Sweet syndrome with pulmonary involvement in a patient with myelodysplastic syndrome

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Abstract

We report a patient with Sweet syndrome involving the pulmonary system in the context of myelodysplastic syndrome. Although Sweet syndrome may involve a variety of organ systems, the pulmonary system is rarely affected and can result in poor clinical outcomes, including acute respiratory distress syndrome. Both cutaneous and pulmonary symptoms respond well to systemic corticosteroid therapy and early diagnosis and treatment can improve the prognosis. Our case highlights the importance of collaboration between hematologists, dermatologists, and pulmonologists to facilitate effective diagnosis, triage, and treatment of these patients.

Keywords: Sweet syndrome, acute febrile neutrophilic dermatoses, pulmonary Sweet, myelodysplastic syndrome

Introduction

Sweet syndrome is a condition characterized by such major criteria as the sudden onset of tender erythematous papulonodules with histopathologic evidence of a diffuse predominantly neutrophilic infiltrate [1]. Additional minor criteria for this diagnosis include: the presence of fever in 40-80% of patients, elevated erythrocyte sedimentation rate, C-reactive protein, leukocytosis, and neutrophilia, excellent response to systemic corticosteroids, and an association with chronic inflammatory disorders such as infection, malignancy, drug exposure, pregnancy, or myeloproliferative disorders [2, 3]. While systemic manifestations such as arthralgia, myalgia, and ocular involvement are common, pulmonary findings are a rare manifestation with only 45 total reported cases and one case published in the dermatologic literature, to our knowledge [4,

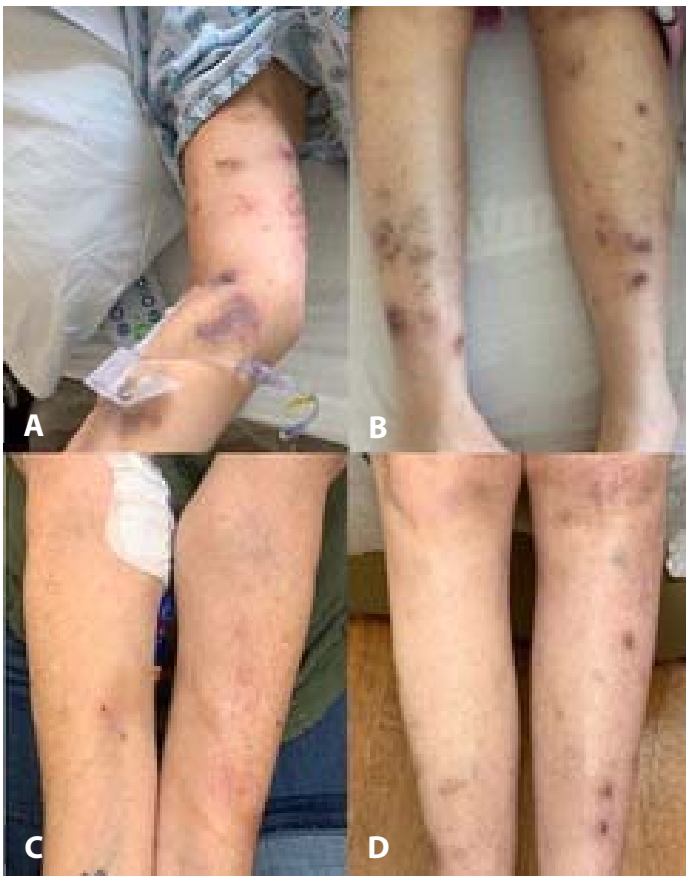

Figure 1: *Clinical photographs of bilateral upper and lower extremities with violaceous papules and nodules.* ***A)*** *Upper extremities and* ***B)*** *lower extremities at initial clinical presentation and* ***C)*** *upper extremity improvement and* ***D)*** *lower extremity improvement after 8 weeks of oral prednisone.*

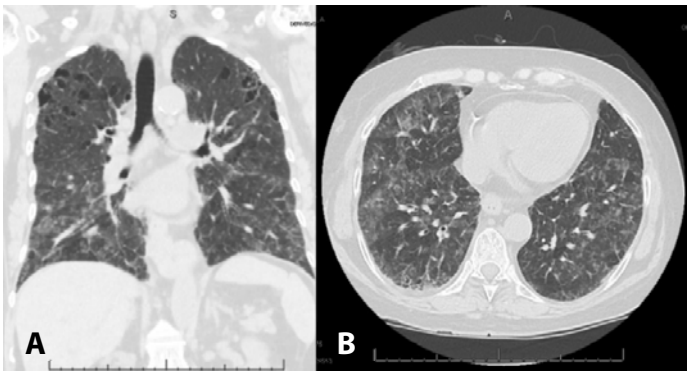

Figure 2*: High resolution chest CT scan. The helical CT imaging of the chest shows bilateral extensive ground glass and nodular opacities on a background of interstitial thickening and emphysema both in **A)** coronal and **B)** sagittal planes.*

5]. In this case report, we demonstrate a rare case of Sweet syndrome with radiologic evidence of pulmonary involvement that rapidly improved with corticosteroids.

