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A painful ulcerative lesion on the lip

Figure 1. Ulcerative lip lesion.

A 59-year-old man from Texas presented to the otolaryngology service with a 2-month history of progressive painful ulceration of the right lower lip, a 1-year history of reduced appetite, and a 20-pound weight loss. He reported a 50-pack-year cigarette smoking history and a history of coronary artery disease and peripheral vascular disease, including aortobifemoral bypass and bilateral iliac stent procedures performed over a decade ago. The patient had limited engagement with primary care and was not taking any medications.

On physical examination, a 1.5-cm ulcerated lesion with raised borders was present at the right oral commissure (**Figure 1**). No other lesions were present on nasal panendoscopy, and the remainder of the physical examination was unremarkable, including normal vital signs.

Laboratory testing revealed the following:

- Hemoglobin 16.2 g/dL (reference range 13.0–17.3)
- White blood cell count 7.3 × 10^9/L (4.0–11.0)
- Platelet count 313 × 10^9/L (140–400)
- Serum sodium 132 mmol/L (136–145)
- Human immunodeficiency virus testing: negative.

PROVISIONAL DIAGNOSIS AND FURTHER EVALUATION

Histologic evaluation of an incisional biopsy specimen of the lesion revealed abundant noncaseating granulomatous inflammation and multiple 2- to 4-µm intracellular forms resembling yeast cells (**Figure 2**). The patient was referred to the infectious diseases service with a provisional diagnosis of cutaneous histoplasmosis.

Enzyme immunoassay of urine for *Histoplasma* antigen and serum complement fixation and immunodiffusion for *Histoplasma* were negative. Since no sample was obtained for culture, the pathology specimen was sent for broad-range polymerase chain reaction testing targeting 28S ribosomal DNA, which detected *Histoplasma capsulatum*.

Computed tomography scan of the chest, abdomen, and pelvis showed centrilobular emphysema, mild hepatosplenomegaly, fluid collections around the aortobifemoral bypass graft, and bilateral adrenal nodularity consistent with disseminated histoplasmosis. The patient declined further vascular surgical exploration for the perigraft fluid collections.

After referral to the endocrine service for hyponatremia, testing revealed compensated adrenal insufficiency,

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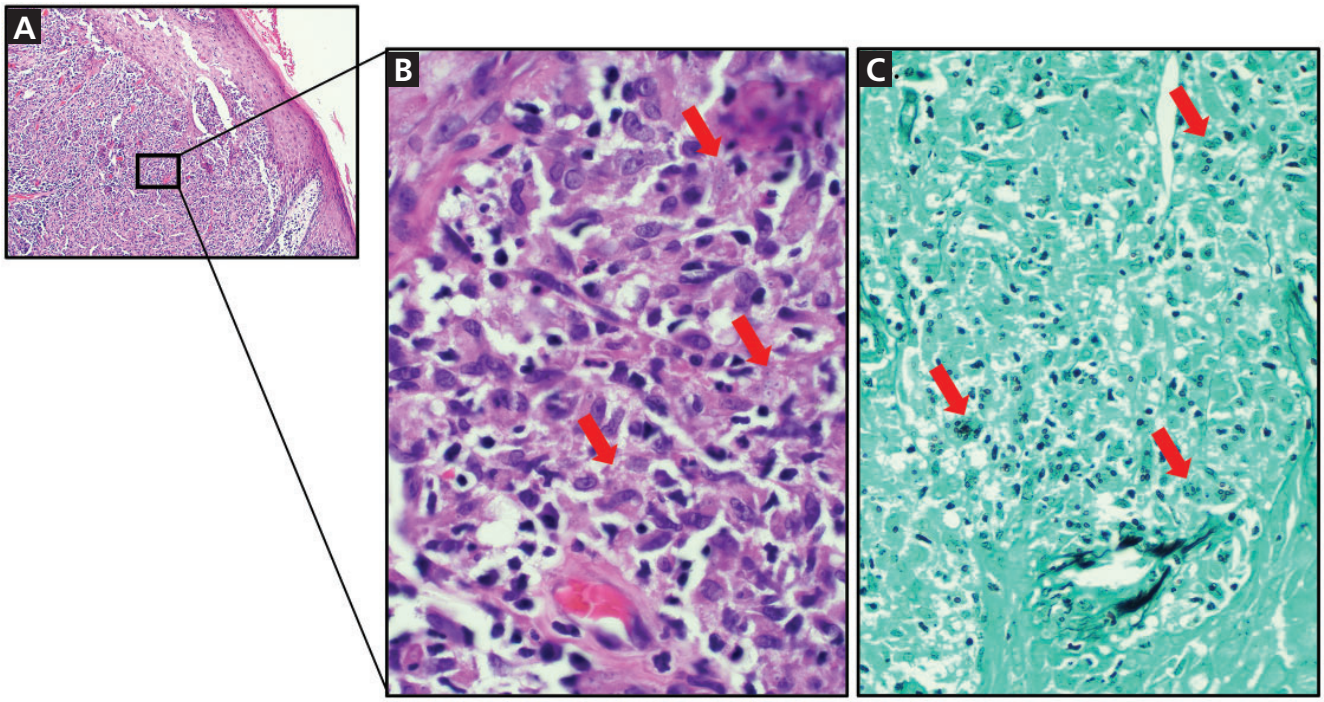

Figure 2. Representative findings of cutaneous histoplasmosis from histopathologic study of a lip lesion specimen. Hematoxylin and eosin staining of a skin section (A) at 4× magnification shows dense dermal infiltrate consisting of acute and chronic inflammatory components with intracellular and extracellular collections of organisms and (B) at 60× magnification shows intracellular and extracellular clusters of *Histoplasma capsulatum* (arrows). (C) Grocott-Gomori methenamine silver staining (magnification × 60) confirms the presence of numerous intracellular forms resembling yeast cells measuring 2 to 4 µM (arrows).

with an elevated plasma adrenocorticotropic hormone level of 107 pg/mL (6–50), normal early morning cortisol of 16 µg/dL (6.7–22.6), and a normal plasma renin-to-aldosterone ratio.

The patient was started on itraconazole oral solution and monitored regularly in the infectious diseases clinic. Symptomatic resolution of the oral lesion occurred within 3 months of initiation of antifungal therapy, and radiologic resolution of the perigraft fluid collections was observed on serial computed tomography imaging done at 6 months and 1 year after therapy was started. After completing 1 year of antifungal therapy, the patient remained stable off therapy.

ORAL MANIFESTATIONS OF CHRONIC DISSEMINATED HISTOPLASMOSIS

Diagnosing and treating histoplasmosis in patients who present with oral ulcers depends on eliciting other symptoms and using necessary testing. Along with lethargy, fever, and weight loss, painful oral cavity ulcerations are a common finding in persons with chronic disseminated histoplasmosis.[1] The differential diagnosis of such a lesion includes herpes simplex virus, syphilis, angular cheilitis, extraintestinal manifestation of inflammatory bowel disease, and squamous cell carcinoma. For immunocompetent adults with chronic disseminated histoplasmosis, advanced age may be the only known risk factor.[2] Given the variable sensitivities of antigen and serologic tests, tissue biopsy may be required for diagnosis.[1,3]

Adrenal involvement is often reported in patients with histoplasmosis.[4] Conversely, vascular graft involvement is rarely reported and, in select cases, resection and replacement of the graft has been pursued.[5]

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DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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