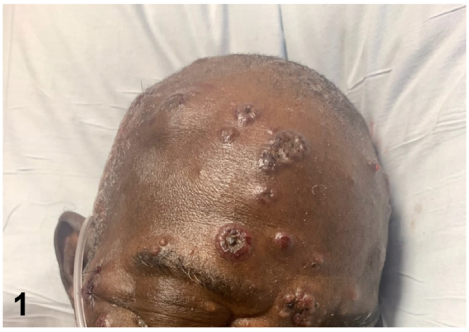
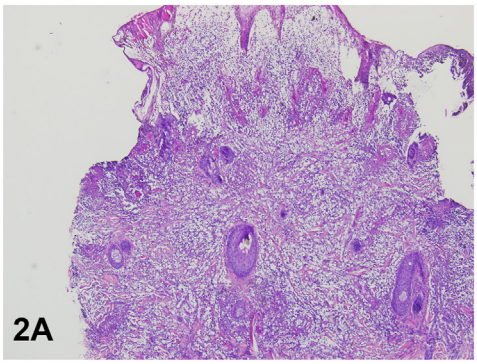
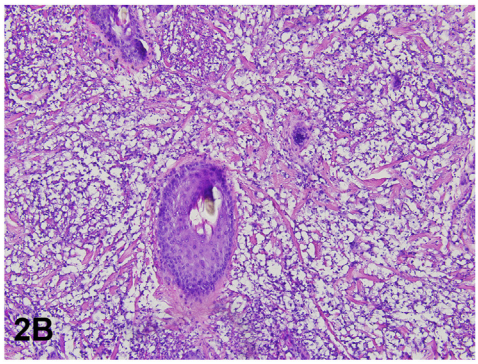
A patient with fever and umbilicated papules

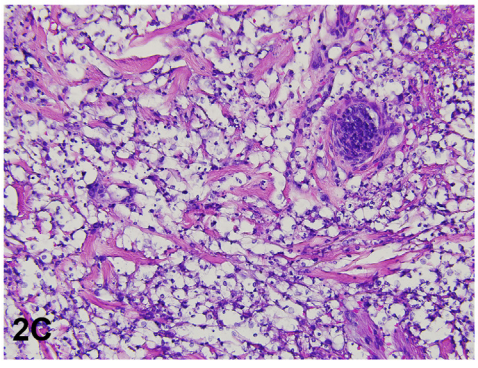
Hesham Alshaikh, MD,[a] Jane Scribner, MD,[a] Bradley J. Saylors, MD,[b] and John Maize, Jr, MD[a,b]

Key words: clinicopathological correlation; cryptococcoid Sweet; neutrophilic dermatosis; Sweet syndrome.









CASE PRESENTATION

A 63-year-old man with no significant past medical history was admitted to the hospital with fever, altered mental status, and rapidly progressing disseminated skin lesions. A physical examination revealed vesicular appearing and umbilicated papules and plaques on the scalp, face, trunk, and upper extremities (Fig 1). The patient's clinical condition continued to decline despite empiric broad antibiotic coverage. Serum cryptococcal antigen, cerebrospinal fluid analysis, and blood, urine, cerebrospinal fluid, and tissue cultures were negative. A punch biopsy submitted for hematoxylin-eosin staining showed dense inflammatory cell infiltrate with

basophilic bodies surrounded by capsule-like spaces (Fig 2, *A-C*). Myeloperoxidase and CD15 highlighted the infiltrate, which was predominantly neutrophilic. Grocott methenamine silver and periodic acid—Schiff staining and all tissue cultures were negative.

Question 1: What is the most likely diagnosis?

A. Cryptococcosis

B. Histoplasmosis

C. Sweet syndrome

D. Sarcoidosis

E. Herpes zoster

Answer:

A. Cryptococcosis — Incorrect. Disseminated Cryptococcus infection is more common in individuals with primary or secondary immunodeficiency. Histopathology typically shows pleomorphic yeast within clear vacuolated spaces. Positive cryptococcal antigen, periodic acid—Schiff, Grocott methenamine silver, and tissue culture support the diagnosis.[1]

B. Histoplasmosis — Incorrect. Histoplasmosis is an opportunistic fungal infection endemic to Ohio and Mississippi river valleys. It is primarily a pulmonary disease, but the skin may be involved, with umbilicated papules that resemble molluscum contagiosum. A biopsy from lesional skin would show evenly spaced intracellular yeast surrounded by pseudocapsules. Grocott methenamine silver, periodic acid—Schiff, and cultures would be positive.[2]

C. Sweet syndrome — Correct. Cryptococcoid Sweet is a unique variant of Sweet syndrome that has been recently described and shows resemblance in both the clinical presentation and histopathologic features to cryptococcal infection.[3] The diagnosis is supported by positive myeloperoxidase staining and negative fungal stains.

D. Sarcoidosis — Incorrect. Patients with sarcoidosis may have cutaneous involvement, which often presents as red-brown dermal papules and plaques that favor the face, neck, and upper extremities. The pathologic hallmark of sarcoidosis is noncaseating granulomatous inflammation.

