



Case report

Out of town guest: A healthy 7 year old from a non-endemic area presents with histoplasmosis granulomatous disease

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ABSTRACT

Histoplasmosis is a common fungal infection, normally infecting people exposed to demolition sites or bat/bird droppings in the central and eastern states. When a child presents with a chest mass and eosinophilia in a non-endemic region the likelihood of an infectious process like pulmonary histoplasmosis is unknown. A seven year old immunocompetent child with a mediastinal mass and eosinophilia presented with acute cough, fever, non-bloody emesis, and four pound weight loss. A neoplastic work up was negative. Further evaluation showed a positive M band (chronic histoplasmosis infection) and negative H band (acute infection). Tissue obtained by thoracotomy demonstrated necrotizing granulomatous inflammation with calcification consistent with histoplasmosis. Patient recovered after completion of a twelve week course of itraconazole. A mediastinal mass in a symptomatic child has a 50% risk of cancer as the primary diagnosis. The Infectious Disease Society of America guidelines recommend treatment of histoplasmosis granulomatous disease with itraconazole if symptomatic and surgery only for obstruction. Thus our patient did not have a clear indication for surgery. In a child with a mediastinal mass, despite low risk factors should they be evaluated for a fungal infection prior to invasive surgery? This case demonstrates that histoplasmosis can cause a granuloma in a non-endemic region and that an infectious etiology ought to be considered when working up a symptomatic child with a chest mass as it may prevent unnecessary surgery.

Introduction

Histoplasmosis infection has a national incidence of 3.4 cases per 100,000 and 6.1 cases per 100,000 in endemic areas [1,2]. Per Center for disease Control the Ohio and Mississippi River Valleys are highly endemic (60–90% of people are exposed in their lifetime) and from there the surrounding states become less endemic, with suspected endemicity reaching as far west as California and east to Virginia and some parts of western Georgia.³ Most cases reported are associated with exposure to soil contaminated by bat or bird droppings like from a demolition site or cave [1–3]. They are several manifestations of histoplasmosis from pulmonary, mediastinal granuloma (< 10% of cases), fibrosing mediastinitis, broncholithiasis, chronic, pericarditis, and other disseminated forms [1,2]. Infection is commonly seen in the immunocompromised and most are asymptomatic, but some may present with flu like symptoms [1–3].

Case report

Over the course of one month a 7 year old Hispanic male from

eastern Georgia started to complain of non-productive cough. He had a history of asthma but the cough persisted despite his parents giving him his albuterol inhaler. While at school, his teacher reported two episodes of non-bloody, non-bilious emesis not related to the cough, for which he was sent to see the school nurse. His temperature in the nurse's office was 104. He was sent home and then followed up with his pediatrician in a small town in rural Georgia.

The patient's mother reiterated the story and added that the patient had a decreased appetite and a 4 pound weight loss. She denied pets in the home, recent travel, sick contacts, foreign or new foods, animal or insect bites, fevers, diarrhea, constipation, and chills. Mother reported that the patient's asthma had been well controlled, he only used albuterol as needed and last used it over three months ago, he is fully immunized, has no allergies to medications, an unremarkable family history, previous normal growth and development, and no surgical history.

Physical exam revealed vitals within normal limits, and a non-tender, palpable, mobile lymphadenopathy mainly 1 cm right submental, 0.7 cm anterior cervical and two 0.5 cm bilateral supraclavicular. Lungs were clear to auscultation. A chest radiograph showed a

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Fig. 1. 7 year old male anterior to posterior chest radiograph with mediastinal fullness/mass.

para-tracheal mass, see Fig. 1. The patient was transferred to a higher level of care.

Upon admission a CT scan was performed, see Fig. 2. The radiologist reported: 3.1 × 2.7 × 3.7 cm paratracheal mass with supraclavicular lymph nodes with a differential of teratoma, thymoma, lymphoma, thyroid related tumor, or granulomatous type process. Because of this initial concern for a neoplastic process the patient was transferred to the hematology/oncology service and an extensive laboratory evaluation was initiated. Ceftriaxone 1 g/m/24hr was started to cover for a potential infectious etiology. Pediatric surgery and infectious disease were consulted. Labs revealed a white blood cell count of $6.8 \times 10^3/\text{mL}$ hemoglobin of 11.5 g/dL, platelets of $307 \times 10^3/\text{mL}$ with a differential of neutrophil 23%, lymphocytes 46%, monocytes 12%, and 18% eosinophils. Other labs included: ESR 30 mm/hr, CRP < 0.012 mg/dL, LDH 197 U/L, uric acid 2.7 mg/dL. The comprehensive metabolic panel, glucose, bilirubin, urinalysis, TSH/T4, HIV, PPD, homovanillic acid, vanillylmandelic acid, angiotensin converting enzyme, and ANCA were unremarkable.

He had an MRI of the brain that was normal. Blood and stool cultures were negative. Serum cryptococcal antigen returned positive at 1:20. A repeat cryptococcal antigen was performed three days later and was undetectable. By immunodiffusion, the histoplasmosis H band was negative and M band antibody was present, which suggested a chronic infection with histoplasmosis within the last six months to three years [1,4].

