The Utility of Fine Needle Aspiration for Diagnosis of Extrapulmonary Coccidioidomycosis: A Case Report and Discussion

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Abstract

Coccidioidomycosis typically presents as pneumonia, but rarely manifests as extrapulmonary disease. We describe a case of Coccidioidal infection that presented as a neck mass and was diagnosed by Fine Needle Aspiration (FNA). Initial clinical suspicion was for mycobacterial infection.

Several modalities are available for the detection of *Coccidioides* species, but culture has been the mainstay of diagnosis. FNA provides a relatively noninvasive and effective modality for tissue-based diagnosis based on characteristic histological findings. It allows the additional advantage of early on-site identification, allowing for triage of the specimen, notification of laboratory staff and prompt initiation of treatment.

This case is intended to demonstrate an atypical presentation of extrapulmonary Coccidioidomycosis and highlight the utility of FNA for diagnosis of such lesions. Clinicians should be aware of the unique advantages of FNA for evaluation of lesions of infectious etiology.

**Keywords:** *Coccidioides*, Fine Needle Aspiration, Extrapulmonary Coccidioidomycosis
INTRODUCTION

*Coccidioides* is a thermally dimorphic fungus endemic to the Southwestern United States and regions of Mexico, Central America and South America. Infections with *Coccidioides* are typically contracted through inhalation of arthroconidial spores. In endemic areas, many infections may be asymptomatic or self-limited. The most common presentation for symptomatic illness is pneumonia, but extrapulmonary manifestations may occur through lymphatic drainage and hematogenous spread in less than 5% of cases. Both immunosuppression and race are predictors of dissemination, with persons African American and Filipino descent being at highest risk. The most common sites of extrapulmonary dissemination are skin, soft tissue, central nervous system and bone.

Diagnosis may be made through a combination of tissue analysis, microbiology culture and serum antibody detection. Two morphologically indistinct species of *Coccidioides* are responsible for human infections: *Coccidioides immitis* and *Coccidioides posadasii*. Speciation is not usually completed since clinical presentation and treatment for the two is identical. Serologic antibody detection tests for *Coccidioides* are usually immunodiffusion or complement-fixation based, but carry the disadvantage that they are labor-intensive and may lack sensitivity, particularly in the early stages of infection. Skin antigen testing is becoming available, but will remain positive in the case of asymptomatic or remote infections. Additionally, patients with extensive disease may be anergic. A blood and urine antigen test has been developed and was found to have a sensitivity of approximately 50-70%. Definitive culture from a clinical specimen remains the gold standard in diagnosis.

CASE REPORT

The patient was a 38 year old Mexican male with a history of Type II Diabetes Mellitus who presented with a four month history of right-sided neck mass. The mass developed quickly and then remained stable in size, and was tender and nonmobile with an erythematous, scaly surface. Three months after the mass was first noted, the patient developed cough, fevers and night sweats. The patient had immigrated to the US from Puebla, Mexico one year prior and worked as a welder. He had traveled home to Mexico shortly prior to the development of the neck mass and upon return was treated with a one week course of moxifloxacin for a suspected case of community acquired pneumonia. Physical exam revealed a right cervical supraclavicular fossa mass which was tender, erythematous and fluctuant.

Admission labs did not demonstrate a leukocytosis (WBC count was 9.8 K/µL) or any electrolyte abnormalities. A chest x-ray showed a prominent ill-defined mass configuration in the right medial supraclavicular region, corresponding to the clinically presenting mass. There were ill-defined patchy opacities in the right lower lobe; the left lung was clear.

A CT of the neck showed a multiloculated, rim-enhancing necrotic mass in the right lower neck, measuring 4.4 x 0.9 cm and involving the right level III, IV, V and supraclavicular regions. Lymphadenopathy was noted in the right level II and III regions as well as necrotic lymphadenopathy in the mediastinum. A subsequent chest CT demonstrated numerous nodular opacities throughout both lungs with focal consolidation and air bronchograms present in the right lower lobe.

Based on the patient’s presentation and CT findings, primary tuberculosis infection was felt to be the most likely cause, but other mycobacteria, fungi, sarcoidosis and malignancy were also considered in the differential.
Serum antibodies to HIV 1 and 2 were negative, as was a Quantiferon gold test.

