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Original Article

Pleuropulmonary Zygomycosis in a Diabetic Child

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Abstract. A 12 yr old girl with type 1 diabetes presented in ketoacidosis and consolidation of left lower lobe along with left pleural effusion. A diagnosis of mucormycosis was made on smear examination of an exudative pleural aspirate. Left lower lobe lobectomy was performed along with drainage of pleural collection with tube thoracostomy. Worsening respiratory distress postoperatively due to increase in empyema fluid necessitated a second surgery. Pleuropulmonary involvement as seen in this patient is an extremely rare occurrence possibly related to the propensity of mucor to invade blood vessels rather than extend outwardly into pleural cavity.

Key words: zygomycosis, lungs, pleural cavity, type 1 diabetes

Introduction

Zygomycosis is an uncommon invasive mycotic infection which disproportionately affects poorly controlled diabetics particularly during episodes of ketoacidosis (1). In children with diabetes it usually manifests as rhinocerebral form and pulmonary involvement is uncommon. We present here a child with Type 1 diabetes (T1D) who had concomitant pleural and pulmonary involvement requiring surgical intervention twice. The rarity of this condition prompted us to report this case.

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Case Report

The patient, a 12 yr-old girl was diagnosed elsewhere with Type 1 diabetes 3 yr back. She came from a hilly terrain with limited access to specialized medical facilities. Because of family dynamics (father works in national army and visits his family once in an year and mother is primary school educated housewife) and child's rebellious nature, her adherence to insulin therapy and consequently diabetic control were poor. Blood sugar monitoring was once or twice in a month and reportedly ranged between 400–600 mg/dL. Intermittent short acting insulin use coincided with blood sugar monitoring. She was on an indigenous oral medication for the past 6 months. She was admitted to our hospital with fast breathing and a low-grade fever for 4 d and drowsiness for last few hours. Physical examination revealed thin built (weight 19 kg and height 125 cm; both below 3rd centiles). Heart rate was 130 and respirations 44 per min with acidotic breathing pattern. Her blood

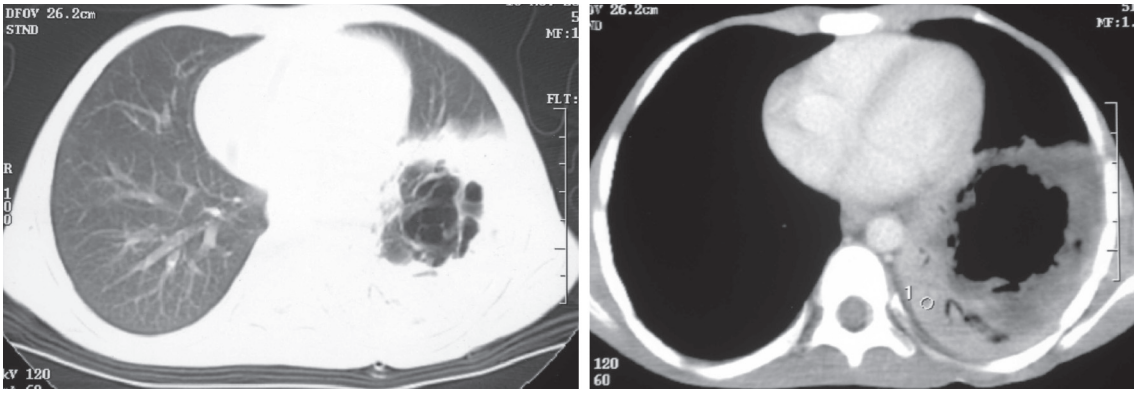

Fig. 1 CECT chest (lung & mediastinal windows) showing cavitatory pneumonia and empyema on left side.

pressure was 100/60 mm Hg. She was febrile with an axillary temperature of 38°C. Breath sounds were diminished in left infra-axillary area. She appeared drowsy and confused. Rest of her systemic examination was unremarkable.

