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*Case Report*

# A Case Report of a Mediastinal Granuloma Related to Histoplasmosis with *Streptococcus dysgalactiae* Subspecies *equisimilis* Superinfection Resulting in Abscess and Subsequent Pericarditis in a Pediatric Patient

Jessica L. Emoto, M.D.[1], Robert R. Wittler, M.D.[2]
The University of Kansas School of Medicine-Wichita, Wichita, Kansas
[1]Department of Internal Medicine-Pediatrics
[2]Department of Pediatrics

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## INTRODUCTION

*Streptococcus dysgalactiae* belongs to the pyogenic group of streptococci and presents with a disease spectrum similar to that of *Streptococcus pyogenes*.[1] *S. dysgalactiae* subspecies *equisimilis* (SDSE) is a beta-hemolytic, Lancefield group C and G streptococci that often colonizes skin lesions as well as the upper respiratory, gastrointestinal, and female genital tracts of humans.[2] While initially thought to be non-pathologic, *S. dysgalactiae* is now a known cause of invasive disease, especially among immunocompromised patients.[2]

A mediastinal granuloma is a rare cause of mediastinal mass, but histoplasmosis is the most common etiology in the United States, especially in endemic areas like the Ohio and Mississippi river valleys.[3] It remains a rare diagnosis in the pediatric literature.[4] We describe a case of a mediastinal mass and abscess due to *S. dysgalactiae* as a superinfection of a mediastinal granuloma related to histoplasmosis.

## CASE REPORT

A previously healthy 16-year-old female was admitted to our children's hospital from a rural Emergency Department (ED) in Kansas for concern of a possible malignant or infectious mediastinal mass. She initially presented one month prior to admission for cough where she was diagnosed with respiratory syncytial virus (RSV). She continued to have worsening cough, fatigue, and developed fevers. She then had shoulder and chest pain with shortness of breath, leading her to present to the ED where a chest computed tomography angiography (CTA) ruled out a pulmonary embolism; a calcified mediastinal mass was discovered instead. The patient had been living in a group home with 13 other adolescents for the six months leading to admission.

On admission, she was alert and in no distress. Vital signs were as follows: temperature, 36.8 °C; blood pressure, 96/58; heart rate, 125; respiratory rate, 20; and oxygen saturation 96% on ambient air. Physical examination showed clear breath sounds with a mild intermittent cough and was only significant for tenderness to palpation over the right scapula. Laboratory findings showed a normal white blood cell count (WBC) of $8.2 \times 10^3$/mcL and low platelets at $125 \times 10^3$/mcL. A chemistry panel was grossly unremarkable. A C-reactive protein (CRP) level was 189 mg/L. Her troponin level was within normal limits. A nasopharyngeal multiplex polymerase chain reaction assay was positive for RSV. A histoplasma yeast antibody titer was positive at 1:16. Histoplasma mycelial antibody and serum and urine antigen were negative. Human immunodeficiency virus (HIV) and Quantiferon-TB tests were negative, and rapid plasma reagin (RPR) testing was nonreactive. The chest CTA from the ED showed a middle mediastinal mass with dystrophic calcifications in the superior margin and a central fluid attenuation that measured approximately 3.3x3.7x4.3 cm that began in the subcarinal region and extended into the hilum and inferior posterior to the right atrium.

The mediastinal mass was thought to be oncologic, but given the high CRP level, the oncologist consulted thought it was more likely to be infectious. A computed tomography (CT) of the chest was repeated to assess potential lymph nodes to biopsy and showed the stable mediastinal mass that was cystic and necrotic in appearance with calcifications suspicious for histoplasmosis or mycobacterial infection (Figures 1 and 2) along with a new right pericardial region fluid collection containing a small amount of gas measuring 4.7x2.3 cm (Figures 3 and 4). There also were enlarged calcified mediastinal lymph nodes and a small pericardial effusion. An echocardiogram showed a potential space next to the right atrium and a trivial pericardial effusion.

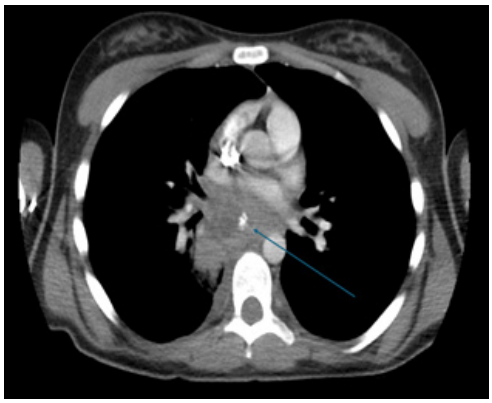

Figure 1. CT chest axial view of the complex cystic/necrotic and calcified mediastinal mass.

