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Recovery from rhinocerebral mucormycosis in a ketoacidotic diabetic patient: a case report

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Abstract
An 18-year-old woman with insulin-dependent diabetes mellitus developed an infection of the paranasal sinuses with *Rhizopus oryzae* resulting in facial swelling, hemiplegia and blindness of the right eye. The therapy of this rhinocerebral mucormycosis consisted of extensive surgical debridement, administration of high-dose amphotericin B, hyperbaric oxygen and control of the underlying predisposing diabetes mellitus. The patient eventually recovered with however, the loss of one eye.

Key words: Mucormycosis, rhinocerebral; Diabetes mellitus; Hyperbaric oxygenation; Paranasal sinuses

Introduction

Mucormycocis is an opportunistic infection caused by fungi of the family *Mucoraceae*. *Mucoraceae* belong together with four other families to the class of Zygomycetes (Lehrer, 1980; Finn, 1988). These fungi are found widespread in nature in soil, dust, spoiled foods and bread (Armstrong, 1989).

*Acute mucormycosis develops in patients with immunosup*pression, trauma or metabolic acidosis (Finn, 1988; Orsel *et al.*, 1990). Mucormycosis can be categorized into a rhinocerebral, pulmonary, disseminated, gastrointestinal or cutaneous form (Venezio and Tucker, 1988). Rhinocerebral mucormycosis is the most common and was first reported in 1885 (Paltauf, 1885). In rhinocerebral mucormycosis the fungi invade from the nasopharynx or paranasal sinuses, spread to the retro-orbital region and may extend into the brain.

Characteristically the fungus invades the walls of vessels resulting in embolization with ischaemia and necrosis. Local acidosis with diminished phagocytic function of granulocytes contribute to the destructive growth of the fungus.

Usually the disease progresses rapidly with a high mortality rate. When infection with mucormycosis is suspected, an early diagnosis is a prerequisite.

Case report

An 18-year-old woman with insulin-dependent diabetes mellitus was admitted elsewhere because of diabetic ketoacidosis. She had suffered from diabetes since childhood and was frequently hospitalized with hyperglycaemic ketoacidoses.

Initial treatment consisted of intravenous fluids with insulin and potassium. She recovered from the ketoacidosis. Three days before this admission, the patient complained of headache and purulent nasal discharge. A maxillary sinusitis was diagnosed. The sinuses were drained by puncture but a Gram-stain and bacterial cultures of the fluid yielded no pathogens. Despite the administration of broad spectrum antibiotics her general condition worsened. Within two weeks after the start of antibiotics she developed facial swelling and a hemiplegia. She was then transferred to our hospital.

On physical examination the patient appeared lethargic and weak. Her rectal temperature was 37.8°C, the pulse rate was 86/min and she was tachypnoeic. The blood pressure was 115/65 mmHg. On ENT examination a diffuse right sided facial swelling with redness and axial proptosis was found. Purulent necrotic material was seen in the right nasal cavity and similar necrotic tissue was seen on the hard palate. There was a facial palsy on the right side and a left-sided hemiparesis. The right eye showed a visual acuity of 1/60 and no oedema of the optic fundi was seen. On laboratory examination a leucocytosis of 15.4×10^9/l was found together with an erythrocyte sedimentation rate of 119 mm/hr, and a serum glucose level of 32.3 mmol/l.

Computerized tomography (CT scan) with administration of high dose contrast revealed an extensive mucosal thickening of all paranasal sinuses on the right side with signs of destruction of the ethmoid and maxillary bony walls. Intracerebral infarction in the area of the right arteria choroidea anterior and a cavern sinus thrombosis was observed (Fig. 1). An intraorbital infection was not suspected on the CT scan at that time. Rhinocerebral mucormycosis was considered and the patient underwent surgery immediately. A right sided lateral rhinotomy was performed together with an extensive surgical debridement of all paranasal sinuses. An abscess of the cheek was drained. The diagnosis of mucormycosis was strengthened at the operation when biopsy specimens from the maxillary sinus showed broad, non-septate mycelial forms. Fungal cultures from multiple biopsies revealed *Rhizopus oryzae*. After the operation antimycotic therapy was started with amphotericin B in a dosage of 1.0 mg/kg bodyweight/day intravenously. Hyperbaric oxygen consisting of 100 per cent oxygen at three absolute atmospheres for 120 min per day was used as additional treatment. Unfortunately, the right visual acuity decreased and two weeks after the operation total blindness of the right eye developed. A CT scan revealed abscesses in the right orbit and in the pterygopalatine fossa (Figs 2 and 3). It was necessary to perform a second operation to debride the pterygopalatine fossa and to enucleate the right eye. Amphotericin B and hyperbaric oxygen treatment were continued and a gauze soaked with an iodine solution was applied daily after cleaning the surgical cavity. The patient recovered