E. Herpes zoster — Incorrect. Herpes zoster may present as an umbilicated vesicular eruption. Disseminated zoster occurs with more than 20 vesicles outside the primary and adjacent dermatome. Cutaneous dissemination is a sign of viremia and is often accompanied by visceral organ involvement. Acantholysis, ballooning degeneration of keratinocytes, and viral cytopathic changes are typically seen with hematoxylin-eosin staining. Adnexal structures are frequently involved, and leukocytoclastic vasculitis may be present.

Question 2: What is the most appropriate treatment for this patient?

A. Intravenous fluconazole

B. Dapsone

C. Systemic corticosteroids

D. Intravenous acyclovir

E. Intravenous amphotericin B

Answer:

A. Intravenous fluconazole — Incorrect. Fluconazole has the advantage of penetrating the blood-brain barrier and can be used as an alternative treatment option to amphotericin B in disseminated cryptococcosis and histoplasmosis.[1]

B. Dapsone — Incorrect. Dapsone has been used off-label for neutrophilic dermatosis and is a second-line treatment agent for Sweet syndrome. It can be used as a monotherapy or in combination with other systemic agents.[4] Monitoring for hemolytic anemia

From the Department of Dermatology and Dermatologic Surgery, Medical University of South Carolina, Charleston, South Carolina[a]; and Trident Dermatology, Trident Medical Center, Charleston, South Carolina.[b]

Funding sources: None.

IRB approval status: Not applicable.

Consent: Consent for the publication of medical information and patient's photograph was obtained prior to submission of the manuscript. The patient understands that his information is to be published in print and online and that it may be publicly available. Also, he understands that it may be used for other educational purposes and that he has the rights to revoke this authorization at any time.

Correspondence to: Hesham Alshaikh, MD, Department of Dermatology and Dermatologic Surgery, Medical University of South Carolina, 135 Rutledge Ave, MSC 578, Charleston, SC 29425-5780. E-mail: Alshaikh@musc.edu.

JAAD Case Reports 2022;27:58-60.

2352-5126

https://doi.org/10.1016/j.jdcr.2022.06.031

and methemoglobinemia is essential, and these side effects are dose-dependent and can occur in all individuals. Agranulocytosis is the most serious idiosyncratic reaction and usually occurs within the first 2 months of therapy.

C. Systemic corticosteroids — Correct. Systemic steroids are the most effective therapy for Sweet syndrome. Response to systemic corticosteroids is one of the diagnostic criteria of Sweet syndrome. Patients often require 1 mg/kg/day of prednisone tapered over 6–8 weeks.[5]

D. Intravenous acyclovir — Incorrect. Intravenous acyclovir is the treatment of choice for disseminated herpes zoster infection.

E. Intravenous Amphotericin B — Incorrect. Amphotericin B is the preferred initial therapy for disseminated cryptococcosis and histoplasmosis.[1,2]

Question 3: Which of the following has the most common association with this condition?

A. Inflammatory bowel disease

B. Hematologic malignancy

C. Granulocyte colony-stimulating factor

D. Solid-organ malignancy

E. Idiopathic

Answer:

A. Inflammatory bowel disease — Incorrect. Patients presenting with Sweet syndrome and concurrent gastrointestinal complaints should be evaluated for inflammatory bowel disease because both Crohn's disease and ulcerative colitis can be associated with Sweet syndrome.[4]

B. Hematologic malignancy — Incorrect. Sweet syndrome is more likely to occur in patients with hematologic malignancy than in patients with solid-organ tumors. Acute myeloid leukemia is the most common associated hematologic malignancy, and it can precede, follow, or appear concurrently with Sweet syndrome.[4]

C. Granulocyte colony-stimulating factor — Incorrect. Granulocyte colony-stimulating factor is the culprit in the majority of drug-induced Sweet syndrome. Recurrence of the syndrome may develop when the patient is rechallenged with the inciting agent.[4]

D. Solid-organ malignancy — Incorrect. Breast, genitourinary, and gastrointestinal carcinomas are the most frequently reported solid organ tumors with Sweet syndrome.[4]

E. Idiopathic — Correct. In most cases, no underlying trigger can be identified, and the diagnosis relies on fulfilling the diagnostic criteria and ruling out infectious etiologies.[5]

Conflicts of interest

None disclosed.

REFERENCES

1. Durden FM, Elewski B. Cutaneous involvement with Cryptococcus neoformans in AIDS. *J Am Acad Dermatol*. 1994;30(5 Pt 2):844-848.
2. Bonifaz A, Vázquez-González D, Perusquía-Ortiz AM. Endemic systemic mycoses: coccidioidomycosis, histoplasmosis, paracoccidioidomycosis and blastomycosis. *J Dtsch Dermatol Ges*. 2011;9(9):705-715.
3. Wilson J, Gleghorn K, Kelly B. Cryptococcoid Sweet's syndrome: two reports of Sweet's syndrome mimicking cutaneous cryptococcosis. *J Cutan Pathol*. 2017;44(5):413-419.
4. Cohen PR. Sweet's syndrome--a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis*. 2007;2:34.
5. Efthimiou P. In: *Auto-Inflammatory Syndromes Pathophysiology, Diagnosis, and Management*. 1st ed. Springer International Publishing; 2019.