

THYMIC ZYGOMYCOSIS IN A GIRL WITH POORLY CONTROLLED DIABETES

D. Dayal^{1,*}, A. Saini¹, K. Sodhi², K. Rao³, N. Gupta⁴, S. Dogra¹, S. Singhi¹

¹Postgraduate Institute of Medical Education and Research - Pediatrics

²Postgraduate Institute of Medical Education and Research - Radiodiagnosis,

³Postgraduate Institute of Medical Education and Research - Pediatric Surgery,

⁴Postgraduate Institute of Medical Education and Research - Histopathology,
Chandigarh, India

Abstract

Zygomycosis is a frequently fatal infection in the immunocompromised and diabetic host. A 12 year old girl with type 1 diabetes presented in diabetic ketoacidosis and consolidation of right lung along with thymic abscess causing persistent respiratory symptoms. A diagnosis of mucormycosis was made on smear examination of the thymic aspirate. Intravenous amphotericin along with surgical excision of the abscess resulted in clinical cure. Thymic involvement as seen in this case is an extremely rare occurrence in a diabetic patient which has not been reported in literature so far .

of the class *Zygomycetes*. The spectrum of zygomycosis ranges from cutaneous to disseminated disease; the rhinocerebral form with a predilection for poorly controlled diabetic patients being the most common manifestation (1). Involvement of mediastinum especially in the thymus area is extremely rare (1, 2). We describe here a girl with Type 1 Diabetes (T1D) who developed a thymic abscess alongwith infection of right lung due to zygomycosis during an episode of ketoacidosis.

Key words: zygomycosis, thymus, fungal abscess, type 1 diabetes.

CASE REPORT

The patient, a 12 year old girl, was diagnosed with T1D three years back when she was admitted in diabetic ketoacidosis (DKA) in our hospital. She came from a socioeconomically poor and illiterate family background. She lived with her grandmother and was on

INTRODUCTION

Zygomycosis is an uncommon, frequently fatal mycosis caused by fungi

*Correspondence to: Devi Dayal MD, Postgraduate Institute of Medical Education and Research - Pediatrics, 3118, Level III, Block A, Advanced Pediatrics Center, Chandigarh 160012, India, Tel: 911722755657 Fax: 911722744401, email: drdevidayal@indiatimes.com

irregular insulin treatment and infrequent glucose monitoring and required frequent hospitalizations for episodes of ketoacidosis. In the current admission, she had fever and non-productive cough for 2 days, developed vomiting and rapid breathing for 1 day followed by drowsiness for last few hours. Physical examination revealed thin built (weight 25 kg and height 130 cm; both below 3rd centiles for age). Heart rate was 120 and respirations 30 per min with acidotic breathing pattern. Blood pressure was 100/60 mm Hg. Her axillary temperature was 38°C. Breath sounds were diminished in right infrascapular and inframammary areas with crepitations in right inframammary area. She appeared drowsy and confused. Rest of her systemic examination was unremarkable.

Laboratory investigations revealed blood glucose of 353 mg/dl, pH 7.19, base deficit of 19 and large ketones in urine. Hemogram showed hemoglobin of 11.7 g/dl and WBC count of 11.870/mm³ (neutrophil 76%, lymphocytes 20%, monocytes 2%, eosinophils 2%). Serum

Na⁺ and K⁺ were 131 and 4.5 mmol/L respectively and urea and creatinine 25 and 0.4 mg/dl respectively. A chest radiograph (CXR) showed some mediastinal widening and right lower zone infiltrates. Initial blood and urine cultures were sterile. She received intravenous (IV) fluids and insulin infusion along with broad spectrum antibiotics and her ketoacidosis improved over 24 hours of hospitalization. Thereafter, she was switched over to short acting subcutaneous insulin at 6 hours and subsequently to premixed (30:70) insulin twice a day with short acting insulin before lunch. In view of persistent cough and tachypnea, high insulin requirements, a previous poor diabetic control and malnourished state, possibility of fungal pneumonia was strongly suspected and a contrast enhanced computed tomography (CECT) of chest done on day 7 of hospital stay revealed 2.8 x 2.3 cm sized necrotic thick walled abscess in the thymus with consolidation of apical segment of right upper lobe and small (~5mm) nodular lesions in sub pleural location in the right

