corp, Armonk, NY) was used for the statistical analyses.

Results

A total of 2178 patients with newly diagnosed AML underwent induction chemotherapy and had follow-up at our institution between the years 2000 and 2011. Six hundred ninety-seven patients (32%) had documented skin biopsies during the course of their AML therapy or during follow-up during this time period. Twenty-nine of these patients received a histological diagnosis of neutrophilic dermatosis. Of these, 8 patients did not meet the von den Driesch modified criteria for diagnosis of SS (3 patients were considered to have skin infections as the underlying etiology, 4 patients had neutrophilic dermatosis but not SS based on histological assessment by a pathologist, and 1 patient was diagnosed with vasculitis). Thus, 21 patients met the von den Driesch

Table 1 Sweet Syndrome in AML Patients

Patient Characteristics	n	Percentage or Range
Total AML Patients	2178	
Total Patients Undergoing Skin Biopsies During Treatment of AML	697	32
Patients Fulfilling Diagnostic Criteria of SS[a]	21	1% of all patients 3% of all patients who received a biopsy
Age		
At diagnosis of AML	55	27-87
At diagnosis of SS	56	27-83
Female Sex	14	66
Laboratory Values at Time of Diagnosis of AML		
Median total WBC count, 10^9/L	4.5	1.1-116.6
Median AML blast, %	43	14-92
Median ANC, 10^9/L	0.8	0.1-45
Median Hb, g/dL	9	7.3-11
Median platelet count, 10^9/L	52	8-156
Classification of AML (2008 WHO)		
AML with recurrent chromosomal abnormalities	3	14.5
AML related to MDS	11	52
Therapy-related AML	3	14.5
AML NOS	4	19
SS Diagnosis Before Allogeneic SCT	5/6	83%
Status of AML at Time of SS Diagnosis		
SS diagnosis before AML diagnosis	1	5
SS diagnosis at the time of AML diagnosis	7	33
SS diagnosis during primary induction therapy	6	29
SS diagnosis during treatment for relapsed AML	7	33
Symptoms at Time of Presentation of SS		
Fever	14	66
Tenderness in the skin lesions	10	48
Systemic involvement	3	14
History of filgrastim (G-CSF) use	3	14
Location of Skin Lesions[b]		
Head and neck	9	43
Upper extremity	10	48
Trunk and back	8	38
Lower extremity	10	48
Laboratory Values at Time of Diagnosis of SS		
Median AML blast, %	25	0-92
Neutrophilia (ANC $\geq 6 \times 10^9$/L)	2	10
Neutropenia (ANC $\leq 1.5 \times 10^9$/L)	11	52
Anemia (Hb <10 g/dL)	19	90
Thrombocytopenia ($\leq 100 \times 10^9$/L)	21	100
Kidney dysfunction (GFR <60 mL/min)	2	10

Abbreviations: AML = acute myelogenous leukemia; ANC = absolute neutrophil count; ESR = erythrocyte sedimentation rate; G-CSF = granulocyte colony stimulating factor; GFR = glomerular filtration rate; Hb = hemoglobin; MDS = myelodysplastic syndrome; NOS = not otherwise specified; SCT = stem cell transplanation; SS = Sweet syndrome; WBC = white blood cell; WHO = World Health Organization.

[a]Von den Driesch modified Su and Liu diagnostic criteria for SS; major criteria: abrupt onset of tender erythematous papules and nodules, and dense neutrophilic infiltrate in dermis without leukocytoclastic vasculitis; minor criteria: presence of fever > 38°C, at least 2 of 4 abnormal laboratory values (WBC > 8000, neutrophils > 70%, ESR > 20 mm/h and positive C-reactive protein), a disease condition associated with SS (such as infection, malignancy, inflammatory disorder, etc), and an excellent response to treatment with glucocorticoids. Diagnosis of SS requires both major criteria and at least 2 minor criteria should be fulfilled.

[b]Several patients had lesions at more than 1 site.

modified criteria for diagnosis of SS and were included in our analysis. This represents approximately 1% of all AML patients treated at our institution in the stated time frame and 3% of all AML patients who underwent skin biopsy.