After fine needle aspiration of the mass, Papanicolaou-stained slides demonstrated numerous spherules ranging in size from 30 to 70 µm, some of which contained endospores. In some areas, ruptured spherules releasing endospores were visible, giving the classic “crushed ping pong ball” appearance. (Figure 3) Diffquik-stained slides demonstrated spherules with less definition of varying sizes. Cultures of the fluid sent to Microbiology grew hyphae with arthroconidia consistent with *Coccidioides* spp. (Figure 4) *Mycobacterium tuberculosis* complex PCR performed on the aspirate was negative and a Gram stain showed no organisms.

**DISCUSSION**

The differential diagnosis for an isolated neck mass is extensive. Since this patient’s presentation was relatively rare for *Coccidioides*, initial clinical suspicion was higher for a mycobacterial infection. Serum antibodies for *Coccidioides* were not sent because the patient originated from the Puebla region of Mexico, which has a subtropical highland climate and is not within the currently-identified endemic range of Coccidioidomycosis. Other infectious etiologies were considered, however, as well as granulomatous processes including sarcoidosis. Lastly, malignancies such as carcinoma metastatic to lymph node or cutaneous lymphoma were considered in the differential.

Typically, such a presentation requires tissue examination. However, avoidance of an excisional biopsy in this setting is desirable. FNA has been successfully used for many decades, and is a routine clinical diagnostic practice throughout the United States. FNA is rapid, can be done in a clinic setting, and is performed without, or only with local anesthesia. It offers powerful advantages in that it is a minimally invasive technique with low morbidity and can access both superficial and deep-seated lesions. A typical FNA results in a tissue specimen adequate for a multitude of diagnostic modalities including microbiologic culture, flow cytometric analysis and molecular studies.

FNA has proven to be an effective tool in the diagnosis of infectious lesions including fungal infections. The stains typically used for FNA slides are Papanicolaou and Romanowsky (Diff Quik), which optimize visualization of nuclear and cytoplasmic detail, respectively. Both are acceptable for identification of fungal and yeast forms. In addition, a granulomatous reaction may be identified in the cells surrounding the organisms.

Previous work examining the utility of FNA for pulmonary *Coccidioides* suggests that it is highly effective and specific. A study by Raab et al. examining 73 cases of pulmonary Coccidioidomycosis described characteristic FNA findings including granular acellular debris and intact and ruptured spherules. Granulomatous inflammation was not always evident and mycelial forms were only present in four cases. In all the cases described, FNA findings were sufficient for definitive diagnosis and surgical intervention for tissue was not required.

There are no systematic large studies which examine the utility of FNA for the diagnosis of extrapulmonary Coccidioidomycosis. Two prior case reports indicate this is possible. Our report confirms this, and emphasizes advantages of FNA, which are not available with other tissue sampling methods. The greatest benefit of FNA in such cases may be on-site evaluation, which is a useful first step in identifying thermally dimorphic fungi. It is important for physicians performing on-site evaluation of potentially-infectious FNA’s to recognize characteristic morphology of *Coccidioides* species and be vigilant in cases of granulomatous inflammation,
since early identification of these organisms can expedite treatment initiation. If spherules and endospores are recognized at the on-site evaluation, diagnosis may precede fungal cultures by several days. Additionally, since these organisms are highly infectious, notification of laboratory personnel is essential to maintain their safety. C. species are classified as select agents by the CDC, meaning that they must be destroyed or sent to appropriate facilities for secure handling.

In summary, Coccidioides infection should be considered in the differential of neck mass. A careful travel history may identify travel or habitation in endemic areas, or may be confounding as in this case. Clinicians should be aware that FNA is an effective tool for diagnosis of extrapulmonary Coccidioidomycosis and can streamline the diagnostic process allowing for early initiation of antifungal treatment.

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REFERENCES


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FIGURES

**Figure 1.** Physical examination of the patient revealed a firm, fixed erythematous mass in the right cervical supraclavicular region.

![Image of a physical examination revealing a mass](image1)

**Figure 2.** CT images show a necrotic tissue corresponding to the neck mass.

![Image of CT scan showing a neck mass](image2)
**Figure 3.** FNA slides demonstrate spherules with refractile walls (arrow), some releasing endospores (Papanicolaou Stain, X400).

**Figure 4.** Lactophenol cotton blue preparation from microbiology sample showing barrel-shaped alternate arthroconidia. Arrowheads indicate the arthroconidia, which are the easily-aerosolized infectious particles. Small arrows point to the disjunctor cells.