Laboratory investigations revealed blood glucose of 340 mg/dl, pH 6.90 and large ketones in urine. Hemogram showed hemoglobin of 11.5 g/dL and WBC count of 11,200/mm^3 (neutrophils 78%, lymphocytes 17%, monocytes 2%, eosinophils 3%). Serum Na^+ and K^+ were 143 and 3.6 mmol/L respectively and urea and creatinine 40 and 0.6 mg/dL respectively. A chest radiograph showed consolidation in left lower lobe and pleural effusion. She received intravenous fluids, insulin infusion and mannitol along with broad spectrum antibiotics and her ketoacidosis improved over 12 h of hospitalization. Thereafter she was switched over to 6 hourly subcutaneous short acting insulin and subsequently to premixed (30:70) insulin twice a day with short acting insulin before lunch. Tachypnea persisted over next 3 days. Because of her diabetic status, lung infection with zygomycosis was strongly suspected and a contrast enhanced computed tomography (CECT) revealed cavitatory pneumonia of left lower lobe and left empyema (Fig. 1). A course of intravenous Amphotericin B deoxycholate was initiated. Needle aspiration from left lower lobe and pleural cavity were done separately as an initial attempt to obtain tissue diagnosis pending a transbronchial biopsy. Lung aspirate was negative but thoracocentasis fluid showed broad aseptate hyphae with right-angled branching conforming to the morphology of mucormycosis. Biochemically and cytologically, the pleural fluid was consistent with an exudate.

Surgical resection of left lower lobe and lingula was done on 12^{th} day of hospital admission and left intercostal tube was placed. The histopathological examination of the resected lung specimen revealed large areas of bland necrosis and many broad aseptate hyphae consistent with mucormycosis (Fig. 2). The surrounding lung parenchyma showed reactive multinucleated giant cells and a dense mixed inflammatory infiltrate in the interstitium.

The post-operative hospital course was complicated by persistent fever and worsening respiratory distress. Chest X-ray showed increased pleural collection and ultrasonography revealed loculations and septations necessitating guided insertion of another intercostal tube which also failed to relieve respiratory distress. A CECT done on 6^{th} post-operative day showed a large empyema with mediastinal shift and collapsed left lung (Fig. 3).

Following this, child underwent second left

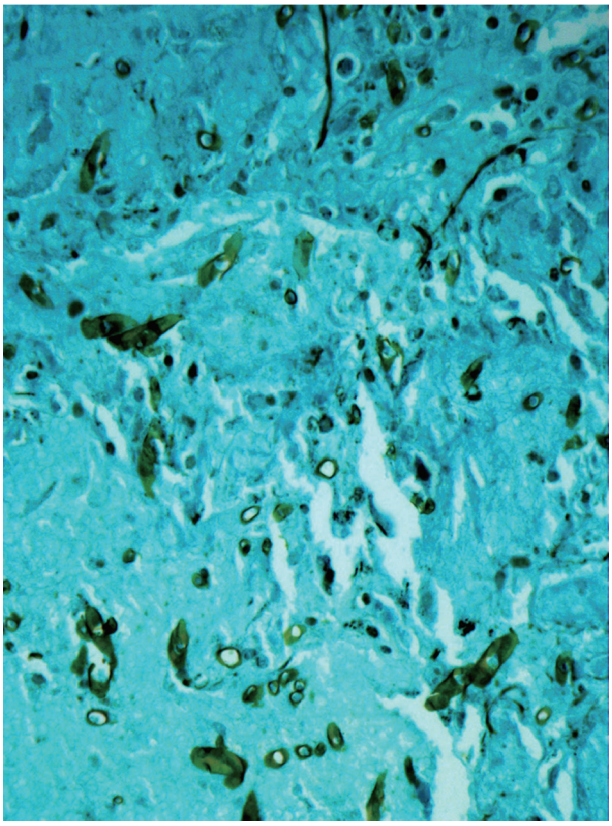

Fig. 2 Photomicrograph of the lung showing variable size and shape fungal profiles which are broad, aseptate and folded on itself on the background of necrotic lung tissue (Grocott's silver stain × 1000).

thoracotomy. A thick membrane was found around left upper lobe and fibrinopurulent fluid in the pleural cavity. After removing the membrane a thorough pleural lavage was performed. Respiratory distress and fever disappeared over the following post-operative week and intercostal drains were removed on tenth postoperative day. All bacterial and fungal blood and pleural fluid cultures obtained on 4 different occasions during 7 wk of her hospital stay were sterile. Glycated hemoglobin done during first week of admission was 11.5% indicating a poor previous control and unstimulated C-peptide level was 0.2 ng/mL. Serial chest radiographs are shown in Fig. 4 a–d.

A final diagnosis of pleuropulmonary mucormycosis was given and child was discharged after completing a 6-wk-course of amphotericin B deoxycholate. She was continued on same insulin regimen after discharge and has a fair glycemic control with glycated hemoglobin ranging between 7.5 and 8.5% over 2 years' follow-up. She has remained well except mild restrictive pattern on pulmonary function tests.