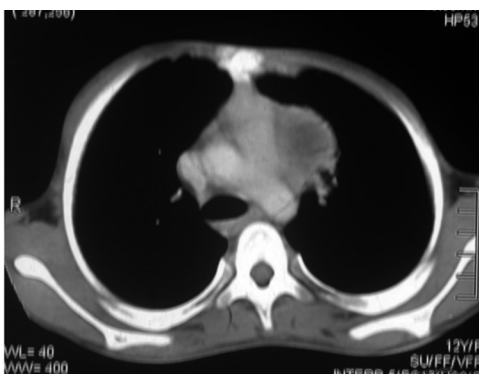


Figure 1. Contrast enhanced computed tomography of chest showing necrotic thick walled abscess in the thymus.

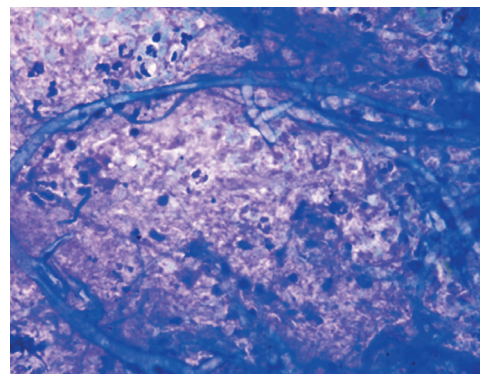


Figure 2. Broad aseptate hyphae with right-angled branching conforming to the morphology of mucormycosis.

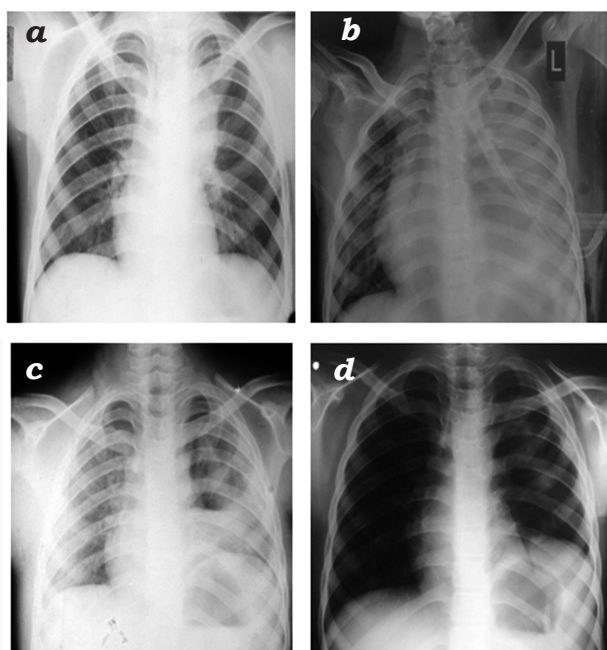


Figure 3. Serial chest X-rays done during hospital admission.

lower lobe (Fig. 1). A course of IV Amphotericin-B was initiated. Ultrasound guided (USG) needle aspiration from thymic lesion done to obtain tissue diagnosis showed broad aseptate hyphae with right-angled branching conforming to the morphology of mucormycosis (Fig. 2).

Surgical exploration was done on the 24th day of hospital stay in view of persistent tachypnea. A well defined abscess was noted in the anterior mediastinum in the location of thymus and about 5 ml of thick pus was extruded from this cavity along with excision of the wall. The pus culture was sterile for any bacteria or fungus. The histopathological examination of the excised tissue representing abscess wall revealed dense organizing inflammatory infiltrate composed of lymphocytes and foamy histiocytes. No

granulomas or fungal elements were seen. The adjoining lung parenchyma showed a similar inflammation.

