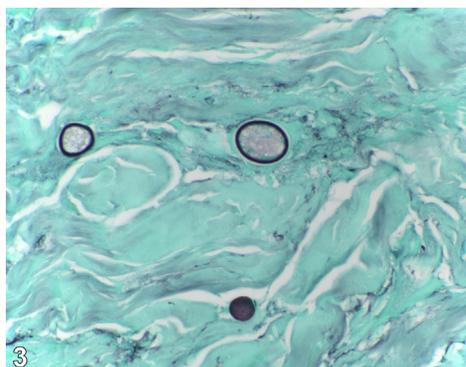
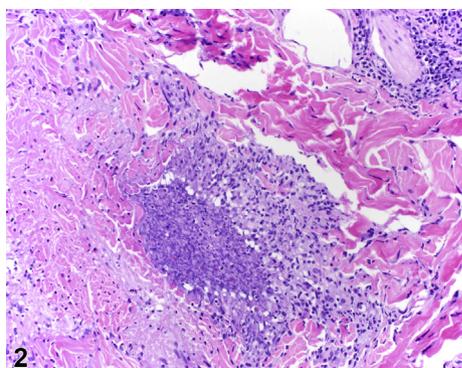


New cutaneous nodules associated with pulmonary symptoms



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A 26-year-old Hmong man, a central California farm laborer with no medical history, presented with 1 week of productive cough and intermittent fevers. A chest radiograph found probable lobar pneumonia with a cavitary lesion, and he was discharged with azithromycin for presumptive community-acquired pneumonia. Despite initial improvement, a pruritic skin eruption developed on his extremities and spread centripetally after completion of azithromycin. Upon re-evaluation in the emergency department, examination found erythematous nodules with central ulceration in the setting of ongoing cough. He denied arthralgia and recent travel but reported an 8-pound weight loss. Punch biopsy specimens were obtained (Fig 1).

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Question 1: Based on the clinical history and histologic findings, which of the following is the most likely diagnosis?

- A. Sarcoidosis
- B. Coccidioidomycosis
- C. Histoplasmosis
- D. Blastomycosis
- E. Cryptococcus

Answers:

A. Sarcoidosis—Incorrect. Sarcoidosis is an inflammatory disease with the histologic hallmark being noncaseating granulomas and imaging likely to reveal perihilar lymphadenopathy. Our patient had necrotizing granulomas on histology (Fig 2) and a lobar pneumonia.

B. Coccidioidomycosis—Correct. Coccidioidomycosis is an infection caused by inhalation of spores of the dimorphic fungi *Coccidioides*, predominantly found in the southwestern United States, with disease expression ranging from self-limited acute pneumonia (known colloquially as *San Joaquin Valley Fever*) to dissemination to the skin, central nervous system or musculoskeletal system.¹ Gomori methenamine-silver (GMS) stain of the punch biopsy (Fig 3) supports this diagnosis by revealing spherules with endospores.

C. Histoplasmosis—Incorrect. *Histoplasma capsulatum* is found worldwide in caves and soil rich in bird and bat droppings. GMS stain would reveal small yeasts with narrow budding.²

D. Blastomycosis—Incorrect. *Blastomyces dermatitidis* has been isolated from moist soil in the Mississippi and Ohio River valleys and around the Great Lakes. GMS stain shows large broad-based budding yeast.

E. Cryptococcus—Incorrect. Because *Cryptococcus neoformans* is mostly responsible for infections found in immunocompromised individuals, it is not the most likely answer choice in our immunocompetent patient with no medical history.

Question 2: Hematoxylin-eosin stain of the punch biopsy showed necrotizing granulomas (Fig 2). Based on the patient's risk factors and the H and E stain findings, which of the following stains would most support your suspicions for the causative organism behind the nodules?

- A. Acid-fast bacilli stain
- B. India ink
- C. GMS
- D. Gram stain
- E. Fontana-Masson

Answers:

A. Acid-fast bacilli stain—Incorrect. The acid-fast bacilli stain uses carbol-fuchsin to stain the lipid walls of acid-fast organisms such as *Mycobacterium tuberculosis*.

B. India ink—Incorrect. *Cryptococcus* has a capsule and would stain as a halo surrounding the yeast with India ink.

C. GMS stain—correct. Hematoxylin-eosin stain would show nonspecific necrotizing granulomas, whereas, of the listed answer choices, GMS stain would be most helpful in identifying Coccidioidomycosis, as it would stain spherules with multiple endospores.² *Blastomyces dermatitidis* would reveal broad-based budding, whereas both *Cryptococcus neoformans* and *Histoplasma capsulatum* would reveal narrow-based budding on GMS stain.²

D. Gram stain—Incorrect. The Gram stain does not normally stain *Coccidioides* species. The GMS stain is most sensitive in detecting fungi in histopathologic preparations.

E. Fontana-Masson stain—Incorrect. Fontana-Masson staining has been demonstrated most consistently for *Cryptococcus neoformans*.³ It is helpful in identifying melanin-producing organisms.

Question 3: Which of the following cutaneous manifestation of this disease would likely produce evidence of fungal dissemination on biopsy?

- A. Erythema nodosum
- B. Erythema multiforme
- C. Sweet syndrome
- D. Acute generalized exanthema
- E. Solitary granulomatous plaque

Answers:

A. Erythema nodosum—Incorrect. Cutaneous manifestations of Coccidioidomycosis are

categorized as reactive or organism specific. Erythema nodosum is considered the most frequent reactive manifestation.⁴

B. Erythema multiforme—Incorrect. Erythema multiforme is characterized by target-like lesions and can include oral findings. It is also considered a reactive cutaneous finding and, as such, would not produce visible microorganisms on biopsy.

C. Sweet syndrome—Incorrect. Sweet syndrome is a very rare feature of Coccidioidomycosis. Biopsy would show abundant neutrophils but not microorganisms.

D. Acute generalized exanthema—Incorrect. Acute generalized exanthema, which can be mistaken for an allergic contact dermatitis, would not produce evidence of fungal dissemination on biopsy.⁴

E. Solitary granulomatous plaques—Correct. Clinically, lesions as a result of dissemination are nonspecific and include ulcerated and verrucous plaques; solitary granulomatous plaques; and papular, nodular, or pustular lesions.^{4,5} The clinical

differential diagnosis includes histoplasmosis, blastomycosis, *Cryptococcus*, and sarcoidosis.

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Abbreviation used:

GMS: Gomori methenamine-silver

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