Case Synopsis

A 59-year-old woman with a past medical history of asthma, gallbladder pancreatitis, and a 30 pack-year smoking history was admitted with fevers of 38.7°C, poor appetite, fatigue, nausea, and 5.9kg weight loss in the setting of pancytopenia. The patient also had one week of tender violaceous papules on both upper and lower extremities (**Figure 1A**, **B)**. Laboratory tests were significant for a white blood count of 4.4×10^9/L, hemoglobin of 6.0g/dL, hematocrit of 16.8%, platelet of 30×10^9/L, C-reactive protein of 38.39mg/L, erythrocyte sedimentation rate of 140mm/h, and negative anti-neutrophilic cytoplasmic antibody. Urinalysis and comprehensive metabolic panel were within normal limits. Initial chest computed tomography scan without contrast (**Figure 2**) demonstrated extensive ground glass opacities more prominent in the lower lobes, believed to be suggestive of an opportunistic infection. The patient was placed empirically on intravenous cefepime, azithromycin, metronidazole, and acyclovir. A bone marrow biopsy was obtained one day after admission and demonstrated hypercellular marrow with 11.6% lymphoblasts consisting of dysplastic myeloid precursors. Cytogenetics tests were positive for amplification of the *lysine methyltransferase 2A* gene (*KMT2A**)*** detected on fluorescent in situ hybridization (FISH), concerning for myelodysplastic syndrome (MDS) with a poor prognosis. Bronchosocopy was performed given persistent fevers and radiographic evidence of ground glass opacities and bronchoalveolar lavage cultures were negative for legionella, acid-fast bacteria, and fungus. Smears

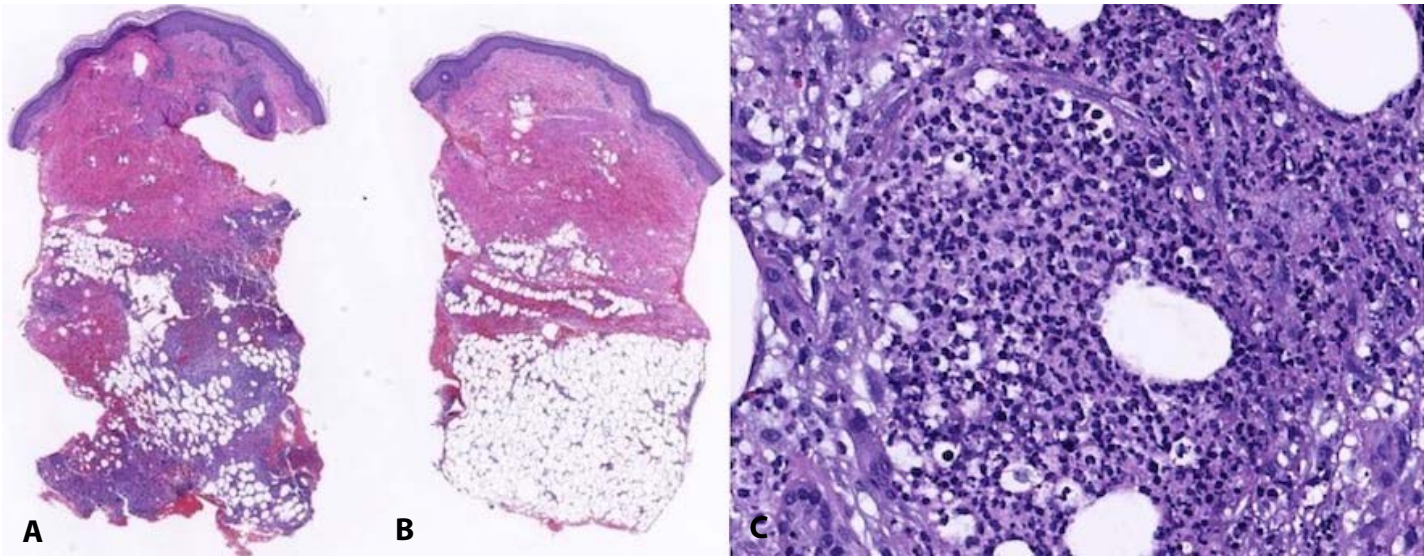

Figure 3*: H&E stain of biopsy of violaceous nodule on left anterior shin. **A)** Low power (2×), and **B)** higher magnification (20×) sections revealed focal parakeratosis and mild spongiosis overlying a deep dermal and subcutaneous neutrophil-rich inflammatory infiltrate with an adjacent reactive fibroblastic reaction and hemorrhage. Gram, Grocott methenamine silver, and periodic acid-Schiff stains were negative.*

demonstrated alveolar macrophages with neutrophils. Despite intravenous antibiotics, the patient had persistent fevers with negative blood and urine cultures. Decitabine therapy was started 11 days after admission to address persistent fevers thought to be secondary to MDS.

