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 mediastinum, 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.

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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

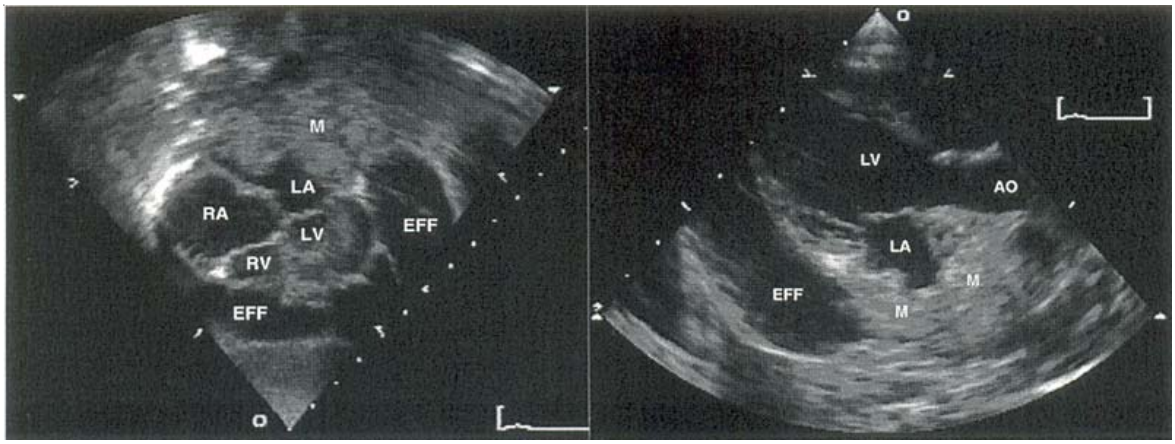

Fig. 1 Echocardiogram demonstrates a large mass infiltrated left atrium. A large amount of pericardial effusion was evident with few fibrin strands. A: subcostal view B: parasternal long axis view. AO= aorta, EFF = pericardial effusion, LA = left atrium, LV = left ventricle, M = mass, RA = right atrium, RV = right ventricle

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

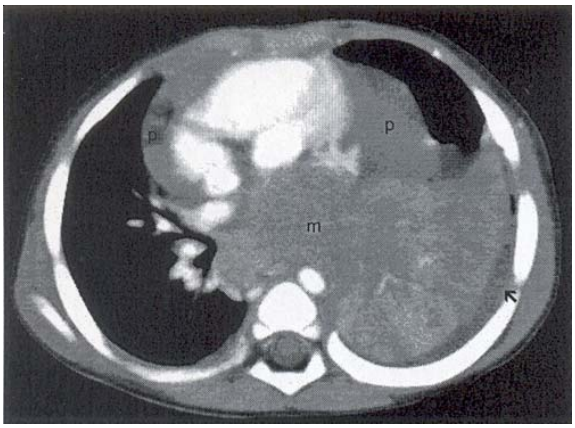

Fig. 2 Axial enhanced computerized tomography scan of chest at subcarina level shows an inhomogeneous enhanced mass (m) at posterior and middle mediastinum. It has invaded the left lung and posterior portion of the pericardial sac. Note pericardial effusion (p), left pleural effusion (arrow), and pneumothorax in the anterior portion of the left chest

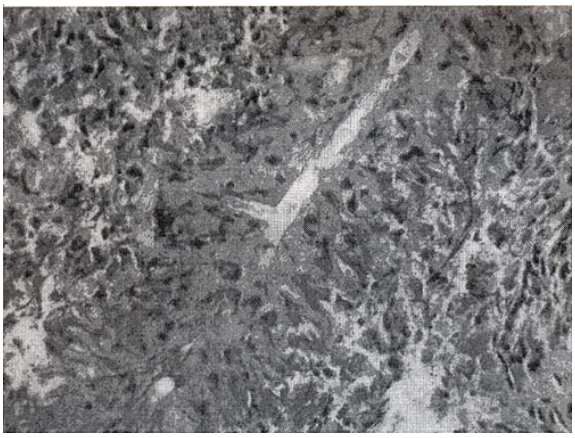

Fig. 3 Histologic section presents thin walled fungal hyphae with perpendicular branching and surrounded Splendore-Hoeppli material. H&E, Objective 40X

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 *Entomopthorales* 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.

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[3,4,6]. 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[3,4].

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.

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ก้อนในช่องทรวงอกคล้ายโรคมะเร็งต่อมน้ำเหลือง: อาการแสดงที่พบได้ไม่บ่อยของโรค zygomycosis ในเด็กภูมิคุ้มกันปกติ

ธันยวีร์ ภูธนกิจ, ยุพดา พงษ์พรต, ธีรศักดิ์ บริสุทธิบัณฑิต, พรรณี วิศรุตรัตน, ศุภชัย เชื้อรัตนพงษ์, นิลยา สุคำวัง, กำธร ธรรมประเสริฐ

ผู้ป่วยเด็กหญิงอายุ 2 ปี มาพบแพทย์ด้วยปัญหาเรื่องไข้ หายใจหอบเหนื่อย 3 สัปดาห์ก่อนมาโรงพยาบาล ภาพรังสีทรวงอก พบเงาทึบที่ปอดด้านซ้ายร่วมกับมีน้ำในช่องเยื่อหุ้มปอด ตรวจคลื่นเสียงสะท้อนหัวใจพบก้อนขนาดใหญ่ในช่องทรวงอกลามไปที่ผนังหัวใจห้องซ้ายบน และน้ำในช่องเยื่อหุ้มหัวใจปริมาณมาก ได้รับการวินิจฉัยเบื้องต้นเป็นมะเร็งต่อมน้ำเหลือง ในการผ่าตัดตรวจพบก้อนขนาดใหญ่สีน้ำตาลเหลืองที่ช่องทรวงอกด้านหลังติดยึดกับต่อมน้ำเหลืองบริเวณขั้วปอด น้ำในช่องเยื่อหุ้มปอด น้ำในช่องเยื่อหุ้มหัวใจ และการอักเสบของปอดด้านซ้าย ผลการตรวจทางพยาธิวิทยาของชิ้นเนื้อพบการอักเสบชนิด granulomatous โดยมีการกระจาย ของเซลล์เม็ดเลือดขาวชนิด eosinophil อยู่ทั่วไป ร่วมกับสายราที่มีผนังกั้นและแตกแขนงในมุมตั้งฉาก ซึ่งเข้าได้กับการติดเชื้อราชนิด zygomycosis การผ่าตัดก้อนเนื้อออกไม่สามารถทำได้เนื่องจากก้อนอยู่ติดกับเส้นเลือดขนาดใหญ่และขั้วปอด สิบวันต่อมาผู้ป่วยเสียชีวิตเนื่องจากทางเดินหายใจถูกอุดกั้นและระบบทางเดินหายใจล้มเหลว