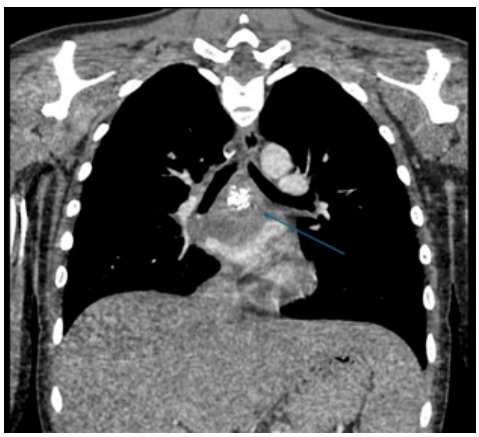

Figure 2. CT chest coronal view of the complex cystic/necrotic and calcified mediastinal mass.

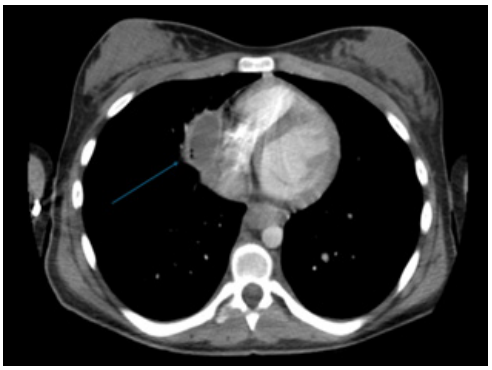

Figure 3. CT chest axial view of the abscess in the right pericardial region.

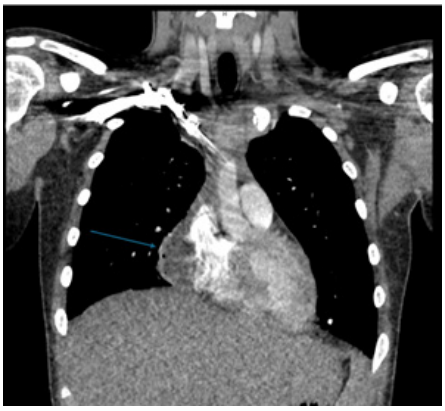

Figure 4. CT chest coronal view of the abscess in the right pericardial region.

Azithromycin was started but antibiotic coverage was expanded with the guidance of infectious disease specialist on day three of hospitalization to vancomycin and ampicillin/sulbactam as the CRP rose to >190 mg/L and her cough worsened. Pulmonology performed endobronchial ultrasound bronchoscopy with transbronchial needle aspiration; the mediastinal mass was biopsied in the medial segment of the right lower lung along with a necrotic lymph node. Cultures from both the lymph node needle aspirate and bronchoalveolar lavage (BAL) of the right lower lobe grew *Streptococcus dysgalactiae* resistant to vancomycin but susceptible to ceftriaxone and clindamycin and intermediate to penicillin. Fungal and mycobacterial cultures from the needle aspirate and BAL fluid showed no growth. Blood culture from admission also showed no growth. Cytology from the needle aspirate showed fibrinoid debris, neutrophils of acute inflammation, alveolar macrophages, and some markedly reactive bronchial epithelial cells; flow cytometry was negative for malignancy. Vancomycin was discontinued. The ampicillin/sulbactam was continued as the patient was clinically improving, and due to concern of polymicrobial infection with mixed aerobic and anaerobic infection since the CT noted some gas in the pericardial fluid collection. Antifungal treatment was not started at that time since her symptoms had improved on antibacterial treatment with the presumption that her symptoms were due to infection from *Streptococcus dysgalactiae*. Additionally, the calcification and histoplasma yeast antibody titer of 1:16 would be consistent with a non-acute or active infection. A pediatric general surgery consultant evaluated the need to drain the abscess, but no intervention was recommended given the location of the abscess and the patient's improved clinical status on antibiotics. She was discharged on day eight of hospitalization on amoxicillin/clavulanic acid to complete a four-week course of antibiotics. A CRP at two weeks post-discharge was <2.9 mg/L.

The patient then presented to a local ED four weeks post-discharge for syncope, vomiting, abdominal pain, chest pain and shortness of breath. A chest CT showed no mediastinal mass, but there was a large circumferential pericardial effusion measuring 1.7x1.2x1.4 cm, calcified subcarinal lymph nodes, and a new lung nodule. She was then transferred to another children's hospital where echocardiogram showed a large pericardial effusion and right atrial and ventricular collapse. The patient underwent pericardiocentesis and started a course of non-steroidal anti-inflammatories (NSAIDs) and colchicine for pericarditis. Ampicillin-sulbactam was started as well as oral itraconazole and she was subsequently changed to clindamycin. Pericardial fluid cultures showed no growth on bacterial and fungal cultures. The patient improved and was able to be discharged on day five of her second hospitalization on two weeks of clindamycin and six weeks of itraconazole for pulmonary histoplasmosis.