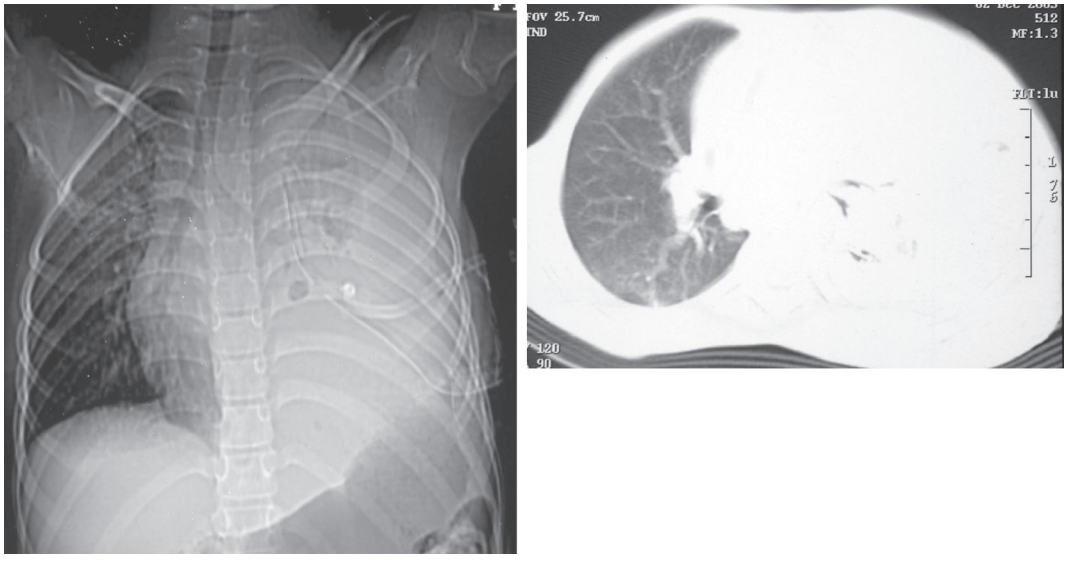

Fig. 3 CECT chest showing large empyema with mediastinal shift and collapsed left lung.

