Case Report

A Mediastinal Mass Resembling Lymphoma: An Unusual Manifestation of Probable Case of Invasive Zygomycosis in an Immunocompetent Child

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A 2-year-old girl presented with prolonged fever and progressive dyspnea for 3 weeks. A chest radiograph revealed a left lung infiltrate and associated pleural effusion. Echocardiography revealed a large posterior mediastinal mass extending to the left atrial wall and massive pericardial effusion. The presumptive diagnosis was lymphoma. At operation, a large brownish-yellow mass was noted at the posterior mediastium, with matted hilar, and subcarinal lymph nodes. Pericardial and pleural effusions with left lung consolidation were also noted. Histopathological examination of biopsy specimens revealed a granulomatous inflammatory reaction with a diffuse eosinophilic infiltrate and broad septated fungal hyphae with right angle branching compatible with zygomycosis.

Surgical removal of the mass could not be performed due to the adjacent great vessels and carina. She subsequently died from airway obstruction and respiratory failure ten days later.

Keywords: Mediastinal mass, Pericardial effusion, Zygomycosis

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The common causes of mediastinal mass in children are neoplasms, including Hodgkin’s disease, neuroblastoma and non-Hodgkin’s lymphoma(1). About one-third of cases are benign and include entities such as teratomas, neurofibromas and lipomas(1). Histologic findings are essential for distinguishing between the two(1). Zygomycosis is a rare fungal infection usually presenting as a subcutaneous infection(2). Visceral involvement is unusual, with mostly gastrointestinal tract involvement having been reported(3,4). Most of them were misdiagnosed preoperatively as malignancy(3,4). Rarely has this presented as a mediastinal mass(5,6). Here, the authors report a probable case of zygomycosis in an immunocompetent child who presented with mediastinal mass resembling lymphoma.

Case Report

A previously healthy 2-year-old girl was referred to our hospital with a pericardial effusion. She initially presented in July 2004 to a local hospital with a one-week history of fever, dyspnea and non-productive cough. She was presumptively diagnosed with bacterial pneumonia and started empirically on an intravenous third generation cephalosporin. One week later, she still had a high-grade fever and progressive dyspnea. A chest radiograph revealed a left lung infiltrate and associated pleural effusion. A thoracocentesis was performed and imipenem was started. Despite these measures, she clinically deteriorated, with development...
of a pericardial effusion noted 7 days later. On physical examination, the temperature was 39.0 °C, the heart rate was 180 beats per minute, the respiratory rate was 52 breaths per minute, and the blood pressure was 96/52 mmHg. There was a pulsus paradoxus of 17 mmHg. Chest examination revealed decreased breath sounds over the left lung fields. Cardiovascular exam revealed a pericardial friction rub. Complete blood count showed a hemoglobin of 12.7 g/dl, a platelet count of 861 x 10^9 /l, and a white blood cell count of 24.8 x 10^9 /l. The differential was 62% neutrophils, 19% lymphocytes, 13% monocytes, and 6% eosinophils. Blood chemistries, renal function and liver function tests were normal.

Echocardiography revealed a large heterogeneous mass extending from the middle and posterior mediastinum to the left atrial wall and posterior part of the aortic root and ascending aorta (Fig. 1). The pericardial effusion was massive. Right atrial and ventricular collapse was present during expiration, suggesting cardiac tamponade. The computerized tomography scans showed an inhomogeneously enhancing mass measuring 6.3 x 3.7 x 5.6 cm at the posterior and middle mediastinum in the subcarinal region. It occluded the left main bronchus, caused narrowing of the pulmonary arteries, invaded the left lung, and extended into the pericardial sac. Pericardial and left pleural effusion were also noted (Fig. 2). Multiple enlarged lymph nodes in the prevascular area were seen.