In Table 1 the baseline characteristics of the patients at the time of diagnosis of AML and SS are summarized. The median age at diagnosis of AML and SS was 55 years (range, 27-87 years) and 56 years (range, 27-83 years), respectively. Most SS patients in this analysis were female (66%). At the time of diagnosis of AML the median percentage of myeloid blast cells in the bone marrow, median absolute neutrophil count (ANC), median hemoglobin (Hb), and median platelet count at diagnosis of AML were 43% (range, 14%-92%), 0.8 $\times$ 10^9/L (range, 0.1-45), 9 g/dL (range, 7.3-11), and 52 $\times$ 10^9/L (8-156), respectively. Based on the 2008 revised World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia, 11 patients (52%) were classified as having AML with MDS-related features, 3 patients (14.5%) each as AML with recurrent genetic abnormalities or as therapy-related AML, and 4 patients (19%) were classified as AML-not otherwise specified.[26] Of note, 1 patient in our population had a medical history of relapsing polychondritis (a disease entity that has a known association with SS),[27,28] before the diagnosis of AML and SS, and had been treated with high-dose steroids in the past for polychondritis.

Sweet syndrome was diagnosed before development of AML in 1 AML patient, at the time of diagnosis of AML in 7 patients (33%), during primary induction chemotherapy in 6 patients (29%), and during treatment for relapsed disease in 7 patients (33%). In terms of front-line/induction chemotherapies received for AML treatment: 16 of the 21 patients (76%) received intensive chemotherapy regimens containing high dose cytarabine (ARA-C) and 5 patients received other regimens (1 each: liposomal ATRA-based [1 patient with acute promyelocytic leukemia]; azacytidine with vorinostat; decitabine with gemtuzumab ozogamicin; laramustine-based therapy, and clofarabine with low-dose ARA-C). Among the 21 patients with SS after induction therapy, 14 patients (67%) achieved a complete response (CR) or complete remission with incomplete

recovery of platelet count (CRp); 7 patients were primary refractory to induction chemotherapy. Among the 14 patients who achieved CR/CRp, 3 patients underwent allogeneic stem cell transplantation in first CR (CR1); 2 patients died in CR1; 2 patients were alive in CR; and the 7 remaining patients had relapse of disease/died.

Pyrexia > 38°C was documented in 14 patients (66%) and tenderness in the erythematous nodules was noted in 10 (48%) patients.

Three patients had been treated with G-CSF, 1 patient had received liposomal ATRA, and 2 patients had received hypomethylating agents (1 each: azacytidine and decitabine) before the diagnosis of SS as part of their management of AML or MDS. In almost all of the patients, the SS-manifested lesions were asymmetrical, diffuse, and multifocal. At the time of diagnosis of SS the median percentage of malignant myeloid blast cells in bone marrow was 25% (range, 0%-92%), neutrophilia (ie, ANC > 6.0 $\times$ 10^9K/μL) was seen in 2 patients (10%), neutropenia (ie, ANC < 1.5 $\times$ 10^9K/μL) was seen in 11 patients (52%), Hb < 10 g/dL was observed in 19 patients (90%), platelet count < 100 $\times$ 10^9/L was noted in 21 (100%), and kidney dysfunction (glomerular filtration rate < 60 mL/min) was identified in 2 patients (10%).

Cytogenetic and molecular analyses are summarized in Table 2. Cytogenetics revealed diploid karyotype in 7 patients (33%), complex cytogenetics (≥ 3 unrelated chromosomal abnormalities) in 5 patients (24%), and −5/del(5q) in 3 patients (14%), t(6;9) in 2 patients (10%) and trisomy 8, t(11;17), t(15;17), and t(3;3) in 1 patient each (5%). Common karyotype abnormalities that constituted the "complex cytogenetics" in the 5 patients are detailed in Table 2, with −5/del(5q) seen in 5 patients, and deletion 3 and deletion 13 in 3 patients each. Therefore, changes in chromosome 5 were the most common abnormality found in the study and occurred in overall 8 patients (38%). The most common genetic molecular abnormality identified using FISH or RT-PCR analysis was in the *FLT3* gene, which was mutated in 7 of 18 analyzed patients (39%). Of these, 4 patients had ITD and 3 had codon-835 tyrosine kinase domain (TKD) mutations. Six of these 7 *FLT3* mutations were in patients who had diploid karyotype on cytogenetic analysis. Additionally, 2 of 7 analyzed patients (28%) harbored nucleophosmin 1 (*NPM1*) gene mutations. One patient had concurrent *FLT3*-835 TKD and *NPM1* mutations. No genetic mutations were identified in rat sarcoma, mast/stem cell growth factor receptor kit, and CEPBA-CCAAT and/enhancer binding protein alpha genes (total patients tested for these mutations 13, 5, and 3, respectively).

