Dusky violaceous necrotic plaques of the chest

Natalie Kollman, MD, Matthew Franklin, MD, and Arlene Rosenberg, MD
Cleveland, Ohio

Key words: diabetes; environmental; fungus; infections; infectious diseases; medical dermatology.
A 42-year-old woman presented to the emergency department with chest pain and dyspnea. She had a medical history significant for uncontrolled type II diabetes and substance abuse (urine toxicology screen positive for marijuana, cocaine, and oxycodone). Laboratory data were significant for diabetic ketoacidosis. Her hemoglobin A1c was found to be 11.7% (normal, 4%-5.6%). A chest computed tomography found an opacity of the left upper lung and air present within the left chest wall. The patient had enlarging pink-to-violaceous dusky necrotic plaques of the left breast (Fig 1). Punch biopsy and wet mount were obtained (Figs 2 and 3).

**Question 1: What is the best diagnosis?**

A. Coumadin-induced necrosis  
B. Calciphylaxis  
C. Levamisole-induced vasculopathy  
D. Mucormycosis  
E. Disseminated candidiasis

**Answers:**

A. Coumadin-induced skin necrosis — Incorrect. Although the classic distribution often involves areas with excessive adipose tissue, such as the abdomen, thigh, or breast, this does not take into consideration the fungi identified on the punch biopsy or the wet mount.

B. Calciphylaxis — Incorrect. Although the typical distribution may include the abdomen, thighs, legs, and breasts, calciphylaxis commonly occurs in the setting of end-stage renal disease or secondary hyperparathyroidism, neither of which are mentioned in the question stem. Additionally, this answer choice does not account for the pulmonary infiltrate or the fungi identified on the punch biopsy or wet mount.

C. Levamisole-induced vasculopathy — Incorrect. Although the picture shows a necrotizing skin condition, and the patient has a history of cocaine use, this answer choice does not account for the pulmonary infiltrate or fungi present in the punch biopsy or wet mount.

D. Mucormycosis — Correct. The patient presented with diabetic ketoacidosis in the setting of poorly controlled diabetes and illicit drug use, both of which are important risk factors for development of mucormycosis. The pulmonary infiltrate and air found within the left chest wall in addition to fungal organisms identified on a punch biopsy and wet mount support an infectious process. The characteristic ribbon-shaped or broad branching non-septate hyphae and sporangium (Figs 2 and 3) are classic for mucormycosis.

E. Disseminated candidiasis — Incorrect. Although uncontrolled diabetes could be a risk factor for disseminated candidiasis, typically patients have underlying immunodeficiencies or other predisposing conditions that were not depicted in the question stem. Additionally, the fungal organisms depicted on the punch biopsy and wet mount are not characteristic for candidiasis.

**Question 2: What put this patient at greatest risk for this condition?**

A. Illicit drug use  
B. Age  
C. Diabetic ketoacidosis  
D. Gender  
E. Environmental exposure

**Answers:**

A. Illicit drug use — Incorrect. Although intravenous illicit drug use may be an associated risk factor for mucormycosis, the intravenous route of administration was not specified in the question stem. Cocaine use is commonly associated with levamisole-induced vasculopathy.

B. Age — Incorrect. Age is not an independent risk factor for mucormycosis.

C. Diabetic ketoacidosis — Correct. This patient had poorly controlled diabetes and was in diabetic ketoacidosis, both of which are the most likely risk factors to cause mucormycosis in this patient. Diabetic ketoacidosis leads to elevated plasma glucose levels, which can upregulate the expression of glucose-related protein 78 (GRP78), which is a heat-shock protein that is present on host endothelial cells. CotH is a fungal spore coat protein present in Mucorales species and functions as a ligand that can bind to GRP78, facilitating angioinvasion. Moreover, hyperglycemia and ketoacidosis act to suppress the innate immune system in addition to facilitating an optimal environment for fungal proliferation.

D. Gender — Incorrect. Gender is not an independent risk factor for mucormycosis.

E. Environmental exposure — Incorrect. Although Mucor species are ubiquitous and commonly found in humid organic matter such as composting...
vegetation or rotting fruit, most people are exposed to these same substances and do not go on to have invasive mucormycosis. Classical risk factors for mucormycosis include immunosuppression, hematologic malignancy, poorly controlled diabetes, diabetic ketoacidosis, iron overload or neutropenia.

**Question 3: Which treatment gives the greatest survival benefit for mucormycosis?**

A. Surgical intervention  
B. Liposomal amphotericin B and surgical intervention  
C. Posaconazole  
D. Liposomal amphotericin B  
E. Liposomal amphotericin B and posaconazole

**Answers:**

A. Surgical intervention – Incorrect. Although limited, cutaneous-only involvement may be amenable to surgical treatment; however, given the severity depicted in the picture and history of pulmonary infiltrate, this case would not be adequately treated with a surgical method alone.

B. Liposomal amphotericin B and surgical intervention – Correct. The combination of liposomal amphotericin B and surgical intervention gives the greatest survival benefit for patients.

C. Posaconazole – Incorrect. Posaconazole is typically used for secondary coverage or salvage therapy. Amphotericin B is the preferred first-line agent, specifically, the liposomal formulation because of its greater efficacy.

D. Liposomal amphotericin B – Incorrect. Although the liposomal amphotericin B is the preferred first-line therapy, studies show the greatest survival rate is with surgical intervention in combination with liposomal amphotericin B.

E. Liposomal amphotericin B and posaconazole – Incorrect. Although primary therapy of liposomal amphotericin B with secondary coverage of posaconazole may be a therapeutic regimen for patients who are not surgical candidates, this therapy has an increased mortality rate when compared with surgical therapy in combination with liposomal amphotericin B. Of note, initial treatment with the combination of amphotericin B and posaconazole did not reduce mortality compared with amphotericin B as monotherapy.

**REFERENCES**

1. Petrikkos G, Skiada A, Lortholary O, Rolides E, Walsh T, Kontoyiannis D. Epidemiology and clinical manifestations of mucormycosis. *Clin Infect Dis*. 2012;54(1):S23-S34.
2. Shields B, Rosenbach M, Brown-Joel Z, Berger A, Ford B, Wanar K. Angioinvasive fungal infections impacting the skin. *J Am Acad Dermatol*. 2019;80(4):869-880.
3. Lipatov K, Patel C, Lat T, Shakespeare A, Wang B, Prakash G. Pulmonary mucormycosis in a patient with uncontrolled diabetes. *Fed Pract*. 2018;35(1):32-36.
4. Stone T, Henkle J, Prakash V. Pulmonary mucormycosis associated with medical marijuana use. *Resp Med Case Rep*. 2019;26:176-179.
5. Jeong W, Keighley C, Wolfe R, et al. Contemporary management and clinical outcomes of mucormycosis: a systematic review and meta-analysis of case reports. *Int J Antimicrob Agents*. 2019;52:589-597.