CASE REPORT

Rhinocerebral mucormycosis in a patient with type 1 diabetes presenting as toothache: a case report from Himalayan region of India

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SUMMARY

Mucormycosis is an angioinvasive infection caused by ubiquitous filamentous fungi of the order Mucorales. It is a rapidly progressive fatal infection mostly reported in susceptible individuals, such as those with poorly controlled diabetes or those with defects in phagocytic function. Rhinocerebral mucormycosis is the most common type of mucormycosis in diabetic patients. This case report describes a 17-year-old girl with type 1 diabetes mellitus presenting with rhinocerebral mucormycosis. The patient presented with a history of toothache and facial pain with oedema of left half of face, periorbital oedema and depressed consciousness. She had hyperglycaemia with diabetic ketoacidosis and rapidly developed hemiparesis progressing to quadriplegia and died within 3 days of admission. The current report emphasises the importance of having a high index of suspicion when dealing with patients with diabetes presenting with facial pain or cellulitis and prompt initiation of medical therapy along with surgical debridement for control of rhinocerebral mucormycosis.

BACKGROUND

Rhinocerebral mucormycosis (ROCM) is the most common form of mucormycosis in patients with diabetes mellitus. This is an uncommon disease which sometimes presents as toothache in a patient with uncontrolled diabetes. The disease presents with a diagnostic dilemma as initial presentation mimics facial or orbital cellulitis thereby suggesting bacterial aetiology. Also it has a very rapidly progressive clinical course and is almost universally fatal if untreated. The authors decided to write up this case because of the need for high index of suspicion in treating patients with this disease.

CASE PRESENTATION

A 17-year-old girl presented in the emergency department with a toothache on the left side of the face for 7 days with subsequent development of pain and swelling on left side of face and periorbital oedema. She was a known case of type 1 diabetes mellitus since 2 years and was on regular insulin thrice a day with poorly controlled blood sugars. She belonged to low socioeconomic status and there was no family history of type 1 diabetes mellitus.

At the time of admission the patient was stuporous, blood pressure was 116/74 mm Hg, pulse rate 126/min, respiratory rate 24/min, random blood sugar was 425 mg/dL and temperature 98°F.

On examination, she was conscious but not following commands, although she was able to move

all four limbs. There was facial oedema, more on the left side with bilateral periorbital oedema, ptosis with purulent discharge and inability to open her left eye. There was no proptosis of either eye. The right cornea was clear and perception of light was present. There was slight bluish black discolouration of skin over the left half of her face near the nose and eye (figure 1). Epistaxis was also present.

INVESTIGATIONS

Total leucocyte count on the day of presentation was 23 700/mm³, differential leucocytes count was 90% polymorphs, 10% lymphocytes and random blood sugar was 425 mg/dL. The serum creatinine level was 0.7 mg/dL. The urine examination showed no pus cells but was positive for ketone bodies. Arterial blood gas analysis showed metabolic acidosis with pH of 7. The CT of the brain and paranasal sinus showed encroachment of maxillary sinus with erosion of the nasal septum (figure 2). Smears prepared from the nasal discharge showed broad non-septate fungal filaments with branching at right angles suggestive of mucorales on Grocott-Gomori methenamine silver stain. Culture of nasal discharge on Sabouraud's media subsequently was positive for *Rhizopus oryzae*.

DIFFERENTIAL DIAGNOSIS

In a patient presenting with facial pain, facial and periorbital oedema, orbital or facial cellulitis and cavernous sinus thrombosis caused by bacterial pathogens (mostly *Staphylococcus aureus*, also streptococcal and Gram-negative species) must be excluded. Our patient presented with elevated

Figure 1 Day 1 of admission showing bluish-black discolouration of left half of face, facial oedema and periorbital oedema.

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Figure 2 CT scan of the brain showing opacification of left maxillary sinus and facial oedema on left side in a patient with mucormycosis.

white cell count and facial cellulitis suggestive of bacterial aetiology. However, the CT scan showed left maxillary sinus opacification with erosion of nasal septum. She also had bluish-black discolouration of face and developed eschar subsequently so ROCM was suspected, which was subsequently confirmed on microbiological analysis.

TREATMENT

The patient presented with features suggestive of orbital cellulitis with a low level of consciousness. A provisional diagnosis of mucormycosis with diabetic ketoacidosis was made. She was promptly started on insulin infusion, antibiotics and amphotericin B based on a high index of suspicion without waiting for a microbiological diagnosis. She was given Amphotericin B deoxycholate at a dose of 50 mg/day diluted in 500 mL of normal saline with monitoring of serum potassium and serum creatinine levels. Blood sugar levels were maintained with an infusion of regular insulin.

On day 2 of admission patient developed eschar over the left half of her face including the nose and showed deterioration in neurological status with development of right hemiparesis (figure 3). Ophthalmological, otolaryngological and neurosurgical consultation were taken and patient advised for debridement and evisceration of left eye but parents opted for medical treatment only.