These labs prompted a pediatric surgeon to perform a thoracotomy where a few milliliters of purulent fluid from the mass was obtained that was sent for culture. Multiple biopsies were taken from the



Fig. 2. Transverse chest CT non lung view revealing mediastinal chest mass 31.2 mm × 27 mm without obstruction.

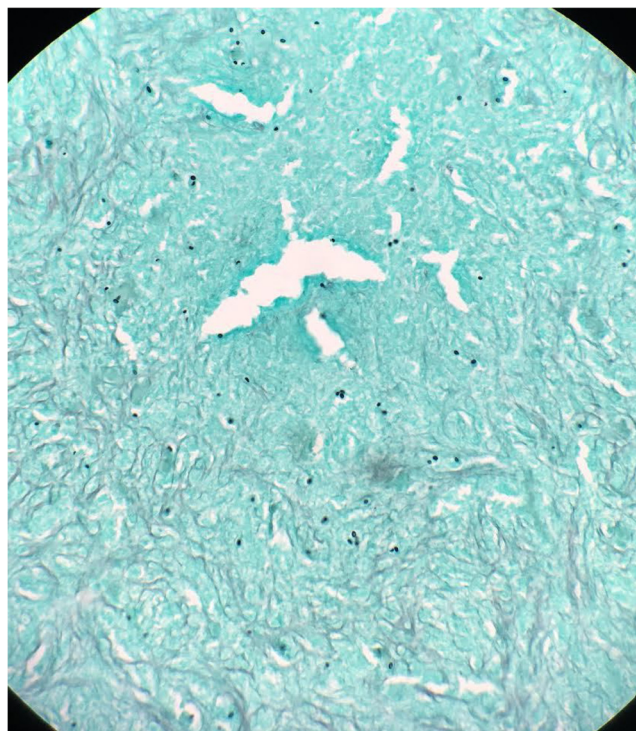


Fig. 3. Biopsy results seen with Grocott-Gomori methenamine-silver stain (GMS) with fungal organisms compatible with *Histoplasma capsulatum*, however there exists morphologic overlap with *Cryptococcus* making it difficult to exclude *Cryptococcal* infection.

mediastinal lymph nodes, right upper lung lobe, mediastinal nodule, and mediastinal mass during the surgery and were sent for biopsy. Post-surgical management required that the patient be transferred to the pediatric intensive care unit because he developed a post-op pneumothorax with a right-sided chest tube. He then returned to the OR for a spinal tap. Cerebral spinal fluid analysis revealed: colorless clear fluid, one red blood cell, one white blood cell, 85 lymphocytes, 15 monocytes; and negative for Indian ink stain, and bacterial and fungal culture

Although the biopsy results were initially unclear as to which fungal organism was present, upon second look the microbiologists, pathologist, and infectious disease physicians agreed that the child had histoplasmosis. Biopsy results revealed necrotizing granulomatous inflammation with calcification, which is consistent with a histoplasmosis mediastinal granuloma, see Fig. 3 [2,5]. In most cases of acute pulmonary histoplasmosis amphotericin B is the drug of choice, however in non-septic cases or in the case of a mediastinal granuloma, itraconazole alone is sufficient [1,2]. He was started on a 12 week course of itraconazole.

The child's remaining hospital course was uneventful. Pain was well controlled with Hydrocodone/Acetaminophen and Ketorolac. Patient was encouraged to undergo incentive spirometry. Serial chest x-rays were performed, which showed progressive improvement of post-op pneumothorax. Chest tube was set to water seal and output was monitored, until removed on later date when the pneumothorax had improved. Patient had intermittent fevers while admitted with drawn cultures returning negative at time of discharge. Patient was afebrile > 24 h prior to discharge.

After further questioning the patient reported that he likes to play outside in the dirt. This could possibly be the source of the histoplasma inoculation as soil may contain bird or bat guano, which may contain the fungus [2]. He denied living near demolition or construction sites. However due to the lack of H bands (which usually clears in 6 months), calcifications present on biopsy, and the size (3.1 × 2.7 × 3.7 cm) it is possible that this infection occurred years prior to presentation [2].

The child was discharged after 12 days in the hospital. For further confirmation of the diagnosis the infectious disease physician did a repeat serum cryptococcal antigen test at one week post discharge and it was undetectable. The patient was compliant to the 12 week course of itraconazole. The infectious disease physician monitored and adjusted the levels of itraconazole at two weeks to maintain a steady state goal of 1–3 mcg/ml [2]. The patient remained asymptomatic at each follow up, finished his course of itraconazole, and reported no return of symptoms.

Discussion

Surgical excision of a histoplasmosis mediastinal mass is recommended to relieve symptoms of compression, otherwise the infectious disease society recommends itraconazole for 6–12 weeks [1,2]. Eosinophilia may be a lab finding suggesting a fungal infection is present. Children with a mediastinal mass should be evaluated for fungal etiologies prior to invasive surgery. This practice may prevent unnecessary surgeries and possible complications. Further studies are needed to identify and update the prevalence of histoplasmosis in non-endemic areas.

Conflicts of interest

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Defense. The authors pose no conflict of interest.

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