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Rhino-orbital cerebral mucormycosis in a child with type 1 diabetes: A case report

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Abstract

Rhino-orbital cerebral mucormycosis is a rare but potentially severe fungal infection in children with high rate of morbidity and mortality. In pediatric patients, uncontrolled diabetes mellitus is considered to be a predisposing factor only in 15% of cases. To prevent and reduce mortality rate of this severe disease, early diagnosis based on clinical findings and biopsy is highly recommended. Herein, we report a case of rhino-orbital cerebral mucormycosis in a 12-year-old girl with type 1 diabetes to demonstrate that a multimodal management approach, involving early surgery which consists in frequent endoscopic sinus debridement and appropriate antifungal therapy, is essential to effectively reduce the spread of infection and achieve effective outcome.

Keywords

Mucormycosis, children, type 1 diabetes, surgery, antifungal medicine

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Introduction

Mucormycosis is an angioinvasive and fulminant fungal infection which usually begins in the nose and paranasal sinuses following inhalation of fungal spores, and is mostly reported in immunocompromised patients.1–3 Diabetes mellitus is the most common predisposing factor for mucormycosis in adults. However, this risk factor was seen only in 15% of pediatric mucormycosis cases.[4] In children, rhino-orbital cerebral mucormycosis (ROCM) is the most common presentation and accounts for approximately 60% of the reported cases.[4,5] The diagnosis of this case maybe particularly difficult in this population, especially in early stages.[1,3]

Case

A 12-year-old girl with poorly controlled diabetes was referred to our department presenting with right-sided facial edema associated with greenish rhinorrhea and diplopia. On physical examination, she was febrile; her pulse was 110 beats/min, blood pressure was 120/60 mm Hg, and her respiratory rate was 22 breaths/min. She had edema on the right side of the face (Figure 1(a)). Ophthalmic examination showed decreased visual acuity in the right eye associated with palpebral oedema, intact extra-ocular movements, and positive corneal reflex. The left eye was normal. Nasal endoscopy revealed inflamed nasal mucosa with crusts over middle turbinate without any signs of tissue necrosis. A diabetic ketoacidosis (DKA) was diagnosed with glucose levels 22 mmol/L, pH level 7.20, and ketonuria. Leukocyte levels and C-reactive protein were 15×10^9/L and 200 mg/L, respectively. A contrast-enhanced computed tomography (CT scan) of brain and paranasal sinuses was performed. It was suggestive of sinusitis involving right ethmoid and maxillary sinus extending into the inferior wall of right orbit (Figure 2). Osteolysis of the lateral and medial walls of maxillary sinus and orbital floor was noted. Brain parenchyma was normal.

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Figure 1. (a) Initial findings at diagnosis: oedema on the right side of the face. (b) Three days after the first intervention: regression of orbital edema with loss of suborbital skin substance.

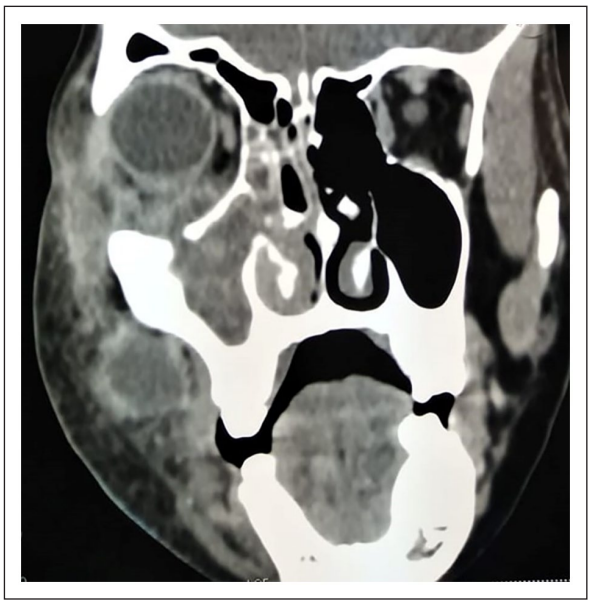

Figure 2. Findings in the CT scan of brain and paranasal sinuses: right ethmoid and maxillary sinus involvement with extension into the inferior wall of right orbit with osteolysis of the lateral and medial walls of the maxillary sinus. The brain parenchyma was normal.

The patient underwent right maxillary sinus drainage with middle meatotomy. Purulent secretions have been found associated with highly inflammatory ethmoid maxillary mucosa.

Bacteriological and mycotic examination of secretions was negative. Thus, the patient was started empirically on intravenous cefoperazone-sulbactam, metronidazole, with eye drops. DKA was treated with insulin infusion and intravenous fluid while arterial blood gases and electrolytes were closely monitored. After 3 days, diffuse swelling on the right side of the face has been observed together with large ulceration in the infra-orbital region, progressive loss of consciousness and left hemiparesis (Figure 1(b)). The patient was taken to intensive care unit (ICU). A second brain CT scan with contrast was ordered and showed, in addition to lesions previously described a right temporal intracranial collection with enhancing wall measuring 10 mm × 23 mm × 12 mm and right cavernous sinus thrombosis (Figure 3). A repeat nasal endoscopy revealed extensive crusting covering right middle turbinate region. In view of such rapid progression, there was high clinical suspicion for mucormycosis; hence, an extensive debridement of the ethmoid, maxillary, and sphenoid sinuses was implemented immediately. Multiple biopsies were performed, and crusting was sent for fungal smear and culture. Histopathologic results from tissues retrieved during extensive sinus debridement revealed, staining large non-septate hyphae branching with the hematoxylin and eosin and highlighted with periodic acid–Schiff stain which corroborated the diagnosis of mucormycosis (Figure 4).