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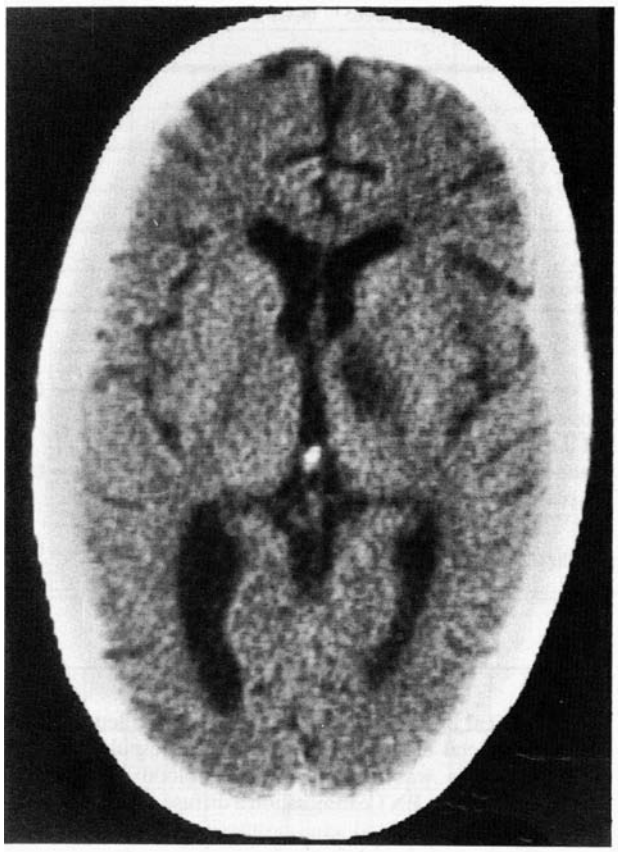

FIG. 1
CT scan of brain, showing infarction of the right arteria choroidea anterior.

slowly and was finally discharged from the hospital 100 days after admission. She had received a total dose of 3.5 gram of amphotericin B and approximately 60 hyperbaric oxygen treatments.

Three years after operation there are no signs of recurrent mucormycosis. An orbital prosthesis has been fashioned. The patient is now fully ambulatory and the hemiplagia has almost recovered without any residual symptoms. Facial nerve function however did not return at all.

Discussion

Rhinocerebral mucormycosis is an uncommon and rapidly progressive fungal infection that occurs especially in association with diabetes mellitus (Finn, 1988). Before amphotericin B became available (Couch *et al.*, 1988) the mortality rate was approximately 70 per cent. Usually the infection starts in the paranasal sinuses, or less frequently in the palate or pharynx (Finn, 1988). The disease progresses through the retro-orbital region and from the apex of the orbit into the brain. Invasion of the fungus into the orbit and the central nervous system is a poor prognostic sign. The initial symptoms of rhinocerebral mucormycosis consist of lethargy, headache and visual loss. Necrotic tissue on the palate or nasal mucosa is a diagnostic clue. Proptosis, periorbital cellulitis and disturbance of the eye movements caused by III, IV and VIth cranial nerve palsies may follow. Intracranial spread of infection can result in neurological disorders. When the paranasal sinuses are involved, X-ray examination may reveal a clouding of the paranasal sinuses and a diffuse bone destruction or sequestration of the walls of the sinuses. Air fluid levels are rarely present (Tyagi *et al.*, 1990). Computerized tomography (CT) should be used to evaluate the extension of the infection into the orbit, pterygopalatine fossa and the brain (Finn, 1988).

