

Mucormycosis

CASE REPORT AND REVIEW

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SUMMARY

A case of non-fatal rhinocerebral mucormycosis occurring in a 5-month-old infant is described, and the literature reviewed.

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Mucormycosis is a rare but dangerous disease, which is usually diagnosed at postmortem examination.

The *Mucoraceae*, members of the class *Phycomycetes*, have for 85 years been known to be pathogenic in animal and man. The genera *Absidia*, *Mucor*, and especially *Rhizopus*, cause severe infections of the orbit and maxilla with infiltration of the brain, usually resulting in death. The other genera usually attack the lungs or gastrointestinal tract. The genus *Entomophthora coronata*¹ causes nasal polyps, subcutaneous induration without ulcers, and infections of the frontal and paranasal sinuses.

In 1943 Gregory *et al.*² described the first case in man. To date, over 200 cases³ have been published in the available literature, and death due to the infection was caused in about 50% of cases.

CASE REPORT

A 5-month-old Black male infant was admitted to Pelonomi Hospital on 20 June 1973 (Fig. 1). The history showed that the infant had suffered gastro-enteritis, which was successfully treated two weeks prior to admission. A few days after that a swelling of the left cheek, eye and eyelids appeared, followed by a 'sore' on the hard palate. There were no other complaints. He was a breast-fed infant, feeding normally and gaining weight.

On clinical examination he was in good general health, with no signs of weight loss or dehydration. The temperature was 38,1°C, the pulse rate 108/min, regular and strong, and the respiration rate 24/min. The left maxillary area was swollen with proptosis of the eye and oedema of the upper and lower eyelids. The nose was displaced to the right, and the left nostril was blocked. On the left side of the hard palate, a slight swelling about 2 cm in diameter was noticed, surrounded by a thin black necrotic area.

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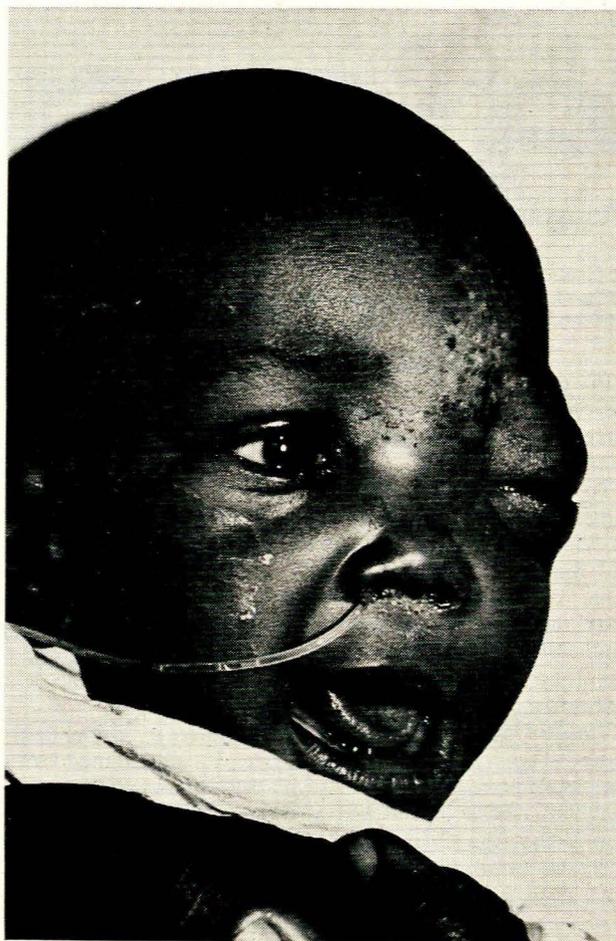


Fig. 1. Swelling of the left side of the face with proptosis and oedema of eyelids.

The infant appeared mentally irritated, but the level of consciousness was normal. The cranial nerves were found to be intact. The right pupil was normal, but the left pupil was dilated and did not react to light. The reflexes were normal, although possibly slightly hyperactive on the right side.

Special Investigations

X-ray films taken of the chest, lungs and heart were normal. There was clouding of the left maxillary and ethmoid sinuses, probably due to a mass in this region.

No clear erosion of the hard palate or orbital bones was seen.

Microbiology: No mycobacteria were found according to a pus swab from the palatal ulcer taken on 21 June 1973. The culture revealed *E. coli*, *Streptococcus faecalis* and *Candida*.

A pus swab taken from the nose on 25 June 1973 showed coagulase-positive *Staphylococcus*, *Streptococcus faecalis* and *E. coli*.

A pus swab from the left maxillary antrum taken at follow-up on 3 November 1973 again showed *E. coli* and *Streptococcus faecalis*, but no mucormycosis could be cultured.