OUTCOME AND FOLLOW-UP

On day 3, the patient developed hypernatraemia with hypokalaemia which were managed with free water through Ryle's tube and potassium replacement. Despite optimal antifungal therapy and prompt reversal of diabetic ketoacidosis with achievement of euglycaemia, the patient had a rapidly progressive clinical course and subsequently developed quadriparesis and eventually died on the fourth day of admission of cardiorespiratory arrest. In this patient cause of quadriparesis could not be elicited as MRI and MR venography facility was not available at our centre. The focal neurological deficit could be either due to progressive and rapid involvement of vascular structures, cavernous sinus or intracranial contents.

DISCUSSION

Mucormycoses are a group of invasive infections caused by filamentous fungi of the Mucoraceae family.¹ This fungus is

Figure 3 Eschar over left half of face on day 2 of admission.

widespread and occurs in soil, manure, vegetable, fruits and as bread mould. *R. oryzae* is the commonest fungus isolated. Other fungi occasionally isolated include *Mycoclados (Absidia)corymbifera*, *Rhizomucor pusillus*, *Apophysomyces elegans*, *Saksenaea vasiformis*, *Mucor* species and *Cunninghamella bertholletiae*.² In a case series of 75 cases from India *R. oryzae* (69%) was the most common isolate followed by *A. elegans* (19%).³

Most human infections result from inhalation of fungal sporangiospores that have been released in the air or direct inoculation of organisms into disrupted skin or mucosa.⁴ Mucormycosis is primarily seen in patients with chronic conditions, particularly uncontrolled diabetes mellitus and haematological malignancies, because these patients are immunocompromised. Patients with extensive burn injuries, renal failure, prolonged corticosteroid use and deferoxamine treatment have also been reported to have mucormycosis.⁵

On the basis of the clinical presentation and particular site of involvement six manifestations of the disease can be described: rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and localised infections not otherwise belonging in the previous categories.⁶ ROCM is the most common form of mucormycosis in patients with diabetes mellitus.⁷⁻⁸ It may also occur in patients with underlying malignancies, recipients of haematopoietic stem cell or solid organ transplants, and individuals with other risk factors.⁹ The infection develops after inhalation of fungal sporangiospores into the paranasal sinuses. The infection may then rapidly extend into adjacent tissues. Upon germination, the invading fungus may spread inferiorly to invade the palate, posteriorly to invade the sphenoid sinus, laterally into the cavernous sinus to involve the orbits, or cranially to invade the brain.¹⁰ The fungus invades the cranium through either the orbital apex or cribriform plate of the ethmoid bone and ultimately kills the host. Occasionally, cerebral vascular invasion can lead to haematogenous dissemination of the infection with or without development of mycotic aneurysms.¹¹ The initial symptoms of ROCM are consistent with those of sinusitis and periorbital cellulitis and include eye and/or facial pain and facial numbness followed by blurry vision.¹²

Mucorales invade blood vessels and cause necrosis of vessel walls and mycotic thrombi. While healthy humans are resistant to such an infection, immunocompromised patients are generally more vulnerable to the angioinvasive hyphal forms of these fungi. Patients with diabetes have decreased granulocyte phagocytic ability with altered polymorphonuclear leucocyte response, consequently are more susceptible. Diabetes mellitus is

associated with 40% of mucormycosis cases overall and 70% of patients with ROCM.¹³

ROCM may present with features of sinusitis-like nasal congestion, facial pain, headache and facial oedema. ROCM typically originates in the nasal or oral mucosa, spreads to the paranasal sinuses, and enters the orbit via the ethmoid and maxillary sinuses or via the nasolacrimal duct.¹⁴ Intracerebral extension may occur from the orbit via orbital apex, orbital vessels or via cribriform plate.¹⁴ The disease is rapidly progressive, so prompt diagnosis and aggressive therapy are essential for successful containment of disease.

The diagnosis of mucormycosis can be made by direct microscopy or histopathological examination, or by culture on Sabouraud's agar. The detection of aseptate hyphae with right angled branching is pathognomonic.¹⁵ The treatment involves good control of blood sugar with reversal of diabetic ketoacidosis, early initiation of amphotericin B therapy and surgical debridement. Owing to extensive vascular thrombosis there is poor drug delivery to the site of the infection. Therefore, medical management with amphotericin B alone is not effective; surgical debridement is essential.

The factors associated with poor survival in ROCM include delay in diagnosis and treatment, hemiparesis, bilateral sinus involvement and facial necrosis.¹⁶ Zygomycosis is a threat in uncontrolled diabetes, renal failure and chronic renal disease.

Although, ROCM is a rare disease but it should be included in the differential diagnosis of patients presenting with pain and oedema of face, facial paraesthesia and facial paralysis with risk factors such as diabetes, haematological malignancies, prolonged corticosteroid intake or renal failure. Earlier recognition of the condition, prompt reversal of risk factors, adequate control of blood sugar, early initiation of medical therapy and meticulous surgical debridement may improve patient outcome.

Learning points

- ▶ In a patient with type 1 diabetes mellitus with toothache and facial or orbital cellulitis we should rule out rhinocerebral mucormycosis (ROCM).
- ▶ Although it is a relatively uncommon disease but it has an aggressive course and is potentially fatal.
- ▶ Prompt initiation of amphotericin B therapy with good glycaemic control form the cornerstone of therapy.
- ▶ Surgical debridement is also essential.

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