On post-discharge day three, the patient developed a fever and neck and shoulder pain. She was re-admitted at the referral children's hospital where laboratory studies showed: WBC 18.39 (x10^3/mcL), CRP 24.5 mg/dL, and ESR 68 mm/h. A chest ultrasound (US) showed a small right pleural effusion and a moderate left pleural effusion. A small pericardial effusion with no right atrial or ventricular collapse was found on echocardiogram. The patient was started on high dose steroids and rheumatology was consulted. Anti-nuclear antibodies were elevated with negative reflex; the studies were inconsistent with any systemic rheumatologic process. Clindamycin and itraconazole were continued. Repeat chest US on day four of hospitalization showed resolution of the right and improvement of the left pleural effusion. Laboratory studies on day five of hospitalization showed: WBC 11.56x10$^3$/mcL and CRP 2.1 mg/dL. The patient had clinical improvement and was discharged home on a steroid taper, clindamycin to complete a two-week course for the previously noted SDSE infection, and itraconazole to complete a six-week course for histoplasmosis.

## DISCUSSION

SDSE is a pyogenic streptococcus strain that is a human pathogen, whereas *Streptococcus dysgalactiae* subsp. *dysgalactiae* is alpha-hemolytic or non-hemolytic and is typically an animal pathogen.[5] SDSE is commensal in the oropharyngeal flora and has been commonly associated with pharyngitis in children. Severe infections tend to affect those with risk factors like a history of injection drug use, elderly patients with comorbidities, or immunocompromised patients.[2] Our case is unique in that it describes a previously healthy pediatric patient who presented with a mediastinal mass and pericardial abscess that both grew SDSE. This patient's mediastinal mass was likely a mediastinal granuloma (MG) given the appearance on CT imaging. MG is typically found subcarinal or paratracheal and occurs as a group of necrotic lymph nodes coalesce into a mass. Patients are often asymptomatic with MG found incidentally years after histoplasma infection or with no known history exposure. Our patient likely had histoplasmosis prior to presentation;

prior to presentation; calcifications are unlikely to be seen if the MG formed within a few months of infection. While the patient did not have positive serum or urine histoplasma antigens, she did have a positive histoplasma yeast antibody titer of 1:16 which is consistent with past infection. A single histoplasma titer of ≥1:32 is presumptive evidence of active or recent infection.[6] In a case series of pediatric mediastinal granuloma related to histoplasmosis[4], histoplasma antibody was positive in 100% and histoplasma antigen was negative in 90% of patients. Fine needle aspirations (FNA) were positive in 31% whereas BAL was negative for histoplasma where performed. Like with our case, histoplasma cultures tend to be negative in MG and small samples taken by excisional biopsy or FNA are not fruitful; large samples are required as the organisms are usually scattered and scarce.

Per the 2007 Infectious Diseases Society of America guidelines on histoplasmosis[7], treatment of MG with an anti-fungal is not necessary unless the patient is symptomatic. Our patient's symptoms during her first hospitalization were thought to be from the SDSE infection given her improvement on antibacterial therapy without antifungal therapy. Pericarditis occurs as a complication of inflammation in adjacent mediastinal lymph nodes rather than infection of the pericardium. Pericardial infection is a rare complication of disseminated infection. Pericarditis with histoplasmosis generally responds to NSAIDs. Large pericardial effusions may require drainage which was performed for this patient and cultures showed no growth adding evidence that this was an inflammatory process, not infectious. Corticosteroids are recommended if there is hemodynamic compromise or unremitting symptoms with NSAIDs. Itraconazole is recommended if corticosteroids are given.[7]

A retrospective cohort study[8] of children with mediastinal lymph nodes with suspected or confirmed histoplasmosis showed that lymph node biopsies were rarely of diagnostic value. They also described three cases of large mediastinal burden with mass where two of the three cases underwent extensive surgical debulking and found that there was not always benefit and added the risk of surgical complications. This study also showed that antifungals and steroids were of unclear benefit and may not change disease course.

Bacterial superinfection is a known complication of MG, and it tends to occur following diagnostic biopsy or from esophageal fistulization with infection of enteric flora.[3] Our patient likely developed superinfection with SDSE secondary to esophageal fistulization, but there was no preceding biopsy. Fistulization was not confirmed by endoscopy or seen on CTA chest. It is also possible that the SDSE was a contaminant, but both the BAL and needle aspirate had moderate growth of SDSE and there was clinical improvement along with subsequent improvement of the CT with antibacterial treatment.

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