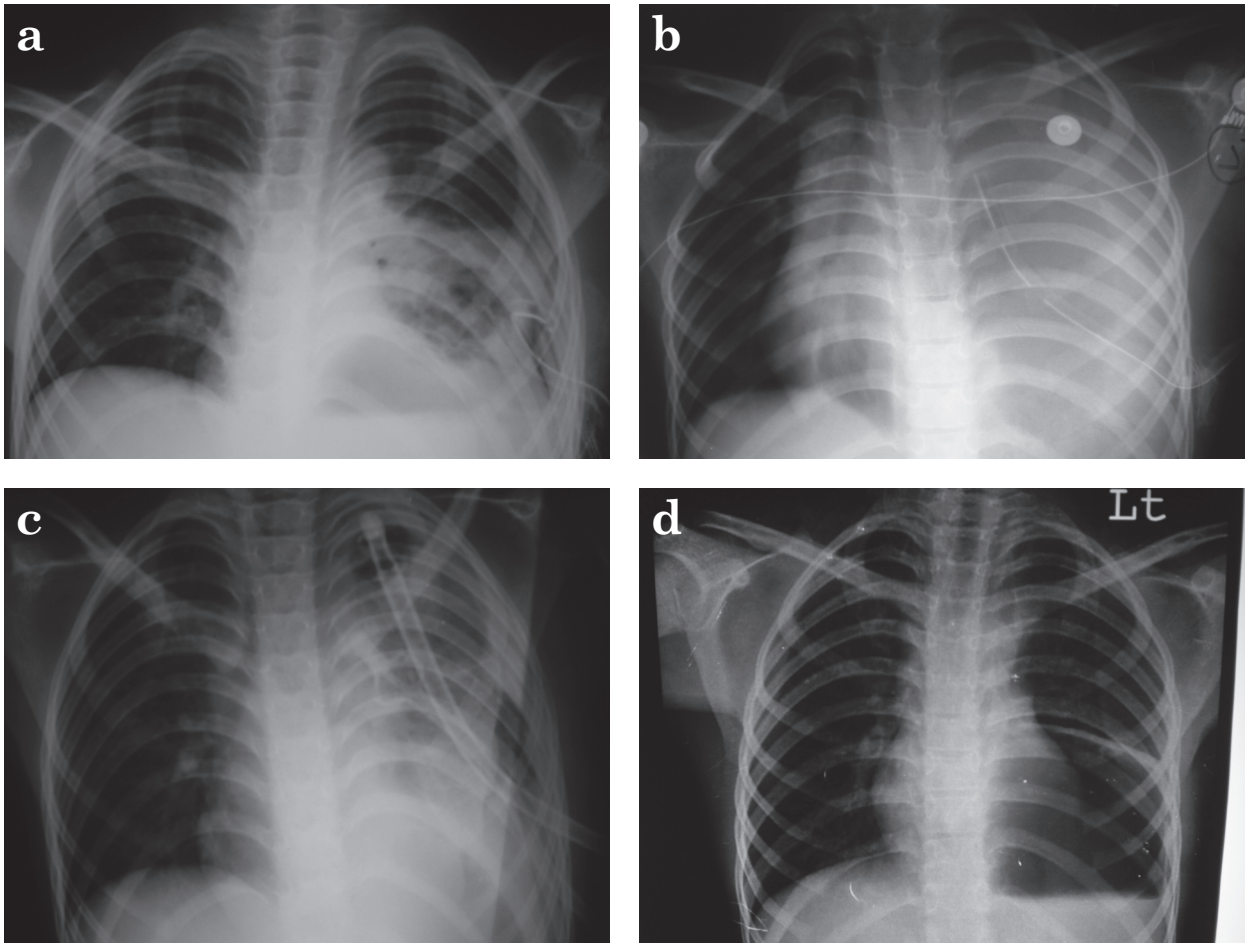

Fig. 4 Serial chest X-rays during hospitalization. a: At admission showing left lower lobe consolidation and pleural effusion. b: Before 2nd operation showing massive left pleural collection with mediastinal shift. c: After 2nd operation showing minimal pleural collection. d: 1 yr follow up showing status post left lobectomy and normal lung fields.

Discussion

Zygomycosis is an uncommon, often fatal, fungal infection complicating diabetes mellitus, hematological malignancies and other debilitating illnesses (1). Poorly controlled diabetes particularly predisposes to this infection due to dysfunctions of macrophage phagocytosis, neutrophil chemotaxis and oxidative killing often present during ketoacidosis (2). Ketoacidosis also induces a temporary block in binding of iron to transferrin providing free iron which is an obligatory growth factor for zygomycoses (3). In our patient also poor long-term diabetic control and progression to ketoacidosis predisposed her to develop mucormycosis.

The diagnosis in this patient was made on smear examination of pleural aspirate. Fine needle aspiration cytology (FNAC) has been described as a relatively non-invasive alterative to the standard transbronchial biopsy (4). Since mucormycosis is a highly fatal infection, FNAC is helpful in making a timely diagnosis as in the index case thus preventing death.

The diagnosis of mucormycosis has improved over the last few decades with more diagnoses

being made premortem now (1, 5, 6–8). Better awareness, expertise and infrastructural facilities for mycological diagnosis seem responsible for this trend (9). Extensive surgical resection along with amphotericin B offers the best chances of survival (1, 5, 8). Amphotericin B alone is usually unsuccessful due to inability to achieve adequate tissue concentrations in the affected tissue resulting from vascular invasion, thrombosis, occlusion and infarction (10). Recent reports suggest possibility of cures with liposomal amphotericin B (11) and posaconazole (12).

Mild pleural effusions may be associated with lung mucormycosis and usually represent inflammatory process but not a contiguous spread that requires demonstration of fungus in the pleural space. In 2 large series on pulmonary zygomycosis, such pleural effusions have been noted to occur in 8 and 6% patients (1, 5). In another recently published paper, deep extension (defined as extension into chest wall, pulmonary artery, aorta or heart) was noted in 7% patients of pulmonary mucormycosis but it was not clear how many of these 15 patients actually had pleural involvement (8). Isolated cases with documentation of actual invasion by fungus into pleural cavity have been reported previously but massive empyemas requiring surgical drainage as seen in our patient, is extremely rare (13, 14). A possible explanation for this rarity of occurrence is angioinvasiveness of mucormycosis. The organisms tend to grow inwardly and invade major lung vessels and outward extension into the pleural cavity may not occur readily. Since infection was simultaneously demonstrated in the lung as well as pleura, our case truly represents a concomitant pleuropulmonary involvement.

Pulmonary zygomycosis is an uncommon diagnosis in children. Only 16% of the 157 pediatric cases of zygomycosis that have occurred till now had pulmonary infection (15). Although Type 1 diabetes has been reported as a common underlying condition in children with zygomycosis, pulmonary involvement appears to have occurred very rarely in this subset of patients; the predominant clinical form being rhinocerebral (15). Ours appears to be the first case of simultaneous pulmonary and pleural zygomycosis in a diabetic child.

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