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A Case of Cryptococcosis Misdiagnosed as Coccidioidomycosis from a Lung Biopsy

Background: Cryptococcosis is increasing in HIV-negative individuals, who may be asymptomatic or present non-specifically. Serum antigen testing has greater sensitivity for cryptococcosis than stain, culture, and microscopy. We present a diagnostically challenging case of cryptococcosis with an inconclusive pathology report.

Case Presentation: A 54-year-old HIV-negative veteran with type 2 diabetes, chronic migraines, and a 20 pack-year smoking history presented with a dry cough, dyspnea on exertion and intermittent sternal chest pain for the past year. He denied recent travel. CT and PET scans revealed multiple hypermetabolic nodules and masses in the left lower lung lobe, the largest 5.0 x 3.0 x 5.4 cm. Biopsy showed necrotizing granulomas and was negative for malignancy. Mucicarmin stain and acid-fast bacilli smear were negative. Pathology report indicated GMS and PAS positive microorganisms resembling *Coccidioides*. Sputum culture and stain showed routine respiratory flora. *Coccidioides* complement fixation was negative but serum cryptococcal antigen (1:10 titer) and Quantiferon-TB Gold Plus were positive. CNS infection was ruled out due to unremarkable CSF studies and negative CSF Cryptococcal antigen.

Conclusion: This case highlights complexities in diagnosing pulmonary cryptococcosis. GMS and PAS stains, though helpful for preliminary fungal infection diagnosis, may not reliably identify specific pathogens. The potential for negative Mucicarmin stains in unencapsulated *Cryptococcus* also complicates diagnosis. A positive serum cryptococcal antigen titer is uncommon in the absence of disseminated disease but was seen in this patient and confirmed the diagnosis. His headaches were likely due to his chronic migraines. The patient was started on oral antifungal therapy with mild improvement. *Cryptococcus* must remain on the differential for any history of pulmonary nodules, even in HIV-negative individuals without overt signs of infection or known exposures.