We further investigated *FLT3* (n = 13) mutational status in FFPE skin lesions (ITD = 4, *D835* = 9), with the aim to attempt to correlate the mutational aberration in skin and bone marrow samples. Results for *FLT3-D835* testing in 7 skin samples were concordant with bone marrow (BM) findings in 5 samples including 1 positive and 4 negative results. In 2 cases, the BM sample showed *FLT3-D835* mutation, and the skin sample was negative for the mutation. *FLT3*-ITD analysis was unsuccessful in all 4 FFPE skin samples likely due to the large size of the RT-PCR product and degradation of DNA on the FFPE preservation.

Glucocorticoids, antibiotics, and supportive wound care were the most frequent therapeutic interventions in patients with AML and SS. Eight patients (38%) received systemic glucocorticoids and 2 (10%) received topical steroids. Nineteen (90%) received antibiotics and all patients received supportive wound care. Clinical documentation regarding improvement or progression of SS lesions was available for 16 of 21 patients (76%) and improvement in the skin lesions was documented in all of these patients. However, SS relapsed in 3 patients requiring multiple courses of glucocorticoids. In the remaining cohort (5 of 21; 24%) of the patients, follow-up documentation about clinical improvement or progression was not available mainly because of loss of follow-up or death during treatment of the AML. The median time to documentation of clinical improvement in SS signs and symptoms was 14 days (range, 4-153 days). The median overall survival for the 21 AML patients from the date of AML diagnosis to the time of death was 14 months (95% confidence interval, 12.6-15.4 months); this was not significantly different from the rest of the 2166 AML patients initially screened (median overall survival, 13 months; 95% confidence interval 11.8-14.1 months).

Table 2 Cytogenetic and Molecular Genetic Analysis in Acute Myelogenous Leukemia Patients With Sweet Syndrome

Patient Characteristics	n	Percentage
Cytogenetic Analysis (n = 21)		
Diploid cytogenetics	7	33
Complex cytogenetics (≥3 chromosomal abnormalities)	5	24
−5/del(5q) (as sole abnormality)	3	14
t(6;9)	2	10
Trisomy 8	1	5
t(11;17)	1	5
t(15;17)	1	5
t(3;3)	1	5
Karyotype Abnormalities Constituting "Complex Cytogenetics" (n = 5)[a]		
−5/del(5q)	5	100
−3	3	60
−13/del(13q)	3	60
−7/del(7q)	2	40
−12	2	40
−17	2	40
Others[b]	1 each	20
Molecular Genetics Analysis		
FLT3 (total tested = 18)		
Internal tandem duplication	4	22
D835	3	17
NPM1 (total tested = 7)	2	28
RAS (total tested = 13)	0	0
C-KIT (total tested = 5)	0	0
CEBPα (total tested = 3)	0	0

[a]Complex cytogenetics patients only (n = 5).
[b]Others: −1, del(6q), −9, −11, −12, −14, −15, del(20q), add(2p), add(3q), add(6q), add7, add(8q), +11, add(16p), add(17p), add(22q).

Discussion

In this study we sought to characterize the clinicopathological features of AML patients who developed SS and to document recurring cytogenetic or molecular aberrations in these patients.

These recurring aberrations might serve to identify patients who are at greatest risk of developing SS during therapy or follow-up of AML. As previously reported, SS in AML patients might present as a paraneoplastic manifestation or as a drug-induced SS due to medications commonly used in the treatment of AML.[1] The clinical manifestations of SS are the result of site-specific infiltration of mature neutrophils to sites such as the dermis and occasionally in other visceral organs (eg, lung, kidney) leading to systemic manifestations like fever, arthralgia, and cutaneous lesions, and sometimes an inflammatory response syndrome. Because SS is associated with various benign and malignant conditions, it has been hypothesized that altered levels of various cytokines and signaling molecules such as G-CSF, interleukin (IL)-1, IL-2, IL-6, IL-8, IL-17, tumor necrosis factor-alpha (TNFα) and interferon γ might contribute to alterations in neutrophil function. Indeed, case reports of SS in individual patients have confirmed alterations in levels of these molecules in the plasma.[29-34] Aberrant production of proinflammatory cytokines IL-6, TNFα, and anti-inflammatory cytokine IL-10 is observed in AML patients, which might also ultimately affect survival.[35] Also, AML and MDS have been associated with defective neutrophil functions including adhesion, migration, chemotaxis, and phagocytosis.[36-38] Thus, such alterations in pro- and anti-inflammatory cytokines and neutrophil function might prevent the occurrence of normal chemotaxis, and thereby contribute to the dermal clumping of the mature neutrophils.