A dermatology consultation was subsequently obtained 24 days after admission for persistent violaceous nodules on the lower extremities. A biopsy of a lesion on the left anterior shin showed focal parakeratosis and mild spongiosis overlying a deep dermal, subcutaneous, and peri-eccrine neutrophil rich inflammatory infiltrate (**Figure 3**). Tissue culture was negative for aerobic and anaerobic bacteria, acid-fast bacteria, atypical mycobacteria, nocardia, and fungus. One day following consultation, the patient developed acute hypoxic respiratory distress and was transferred to the ICU. Repeat chest CT showed interval worsening of bilateral ground glass opacities and nodular opacities throughout both lungs. The patient was treated with vancomycin and piperacillin-tazobactam for possible pneumonia along with intravenous methylprednisolone.

The neutrophil-rich infiltrates on biopsy along with radiologic pulmonary findings was concerning for a diagnosis of Sweet syndrome with pulmonary involvement. Consequently, the antibiotics were stopped and the patient continued intravenous methylprednisolone followed by a 6-week oral prednisone taper. The patient experienced rapid improvement in her pulmonary symptoms and her fevers resolved. Follow-up two months after discharge demonstrated complete resolution of ground glass opacities and pleural effusions on CT along with marked improvement in cutaneous symptoms (**Figure 1C**, **D)**.

Case Discussion

In this case, we present a patient with clinical, histopathologic, radiologic, and bronchoalveolar lavage evidence of Sweet syndrome with pulmonary involvement in the context of negative cultures and MDS. The patient's constitutional and respiratory symptoms did not improve with empiric antibiotics, suggesting lack of infection. The differential diagnosis also included Sweet syndrome, pyoderma gangrenosum, neutrophilic eccrine hidradenitis, ulcerating neutrophilic panniculitis related to alpha-1-antitrypsin deficiency syndrome, and vasculitis. However, the rash preceded decitabine administration and the lack of ulcerating lesions or elevated liver function tests did not support pyoderma gangrenosum or alpha-1-antitrypsin deficiency syndrome, respectively. Pathology, negative ANCA, and normal urinalysis were also less suggestive of vasculitis. Furthermore, our patient fulfilled two major criteria for Sweet syndrome: the presence of erythematous violaceous papulonodules and dense neutrophilic infiltrate on biopsy. Additionally, she fulfilled four minor criteria, including: general malaise and fevers >38°C, a concomitant diagnosis of MDS, elevated C-reactive protein, erythrocyte sedimentation rate, and neutrophilia on bronchoalveolar lavage, and a rapid response to systemic corticosteroids [6]. The ground glass opacities, interstitial infiltrates on chest CT, neutrophilia on bronchoalveolar lavage, and acute hypoxic respiratory distress with prompt response to corticosteroids indicated pulmonary involvement as well.

Symptoms of pulmonary Sweet typically involve progressive dyspnea and a dry nonproductive cough that typically present concomitantly with cutaneous lesions [7]. Chest X-ray and chest CT show diffuse unilateral or bilateral interstitial infiltrates, with some cases demonstrating pulmonary ground glass opacities and pleural effusions. Bronchoalveolar lavage often reveals a high neutrophil content (>50%) with negative cultures, whereas transbronchial biopsies show dense, sterile neutrophilic alveolar infiltrates. In 16 of 34 cases of Sweet syndrome with pulmonary involvement the skin manifestations presented first, whereas in 12 cases the two occurred simultaneously [7, 8]. In this case, our patient was found to have violaceous papulonodules prior to having a screening chest CT, which demonstrated bilateral lower lobe infiltrates and ground glass opacities. Although our patient recovered lung function with significant improvement of cutaneous lesions on systemic

corticosteroids, Sweet syndrome with pulmonary involvement has, in five cases, rapidly progressed to acute respiratory distress syndrome and death [7]. Furthermore, as seen in our patient, of 34 previous reported cases of pulmonary involvement in Sweet syndrome, 18 cases involved the presence of hematologic disorders, including MDS, myeloproliferative disorder, and agnogenic myeloid metaplasia [9, 10].

Conclusion

We report a patient with Sweet syndrome with pulmonary involvement in the setting of MDS. We hope that this case will add to the literature regarding systemic manifestations of Sweet syndrome. This case serves as an important reminder of the rare systemic manifestations of Sweet syndrome while also demonstrating the importance of interdisciplinary collaboration between dermatologists, pulmonologists, and hematologists to optimize the management and outcomes of patients suffering from Sweet syndrome.

Potential conflicts of interest

The authors declare no conflicts of interest.

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