CASE REPORT

Pulmonary Necrotizing Granuloma Due to Subclinical *Histoplasma* Infection

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Abstract

Aim and objective: To describe the management and outcome of an isolated pulmonary granuloma due to subclinical *Histoplasma* infection in a pediatric patient.

Background: Fungal infections can lead to variable presentations and include isolated organ involvement or disseminated disease. Histoplasmosis is an infection caused by the fungus *Histoplasma* and is particularly endemic to the Ohio and Mississippi river valleys.

Case description: A 16-year-old male presented with shortness of breath and pleuritic chest pain for a 1-year duration. He lived in a home that was occupied by bats. Chest X-rays and computed tomography revealed a right paratracheal calcification. The patient underwent esophagoscopy and right thoracoscopic hilar mass resection. On pathology, the sections showed necrotizing granulomata with giant cells, but no organisms were identified despite full pathological workup. *Histoplasma* yeast titers were subclinical at 1:8. No further medical management was pursued, and the patient demonstrated resolving symptoms on follow-up.

Conclusion: Management of isolated granulomatous disease in pediatric patients is poorly characterized. The most common cause of necrotizing granulomatous inflammation are infections including mycobacteria and fungal infections, but organisms may not be seen on pathological workup. The exact cause of the granuloma may be idiopathic. Treatment is reserved for patients with a severe disease process and degree of symptoms. Practitioners in areas endemic to *Histoplasma* should suspect it as a cause of isolated lung nodules in the right clinical setting.

Clinical significance: Workup of pulmonary granulomas requires a detailed history and physical exam, and isolated pulmonary granulomas in the pediatric population are rare. Practitioners are encouraged to consider infectious etiologies and consider surgical consultation for diagnosis and treatment.

Keywords: Granuloma, Infectious disease, Pediatric surgery, Pulmonary, Thoracic surgery.

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Background

Histoplasma capsulatum is a fungus that is primarily located in the Ohio and Mississippi Valley regions of the United States. Inoculation is caused by inhaling its spores. While many people will not experience symptoms, those who do not clear the infection have variable clinical presentations along a spectrum of isolated organ involvement to disseminated disease.[1]

Granulomatous lesions are commonly found in the lungs, and the majority of cases are due to fungus, bacteria, or foreign objects.[2] Necrotizing granulomata (NG) in particular are often caused by mycobacteria and fungal infections.[3] The presentation and management of isolated granulomatous lesions in pediatric patients are poorly characterized in the literature. Patients who present with isolated pulmonary nodules and who live in endemic areas where fungal species are known to exist should raise suspicion of fungal infection. Clinical, radiological, and pathological data can support the diagnosis. However, pathological workup in specimens taken from patients may not demonstrate an identifiable organism as the cause of the granuloma.[4] Surgical and medical treatment should be reserved for those patients presenting with symptoms or more severe disease processes. We present a case of a 16-year-old boy who presented with a symptomatic isolated pulmonary necrotizing granulomata and whose symptoms resolved after surgical excision.

Case Description

The patient is a 16-year-old male evaluated for shortness of breath. His symptoms started during a basketball game the year prior when he turned his body suddenly. He reported pleuritic chest pain in the mid-chest on deep inspiration and shortness of breath since that event. He denied any productive cough or hemoptysis. He denied any fever, chills, nausea, vomiting, or recent weight loss. A chest X-ray was performed, which demonstrated a right paratracheal calcification that measured 3.2 cm and was most consistent with a calcified lymph node (Figs 1A and B). This was also present on imaging he had received 3 years prior. He was referred to the pediatric surgery clinic for possible excision of the calcification. Computed tomography (CT) of his chest demonstrated a 2.4 × 1.4 cm right paratracheal calcification (Figs 1C and D). Of note, the patient and his family lived in a house that was occupied by bats.