Our results show that skin disorders are a relatively frequent occurrence in AML patients with skin biopsies performed in 32% of all AML patients treated at our institution. In the general population, SS is a relatively rare phenomenon with some estimates quoting an incidence of 2.7 cases per million people per year. In our study, however, the observed incidence was less than 1% of AML patients. Based on the 2008 revised WHO classification of myeloid neoplasms and acute leukemia, we were able to classify 11 of our patients as having AML with MDS-related features, which is considered a high-risk for relapse and poor response to therapy with hematopoietic stem cell transplant.[39] MDS has a known association with SS, so this result was not unexpected.[40-43]

The cytogenetic profile of our population showed increased frequency of high-risk AML cytogenetics anomalies including complex cytogenetics, −5/del(5q), and t(6,9). In patients who had diploid cytogenetics, the most commonly identified molecular mutations involved the *FLT3* gene (either ITD or TKD mutation of *D835*) that encodes a class III receptor tyrosine kinase expressed in 70% to 100% of leukemia cells. Constitutional activation of *FLT3* due to ITD or TKD mutations confers a high risk for relapse and inferior overall survival.[44,45] The reason for increased frequency of SS in AML patients with poor risk cytogenetic and molecular abnormalities is unclear. The median overall survival of approximately 14 months in our study population might be attributable to multiple etiologies, including the greater frequency of poor risk cytogenetics and molecular aberrations in this cohort of patients. Performing FISH or RT-PCR analysis using molecular probes for cytogenetic and molecular aberrations in skin samples from SS patients might help to determine the clonality of the neutrophilic infiltrates thus furthering our understanding of the pathogenesis of SS in AML. Recently, an SS-like clinical entity involving the skin, soft tissues, and lung was noted in several *FLT3*-ITD mutated AML patients who were being treated with a *FLT3* inhibitor, quizartinib (AC220). One hypothesis to explain the putative mechanism is that this is due to induction of terminal differentiation of myeloid blasts to mature neutrophils.[46] Treatment-related terminal myeloid differentiation of AML blasts into mature neutrophils, as described with quizartinib, might explain development of SS in some of our patients after G-CSF, liposomal ATRA, and azacitadine treatments.[19,20,24,46]

Our study, similar to previous studies, showed that SS was more common in women and occurred at various stages of AML including before diagnosis, at diagnosis, at primary induction therapy, or during remission or at the time of relapse, suggesting that SS might actually act as an indicator of underlying malignancy or its relapse.[9,34,47] Although fever, neutrophilia, and increased ESR level are part of the diagnostic criteria for idiopathic SS and MA-SS, these were observed in only a subset of our patients. Only two-thirds of our patients presented with fever, however, most had neutropenia with an ANC $< 1.5 \times 10^9$ K per microLiter (K/μL), and almost all had anemia and thrombocytopenia (notably, the cytopenias observed in our population could be a manifestation of AML/MDS or a result of therapy for myeloid malignancy). Our findings are similar to previous reports that SS in hematological malignancies might occur even in the face of neutropenia and that it might not always manifest the classical signs and symptoms of idiopathic SS.[9,48-50] In our study population, documented improvement of the SS-associated skin lesions occurred in 16 of 21 (76%) patients for whom adequate follow-up data were available. This is notable, especially because approximately half of the patients received glucocorticoids and most received antibiotics. The improvement in SS skin manifestations without glucocorticoids might be attributable to treatment of underlying AML or infection resulting in restoration of normal granulocyte function.

Conclusion

Sweet syndrome should be considered in the differential diagnosis of any AML patient who presents with skin rash (differential diagnosis includes infection, leukemia cutis, drug-induced reaction). SS occurred in approximately 1% of AML patients at our institute, and AML with myelodysplasia-related features, −5/del(5q), and *FLT3* mutations were common in patients with SS. The diagnosis of SS in AML did not affect the median survival of the patients in this limited sample size.

Clinical Practice Points

- Sweet syndrome should be considered in the differential diagnosis of any AML patient who presents with skin rash (differential diagnosis includes infection, leukemia cutis, drug-induced reaction).
- Sweet syndrome occurs in 1% of AML patients, and AML with myelodysplasia-related features, −5/del(5q), and *FLT3* mutations are frequent in patients with SS.
- Sweet syndrome generally responds promptly to treatment with glucocorticoids.

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Disclosure

The authors have stated that they have no conflicts of interest.

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