“NOT SO SWEET” SYNDROME

CHANDLER MCCAIN, PA-C FELLOW, AMY JAYSON, PA-C
HARDIK THAKKAR, PA-C, KEVIN EATON, PA-C, STEENLAND, MD, VERMA, MD
Department of Internal and Hospital Medicine, Moffitt Cancer Center, Tampa, FL

Case Presentation

A 54-year-old female with myelodysplastic syndrome, on Azacitidine, a demyelinating agent, presented with three-day history of bilateral knee pain, conjunctival erythema, and intermittent fevers. Past medical history significant for HSV. Vitals prominent for 101° F temperature and a heart rate of 110 bpm. Physical exam revealed tender and erythematous papules, nodules, and plaques, on the bilateral upper and lower extremities, face, and scalp. She also had bilateral conjunctivitis, and severe lower extremity joint pain. Labs pertinent for leukopenia (WBCs 1.75 k/uL), elevated ESR (124 mm/hr)/CRP (17.67 mg/dL) and neutropenia (ANC of 0.40 k/uL).

Infectious causes of neutropenic fever were ruled out and dermatology was consulted due to suspicion for sweet syndrome (SS). The patient was admitted and started on Prednisone 80 mg with a plan to taper over 4-6 weeks. Within 24 hours, her symptoms began to improve, and she was discharged 4 days after admission. The patient’s positive response to steroids and cutaneous lesion biopsy confirmed the diagnosis of sweet syndrome, also known as acute febrile neutrophilic dermatosis.

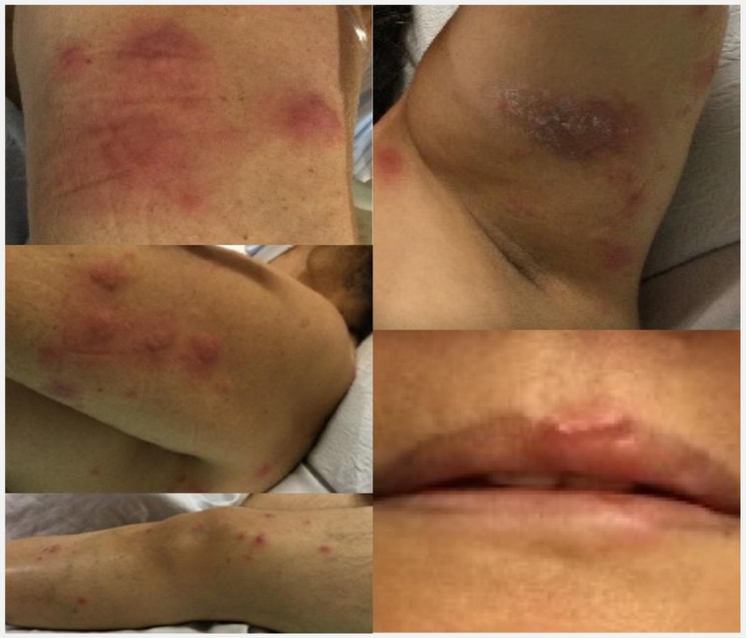

Figure 1: Tender, erythematous and edematous papules, nodules, and plaques, asymmetrically distributed on the bilateral upper and the lower extremities, face, and scalp

Discussion

Sweet syndrome is a rare inflammatory disorder that is classified into three subtypes based on etiology: classical, malignancy-associated, and drug induced. Classical SS includes patients without history of malignancy or drug exposure. Malignancy-associated SS occurs more often in patients with a hematologic malignancy than a solid tumor malignancy, especially AML or myeloproliferative disorders. Drug induced SS usually develops two weeks after exposure and is most associated with G-CSF.

Pathogenesis has been linked to a combination of hypersensitivity reaction, cytokine induction, and genetic susceptibility. SS presents as an abrupt onset of tender rash (Fig 1.), fevers, ocular inflammation, arthralgias and in severe cases, encephalitis. Rash presents as tender, edematous papules, plaques and nodules that start on the upper extremities or scalp and spread in a craniocaudal fashion. Ocular manifestations are common extracutaneous findings.

A diagnosis of SS requires both major criteria, and three out of four minor criteria to be met. Major criteria: 1. acute onset of painful, erythematous, edematous plaques or nodules 2. histology showing edema, and neutrophil infiltration in the upper and mid dermis, sparing the epidermis, leukocytoclasis, and absence of vasculitis (Fig 2.). Minor criteria: 1. fever 2. presence of malignancy, inflammatory disorder, pregnancy, recent URI or GI infection, or recent vaccination 3. At least three lab abnormalities: ESR > 20 mm/hr, positive CRP, leukocytosis with neutrophil predominance (> 70% neutrophils).

Treatment is initiated with Prednisone 0.5-1 mg/kg/day then tapered over 4 – 6 weeks. Symptoms typically improve within 48 hours and rash resolves in 1 – 2 weeks.

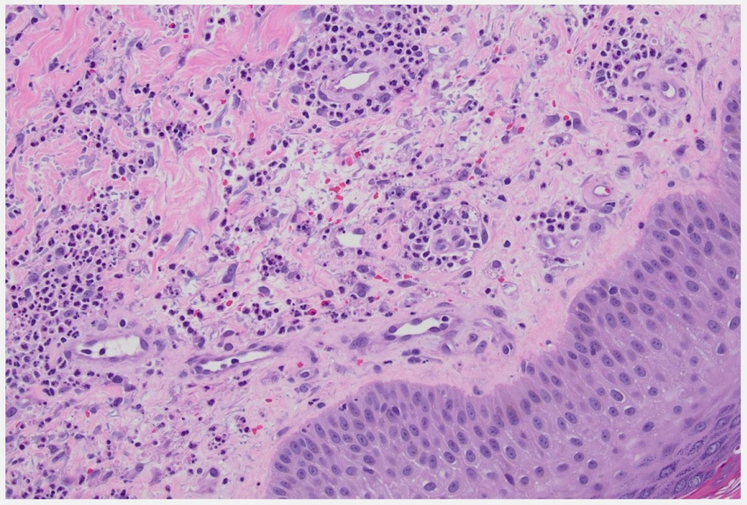

Figure 2. Sections of skin demonstrate a marked dermal neutrophilic infiltrate that surrounds blood vessels, associated with edema and the presence of leukocytoclastic nuclear debris. Vascular endothelial cells show reactive change with swelling, but vasculitis is absent. The overlying epithelium is intact.

Conclusion

This case serves as an educational piece on the rare pathology of sweet syndrome, as well as the complex nature in which the syndrome can present. Although SS most often occurs with neutrophilia, it is possible the patient may instead present with neutropenia due to systemic chemotherapy which can further complicate the diagnosis, as in the case of our patient. In patients with known risk factors, including malignancy or new drug exposure, presenting with symptoms of ocular complaints, arthralgias, and rash, a diagnosis of sweet syndrome should be considered. Early recognition may prevent unnecessary advanced radiologic imaging, antibiotic exposure, and ultimately improve patient outcomes.

References

1. (n.d.). Merola, MD, MMSc, FAAD, FACR J. 2022 Jun 29. weet syndrome (acute febrile neutrophilic dermatosis): Pathogenesis, clinical manifestations, and diagnosis. Callen, MD, FACP, FAAD J, O Ofori, MD A, editors. UpToDate.