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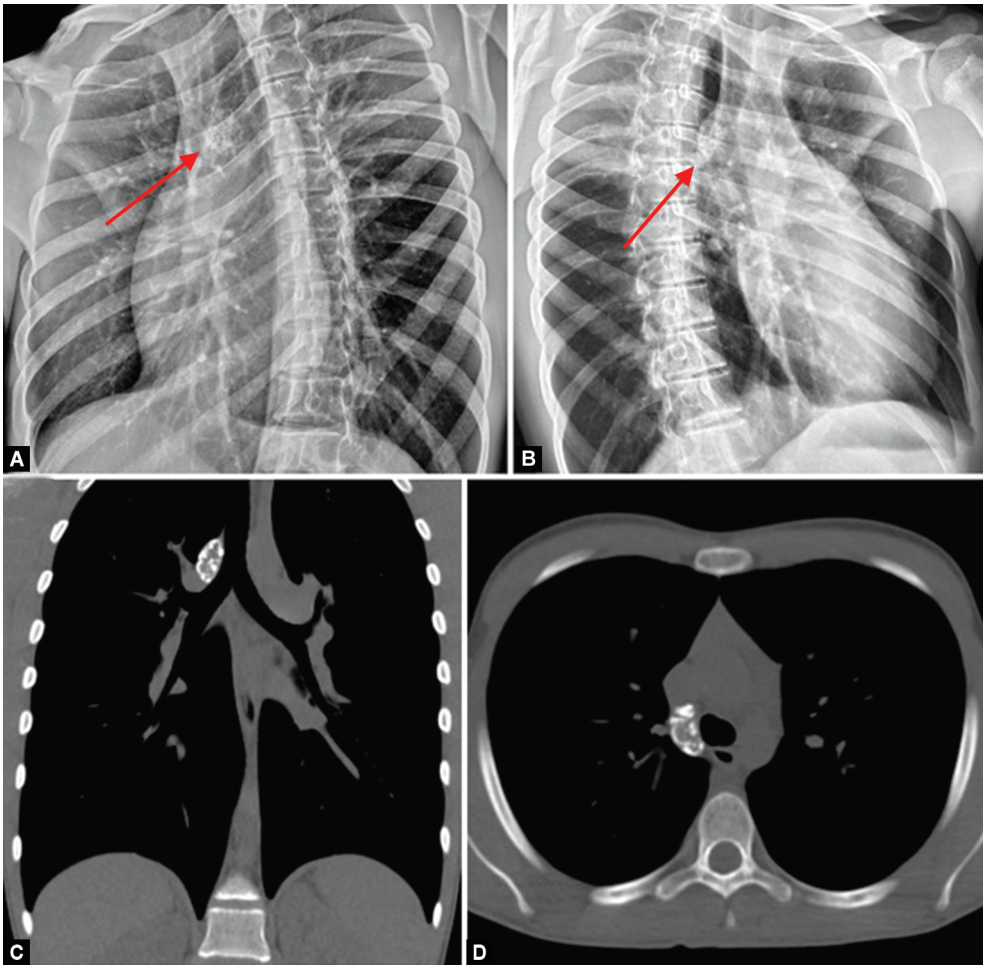

Figs 1A to D: Chest imaging: (A and B) Oblique chest X-ray demonstrating oval, focal calcification in the R paratracheal region; (C) Coronal and (D) axial CT chest without contrast demonstrating right paratracheal calcification measuring 2.4 x 1.4 cm. No mediastinal, hilar, or axillary adenopathy

He had a past medical history significant for GERD. His surgical history was significant for hypospadias correction. Family history was notable for his father who had muscular dystrophy. Laboratory workup, including complete blood count, basic metabolic panel, and hepatic panel, was within normal limits. Workup for histoplasmosis and blastomycosis was negative, but *Histoplasma* yeast antibody titers were subclinical at 1:8. The patient underwent esophagoscopy and right thoracoscopic hilar mass resection. On pathology, the sections showed NG with giant cells. Stains for microorganisms including acid-fast bacillus (AFB), periodic acid Schiff (PAS) fungus, Grocott methenamine silver (GMS), and Gram were performed, but no definitive microorganisms were identified. The controls were stained appropriately.

Operative Management

The endoscope was introduced into his mouth through his esophagus and into his stomach without issue. The patient was positioned in the left lateral decubitus position, and a 1-cm incision was made medial to the tip of the scapula in the 4th intercostal space. A 5-mm trocar was placed. Minimal insufflation was performed since the right lung was collapsed with the double-lumen tube. The mass was not immediately visualized, so an additional 5 mm trocar was placed in the midaxillary line of the 7th intercostal space. Using this port location, a grasper was used to retract the lung anteriorly until the mass was seen. The mass was originally suspected to be closely positioned to the esophagus, but it appeared now to be more associated with the trachea. An additional 5-mm trocar was placed in the posterior axillary line of the 6th intercostal space. From these positions, the retraction was placed on the lung and the mass, and the pleura overlying the mass was opened with a 5-mm Maryland ligasure. Using the ligasure, the azygous vein was ligated and divided, as it was directly overlying the mass. The vagus nerve was noted to be densely adherent to the posterior wall of the mass. The ligasure blade was used to sharply dissect and separate the nerve from the mass with no energy use. Once the vagus nerve was safely dissected off, the remainder of the mass was carefully dissected off the trachea and bronchus and was completely mobilized.