After 6 weeks of systemic antifungal therapy and intensive medical and surgical managements, the evolution was marked by clinical and radiological improvement. The patient was discharged with oral antifungal medication and strict control of her diabetes. In addition, motor re-education program was indicated. Three months later, the patient was in good general condition, without signs of active infection (Figure 5) and is currently on a plan to undergo facial plastic surgery.

Discussion

Mucormycosis in children is an uncommon and serious fungal infection with acute and fulminant manifestation that is

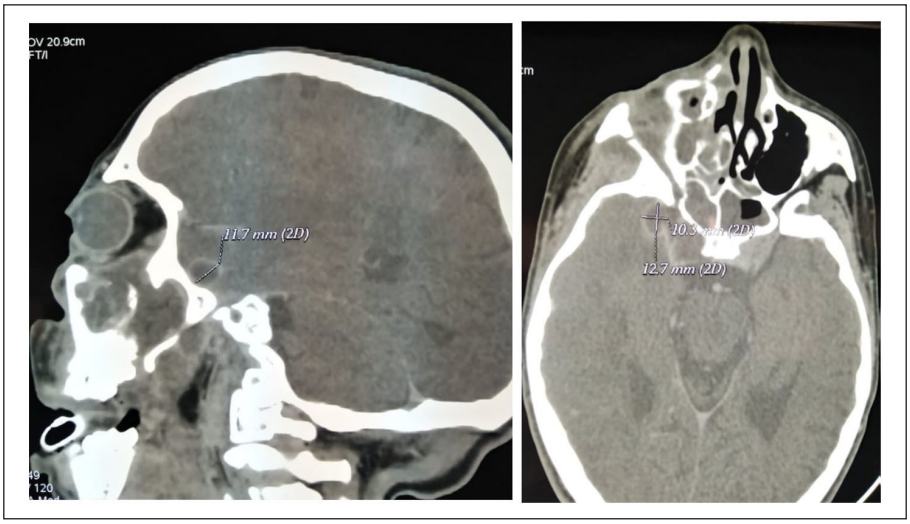

Figure 3. Findings in the CT scan of the brain: right temporal intracranial collection with right cavernous sinus thrombosis.

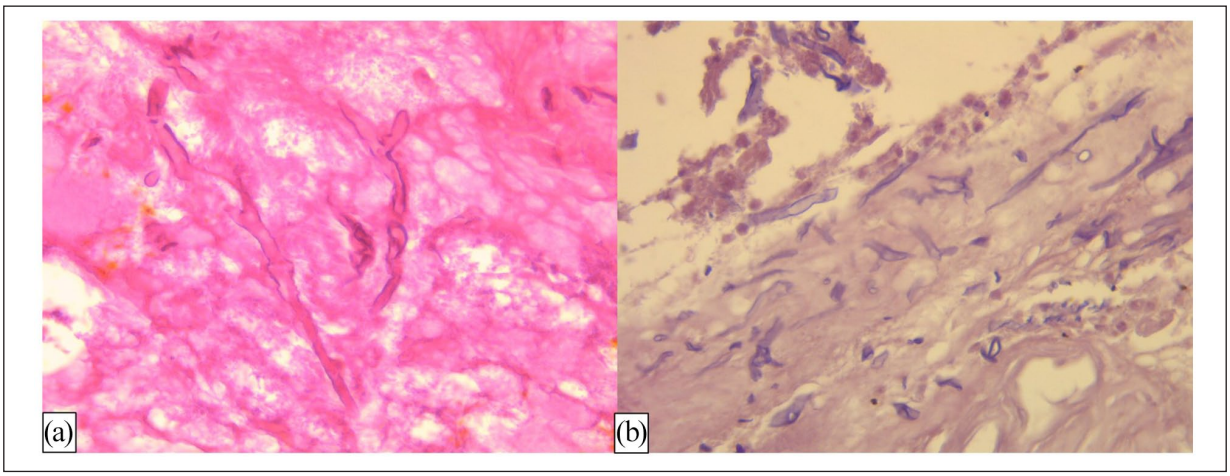

Figure 4. (a) Broad non-septate hyphae branching at 90 degrees (hematoxylin and eosin ×400). (b) Mucormycosis organisms highlighted with periodic acid–Schiff (PAS) stain.

caused by ubiquitous filamentous fungi of the Mucorales.[1,2] This life-threatening infection develops rapidly and spreads by extensive angioinvasion, causing thrombosis of the blood vessels and tissue necrosis.[3]