The following day, with a presumptive diagnosis of a neoplasm, she underwent surgery. A large brownish-yellow mass was noted at the posterior mediastinum, occupying nearly one-third of the left pleural space. Fibrinous pericarditis was present, with 250 ml of fluid in the pericardial sac. The basal segment of the left upper lung was consolidated, and 200 ml of clear yellowish pleural fluid noted in the left pleural space. An incisional biopsy of the mass and pleuropericardial drainage were performed. Pleural fluid examination revealed 6750 red blood cells, 590 white blood cells (8% polymononuclear cells), protein of 2.2 gm %, glucose of 102 mg/dL, and LDH of 475 U/L. Pericardial fluid examination revealed 7250 red blood cells, 64 white blood cells (36% polymononuclear cells), protein of 3.1 gm %, glucose of 109 mg/dL, and LDH of 666 U/L. The
gram and kinyoun stains of fluids were unrevealing. A Wright stain showed no evidence of malignancy. Histopathology of the biopsy specimens revealed a granulomatous inflammatory reaction with a diffuse, predominantly eosinophilic infiltrate and focal suppuration. There were broad, thin-walled, irregular septated fungal hyphae with right angle branching compatible with zygomycosis identified in hematoxylin and eosin (H&E) stained slides (Fig. 3). Fungal culture of biopsy specimen was not done because of the clinical preoperative diagnosis of neoplasm.

Serologic tests for Basidiobolus ranarum and other Entomophthorales agents could not be performed at our center. The patient was investigated for an underlying immunodeficiency. Workup included an immunoglobulin level, which was normal except for increased IgE of 887 IU/mL (normal 0.3-29.5 IU/mL), HIV serology, which was negative, and nitroblue tetrazolium testing, which was normal. Surgical removal of the mass could not be performed due to the adjacent great vessels and carina. Oral itraconazole (10 mg/kg/day) was started. Ten days later, she developed signs of airway obstruction and subsequently died from respiratory failure. An autopsy was not performed.

Discussion

Zygomycosis is a fungal infection usually presenting as a subcutaneous infection(2). Few cases have presented as a mediastinal mass with lung involvement(5,6). Here, the authors report a probable case of zygomycosis in an immunocompetent child who presented with mediastinal mass resembling lymphoma.

Fig. 3 Histologic section presents thin walled fungal hyphae with perpendicular branching and surrounded Splendore-Hoeppli material. H&E, Objective 40X

The diagnosis of zygomycosis was made on the basis of the biopsy findings, which showed hyphal structures with associated Splendore-Hoeppli phenomena and marked eosinophilic infiltration. The organisms in the differential include organisms in the order Entomophthorales or Mucorales. Entomophthoro-mycosis tends to produce disease in normal hosts, causing more indolent clinical syndromes. This is in marked contrast to the classic mucormycosis seen in immunocompromised hosts. The eosinophilic inflammation in tissues helps distinguish Entomophthorales from Mucorales infection, which is characterized by a predominantly neutrophilic infiltrate, with vascular invasion and thrombosis(7). Basidiobolus ranarum is an organism in order Entomophthorales that is associated with visceral organ invasion in humans. However, in this case, culture was not performed. The laboratory findings in the present case are similar to other reported cases of visceral Entomophthoromycosis, which include leukocytosis with significant eosinophilia and elevated immunoglobulin E(5,6). Another differential diagnosis in the present case is infection caused by Pythium insidiosum. However, the common clinical manifestations of pythiosis are keratitis, subcutaneous tissue infection, and disseminated arterial pythiosis(8). The histological findings can be differentiated from the members of the order Entomophthorales on the basis of its smaller uniform sized hyphae, which is very difficult to detect in hematoxylin and eosin (H&E) stained slides(8).

The mode of acquisition of the disease remains poorly understood. The port of entry is believed to be cutaneous inoculation in subcutaneous infection or through inhalation of spores in sinus disease(9). In the present patient, no predisposing cause for acquiring this infection was evident. Similarly, factors responsible for progressive infection are unknown. There is no standard treatment for Entomophthoromycosis. Potassium iodide has been used for subcutaneous infections(2), whereas surgical resection of any obstructing masses, in conjunction with medical treatment using itraconazole or trimethoprim/sulfamethoxazole, has been reported with success in visceral disease(5,4).

Conclusion

The authors report a probable case of zygomycosis in an immunocompetent child who presented with a mediastinal mass. Although neoplasm remains the most likely etiology in children, zygomycosis should be considered in the differential diagnosis as an unusual cause of this entity. Increased awareness of
this clinical entity might lead to an earlier diagnosis and better prognosis.

References