A leak test was performed as the lung was inflated. The lung was seen to fully inflate. The ports were removed, the muscles were reapproximated with 2-0 vicryl, and the skin was closed with 4-0 monocryl and exofin. The patient tolerated the procedure well and was discharged the next day without issue. On follow-up, the patient reported improvement in his symptoms and was recommended to follow-up as needed.

Discussion

This case report describes a boy with a lung mass consistent with an NG. This case is unusual because isolated pulmonary granulomas

have been scarcely reported in the pediatric literature, there were no identifiable etiologies for the NG based on histological analysis, and he had resolution of his symptoms after operative intervention.

A granuloma is a non-specific histopathological finding, so a multidisciplinary approach is required for a precise diagnosis and includes clinical, radiological, and pathological evidence. A multitude of modalities exists to evaluate granulomas. Their scope of practice is limited and can be utilized in the appropriate clinical setting but include bronchoalveolar lavage, endobronchial ultrasound-guided transbronchial needle aspiration, transbronchial cryobiopsy, high-resolution CT, and positron emission tomography (PET).[3] Genetics analysis may be considered in sarcoidosis.[3] Nonetheless, they can improve the accuracy of diagnosis.

The most common causes of NG inflammation are infections including mycobacteria and fungal etiologies.[3] Their clinical manifestation and spectrum of pathology are variable. While the majority are often infectious in etiology, a proportion remain unexplained despite appropriate histological and infectious workup.[5] No definitive microorganisms were identified by special stains in the specimen from our patient. However, this does not completely rule out infections, and serologies indicated a possible subclinical *Histoplasma* infection in this patient. If infections are excluded, other possible etiological considerations include inflammatory reactions, exposures or toxins, vasculopathies, autoimmune disease, malignancies, or are considered idiopathic.[3] Clinical correlation is required.

The process of identifying an organism histologically is often challenging, and if no organisms are identified despite adjunctive staining, a descriptive diagnosis is given.[4] The pathological workup demonstrated giant cells in this individual. Histologically, the presence of giant cells is not pathognomonic for one particular granulomatous lung disease but may be a clue to a diagnosis of *Cryptococcus, Blastomyces, Pneumocystis,* hypersensitivity pneumonitis, Wegener granulomatosis, Churg–Strauss syndrome, or aspiration pneumonia.[4]

Because our patient was symptomatic, we elected to excise the lesion. However, in patients who have undergone an appropriate workup and demonstrate no specific etiology for granulomatous reactions without symptoms, treatment may not be necessary and further workup may be plethoric. Current infectious disease guidelines recommend antifungal treatment for histoplasmosis in patients with acute diffuse pulmonary infection, moderately severe symptoms, severe symptoms, chronic cavitary pulmonary infection, progressive disseminated infection, and CNS infections; however, treatment is not recommended for a single pulmonary nodule.[1]

There is currently a paucity of literature describing granulomatous diseases in pediatric populations. Panigada et al. described a case of a 12-year-old boy with a lung consolidation that was consistent with necrotizing sarcoid granulomatosis. Treatment with high-dose prednisone resolved his symptoms, but his symptoms relapsed and additional pulmonary lesions were identified as the steroid was tapered, which was unusual.[6] Al-Binali et al. described a case of an 11-year-old boy with Crohn's disease who developed isolated pulmonary symptoms and showed irregularly scattered non-caseating granulomas on thoracoscopic lung biopsy before developing gastrointestinal symptoms.[7] Young et al. described a rare case of a 15-year-old boy with pulmonary hyalinizing granuloma and retroperitoneal fibrosis not caused by any organisms and was likely caused by an idiopathic autoimmune disease. He was treated with intravenous and oral steroids and responded appropriately. Institutions located in endemic areas to *Histoplasma* are privy to experiencing the full spectrum of complications and treatment options.[8]

Conclusion

Pulmonary granulomas are poorly described in the pediatric literature. The severity of disease and symptoms should drive medical and surgical therapy. Practitioners who live in areas where fungal organisms are endemic should be particularly suspicious of a fungal etiology when presented with pulmonary nodules, and clinical, radiology, and pathology data can assist in making an accurate diagnosis.

Clinical Significance

Workup of pulmonary granulomas requires a detailed history and physical exam, and isolated pulmonary granulomas in the pediatric population are poorly characterized. In the right clinical setting, surgical consultation may be required if the granulomas abut critical structures and produce symptoms that affect the quality of life. Practitioners are encouraged to consider infectious etiologies as the most common pathology but should be aware of other existing disease processes.

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