The diagnosis of rhinocerebral mucormycosis can be made on biopsy. Swabs of the infected regions may be negative. Biopsies stained with Giemsa's stain, haematoxylin-eosin stain or fluorescence may reveal broad, nonseptate hyphae branching at right angles. In our experience, fluorescence (Fungiqual, CIBA) is most sensitive (Wachsmuth, 1988). Members of the mucorales grow rapidly in most culture media after a few days incubation at 30°C. Morphologic features are used to distinguish between the various pathogenic mucorales (Schipper, 1978). The fungi encountered in most cases of rhinocerebral mucormycosis belong to the genera *Rhizopus, Absidia, Mucor* or *Rhizomucor*. *Rhizopus oryzae* accounts for 90 per cent of the disease (Scholer, 1983).

Malignancy with secondary infection and other fungal infections as aspergillosis may mimic a mucor infection and must always be included in the differential diagnosis (Tange *et al.*, 1986).

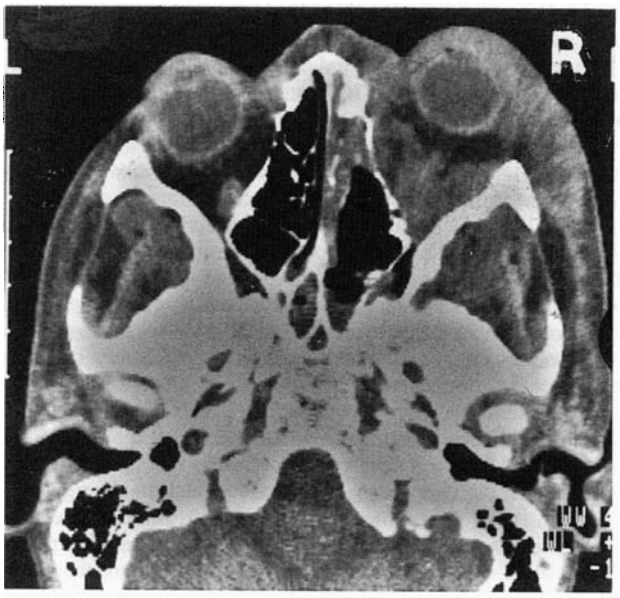

FIG. 2
CT scan showing axial proptosis associated with infiltration of the right orbit.

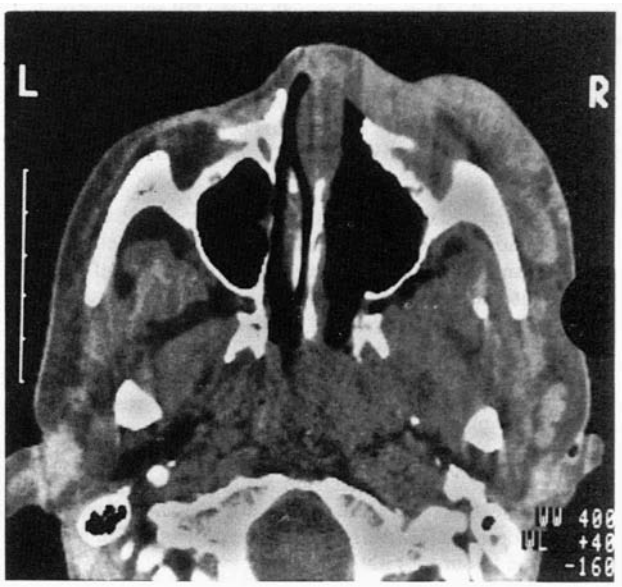

FIG. 3
CT scan showing diffuse infiltration in the right pterygopalatine fossa.