In adult patients, diabetes mellitus is the most common risk factor associated with mucormycosis in India. However, hematological malignancy and transplant are the most observed risk factors in Europe and the United States.[6]

In pediatric population, predisposing factors for this fungal infection mainly include hematological malignancies (46%), hematopoietic stem cell transplantation, and solid organ transplantation.[4] However, diabetes was present only in 5%–15% of cases.[3,4]

While diabetes is reported to be as a risk factor for adults with mucormycosis in developing countries, no such correlation has been established with respect to children. In fact, epidemiological data on children are too limited to provide epidemiological trend. In the literature, we have found only one study comparing children with mucormycosis in developed and developing countries. Only three cases of diabetes were observed in 63 children in the two series.[3]

The association between mucormycosis and diabetes may be a result of multifactorial effects of hyperglycemia and ketoacidosis. In fact, ketones help fungi to utilize and produce ketoreductase, which facilitates its growth.[7] Other underlying conditions were observed such as steroid therapy, iron overload, deferoxamine therapy, and previous trauma.[3,4,8] While 10% of children had no predisposing factor,[3,9] ROCM was the clinical presentation of mucormycosis in 60% of pediatric diabetics. The median age of diabetic children with mucormycosis is 14 years (11–16 years).[4]

The symptoms of ROCM are generally non-specific with varying degrees of severity. The initial clinical presentation could be similar to bacterial cellulitis, especially in the early

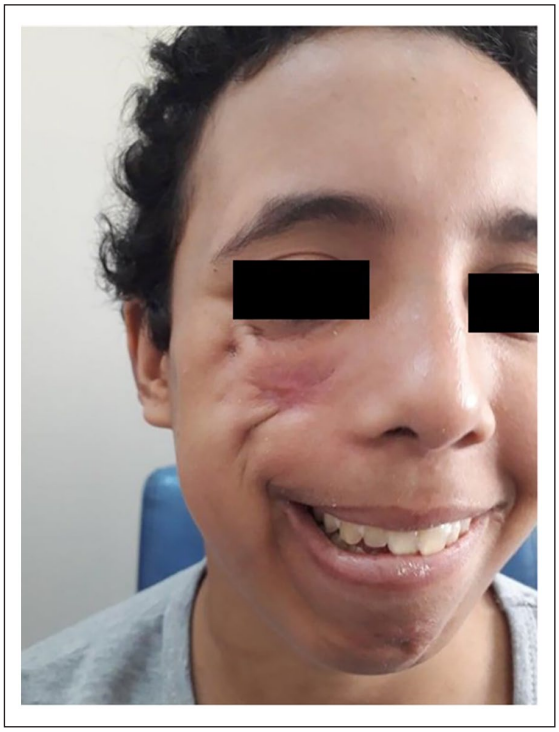

Figure 5. Patient 3 months after surgery.

stage.[9,10] Fungal infection is likely to extend to orbital structures, which may lead to proptosis, chemosis, and in extreme cases to ophthalmoplegia and even loss of vision. Brain damage can manifest in impaired consciousness, unsteady gait, and/or seizures.[11,12]

Therefore, early diagnosis based on identifying organisms in tissue by direct microscopy, histopathological examination, and culture on Sabouraud's agar molecular tests could limit morbidity and mortality rates.[2,3] The detection of aseptate hyphae with right-angled branching is pathognomonic of mucormycosis.[12] Cultures are often negative.[2,11] *Rhizopus arrhizus* has been reported as the most common organism found most frequently in diabetic children with mucormycosis (44%) followed by *Mucor* Sp.[3,4] Imaging is essential for surgical planning because it helps to assess the extent of disease and detect possible complications.[13] CT scan shows bone destruction, clouding, and thickening of nasal and paranasal mucosa,[8,12] whereas magnetic resonance imaging (MRI) is useful for identifying the orbital and intracranial extent of the disease as well as cavernous sinus thrombosis or internal carotid artery thrombosis.[12,13]

Treatment approach should be initiated as early as diagnosis for mucormycosis is established. It is usually based on the combination of systemic antifungal therapy (liposomal amphotericin B), urgent surgical debridement of the tissues involved (especially in rhino-orbital and cutaneous forms) as well as control of underlying conditions.[1,11,12] Amphotericin B has been the drug of choice given either as monotherapy (31.7%) or in combination with other antifungal agents.[3] The duration of treatment is related to several factors, that is, time from illness onset to hospital admission, cerebral infection extension, age, early response to treatment, and timely surgical intervention. Mortality rate in pediatric patients with mucormycosis is high, especially in children with hematological malignancy; it ranges from 41.3% to 66.6%.[3] However, prognosis could be improved through expedient treatment. Finally, to ensure a successful outcome, frequent surgical debridement is crucial for the management of such patients.[9]

Conclusion

ROCM is a severe infection in children with poorly controlled diabetes. Prompt and accurate diagnosis of this invasive fungal infection, early initiation of adequate antifungal treatment, frequent endoscopic sinus debridement, and close monitoring of hyperglycemia are key to reducing its devastating consequences.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

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