The post operative hospital course was complicated by worsening respiratory distress. Repeated CXR and USG showed left pleural effusion necessitating intercostal tube drainage which relieved the distress gradually. A CECT done on 9th post-operative day revealed left pleural effusion with partial collapse and consolidation of the underlying lung parenchyma. Small collections were also seen in the left axillary region as well as in anterior mediastinum at the site of previous abscess.

Following this, child gradually improved and intercostal drain was removed on 17th day post operatively. All blood and pleural fluid cultures sent on different occasions during 10 weeks of her hospital stay were sterile. A final

diagnosis of thymic & pulmonary mucormycosis was made and the child was discharged after completing a 6-wk course of Amphotericin-B. She was continued on the same insulin regimen after discharge and has remained well over one year's follow up with fair glycemic control and glycated hemoglobin between 8.0 and 9.0%. Serial CXRs done during hospital admission are shown in Fig. 3 a-d.

DISCUSSION

The members of the order *Mucorales* in the class *Zygomycetes* cause most human disease, referred to as mucormycosis, characterized by a rapidly evolving course, tissue destruction and angioinvasion. It often complicates diabetes mellitus, hematological malignancies, corticosteroid therapy, immunosuppression, renal failure, high-risk newborns, congenital metabolic acidurias and other debilitating illnesses (2). In a recent systematic review of pediatric cases of zygomycosis, the most common patterns of zygomycosis were cutaneous (27%), gastrointestinal (21%), rhinocerebral (18%) and pulmonary (16%) (2). Though cutaneous and gastrointestinal forms are more common in infancy, older children are most commonly present with rhinocerebral and pulmonary forms. It may rarely occur in unusual locations like trachea, common carotid artery, heart and mediastinum as a contiguous spread from a pulmonary focus or as an isolated involvement (3-5). Involvement of thymus has been described previously as part of a widely disseminated fatal disease in a liver transplant recipient (6). An isolated

involvement of thymus leading to the formation of pus with minimal involvement of lung has never been reported in literature. In our patient also the thymus involvement was clinically unsuspected as there were no symptoms attributable to anterior mediastinal involvement. Again due to lack of specific symptoms, surgical intervention was undertaken after more than 2 weeks of antifungal therapy. Expectedly the histopathology demonstrated only organizing inflammation without fungal profiles.

Mechanisms operating in poorly controlled diabetics for disease predisposition include dysfunctions of macrophage phagocytosis, neutrophil chemotaxis and oxidative killing often present during ketoacidosis (7). An elevation in available serum iron, due to its proton-mediated dissociation from transferrin during DKA, has also been implicated for the increased susceptibility to the ferrophilic fungi (8). Our patient also had known predisposing factors like poorly controlled diabetic status, presence of ketoacidosis and undernutrition.

Since mucormycosis is a highly fatal infection, fine needle aspiration cytology is helpful in making a timely diagnosis as in the index case and in our previous case of pleuro-pulmonary zygomycosis (9). The present increased overall survival of patients with mucormycosis is related to early diagnosis and use of surgical intervention combined with effective antifungal agents like amphotericin B (1, 10). Correcting underlying predisposing conditions like poor glycemic control in diabetes cannot be overemphasized. Liposomal amphotericin B is advocated because of its reduced nephrotoxicity and

improved cell penetration (11).

A recent survey has shown good success rates with oral broad-spectrum triazole posaconazole as salvage therapy for zygomycosis (12).

In conclusion, a high index of suspicion is needed, in appropriate clinical setting, to diagnose and aggressively treat this infection in view of the high mortality rate for susceptible patients. Although T1D has been reported as a common underlying condition in majority of these infections, thymic involvement has never been described in this subset of patients. To the best of our knowledge, this is the first reported occurrence of thymic mucor abscess in a diabetic child.

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