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Therapy of rhinocerebral mucormycosis includes aggressive surgical debridement and administration of amphotericin B in a total dose of 3–4 gram. Despite this treatment, the mortality rate remains high. Laboratory experiments in which fungi were exposed continuously to 10 atmospheres pressure of oxygen at 25°C for seven days, showed that 50 per cent of the stains tested were killed (Robb, 1966). This observation suggested that hyperbaric oxygen therapy may have value as an adjunctive treatment. The benefit of this additional treatment has been demonstrated in four case reports and in a retrospective review of 13 patients (Price and Stevens, 1980; Nathan *et al.*, 1982; Couch *et al.*, 1988; Ferguson *et al.*, 1988). However some comments have to be made. *Rhizopus oryzae* has a very variable behaviour when exposed to hyperbaric oxygen and it appears that this species is more resistent to high oxygen pressure than other fungi (Robb, 1966). In addition, it is very difficult to interpret these laboratory findings to an *in vivo* situation where the administration of hyperbaric oxygen occurs intermittently, where the tissue pO2 is undoubtedly much lower and where the fungus grows invasively with hyphae only. We are not aware of animal experiments or prospective studies that show a beneficial effect of hyperbaric oxygen treatment in this specific kind of infectious disease. In general it is believed that hyperbaric oxygen has a beneficial effect on leucocyte migration and phagocytic function (Couch *et al.*, 1988). Tissue repair is stimulated by hyperbaric oxygen administration especially when vascularization is impaired (Hunt *et al.*, 1969). Therefore a positive effect of hyperbaric oxygen on tissue repair was expected. The effect on the fungus itself remains unclear.

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References

Armstrong, D. (1989) Problems in management of opportunistic fungal diseases. *Reviews of Infectious Diseases* **11:** 1591–1599.

Couch, L., Theilen, F., Mader, J. T. (1988) Rhinocerebral mucormycosis with cerebral extension successfully treated with adjunctive hyerbaric oxygen therapy. *Archives of Otolaryngology and Head, Neck Surgery* **114:** 791–794.

Ferguson, B. J., Mitchell, T. G., Moon, R., Camporesi, E.M., Farmer, J. (1988) Adjunctive hyperbaric oxygen for treatment of rhinocerebral mucormycosis. *Reviews of Infectious Diseases* **10:** 551–559.

Finn, D. G. (1988) Mucormycosis of the paranasal sinuses. *Ear, Nose and Throat Journal* **67:** 813–822.

Hunt, T. K., Zedenfeldt, B., Goldstick, T. K. (1969) Oxygen and healing. *American Journal of Surgery* **118:** 521–525.

Lehrer, R. I. (1980) Mucormycosis. *Annals of Internal Medicine* **93:** 93–108.

Nathan, M. D., Keller, A. P., Lerner, C. J., Davis, J. C. (1982) Entomophthorales infection of the maxillofacial region. *Laryngoscope* **92:** 767–769.

Orsel, S., Bessede, J. P., Sauvage, J. P. (1990) Mucormycose naso orbito cerebrale. Une maladie de moins en moins exceptionnelle. *Revue de Laryngologie* **111:** 221–225.

Paltauf, A. (1885) Mycosis mucorina. *Virchows Archives* (Pathology and Anatomy) **102:** 543.

Price, J. C., Stevens, D. L. (1980) Hyperbaric oxygen in the treatment of rhinocerebral mucormycosis. *Laryngoscope* **90:** 737–747.

Robb, S. M. (1966) Reactions of fungi to exposure to 10 atmospheres pressure of oxygen. *Journal of General Microbiology* **45:** 17–29.

Schipper, M. A. A. (1978) Studies in mycology, no. 17. In *Centraal bureau voor schimmelcultures*. (Baarn, ed.)

Scholer, H. J. (1983) Mucorales. In *Fungi pathogenic for humans and animals*. (Howard, D. H., ed.), New York, p. 9–59.

Tange, R. A., Nijdam, D. C., Schot, L., Schipper, M. E., Bras, J. (1986) Localized aspergillosis involving the nose and paranasal sinusis. *Acta Oto-Rhino-Laryngologica Belgica* **40:** 455–462.

Tyagi, I., Majumder, N. K., Gopalakrishan, S. (1990) Mucormycosis of paranasal sinuses. *Pakistan Journal of Otolaryngology* **1:** 37–41.

Venezio, F. R., Tucker, P. C. (1988) Zygomycosis. In *Handbook of Clinical Neurology 8*, (Harris, A. A., ed.) Elsevier Science Publishers, Amsterdam. p. 467–477.

Wachsmuth, E. D. (1988) Visualization of fungi in histological sections. *Virchows Archives* (Cell Pathology) **56:** 1–4.

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