Haematology: Haemoglobin count was 8,8 g/100 ml and ESR 63 mm/hour (Westergren). Platelets were elevated. Hypochromic, normocytic anaemia with Rouleaux formation and toxic granulation was found.

All biochemical tests were within normal limits; the VDRL test was negative; lumbar puncture was within normal limits; and the Heaf test was negative.

Consultations: The Departments of General Surgery, Neurosurgery, Ophthalmology, and a maxillofacial surgeon were consulted, but the differential diagnosis did not include mucormycosis.

Examination under Anaesthesia

An antrostomy was done on the left maxillary antrum and thick white-and-black mucus was removed, and was sent for histology, culture and sensitivity. There was a remarkable absence of bleeding. The swelling on the hard palate was found to be completely loose, and kept in position by necrotic strands of tissue. This was removed, leaving a large defect on the hard palate communicating with the left nasal cavity (Fig. 2). The black edges surrounding the defect were sent for histology. Once again, the absence of bleeding was striking.

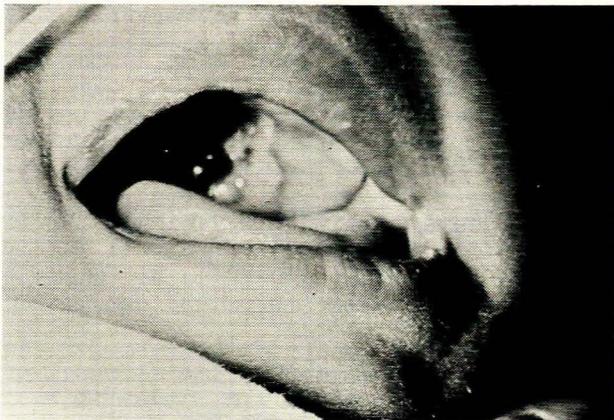


Fig. 2. Large hard palatal defect on the left side.

The pathological report described the specimen received as being 2 cm in diameter, and greyish-red in colour. Microscopic examination revealed fragments of bone, blood

clots, necrotic material, squamous epithelium and granulation tissue, consisting of foreign body giant cells, histiocytes, plasma cells and vascularisation. This material was also infiltrated with polymorphonuclear neutrophilic leucocytes. In between, thick non-septate hyphae were found that branched at right angles. The PAS staining was positive.

Another specimen was cultured, and identified as *Rhizopus nigricans* (Fig. 3).

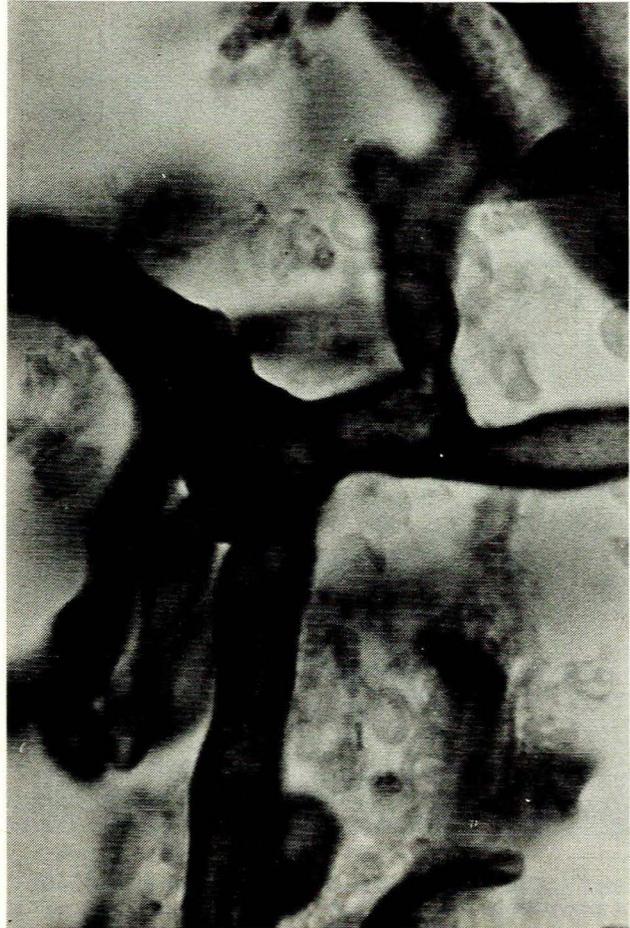


Fig. 3. The causative organism *Rhizopus nigricans*.

Treatment

Although trimethoprim sulphamethoxazole has been used in subcutaneous phycomycosis, the most effective drug for the other forms is amphotericin B.

Because of the well-known toxicity of amphotericin B, it was not possible to continue with intravenous treatment for longer than a week. Absorption from the gastrointestinal tract is poor, but with massive oral dosage of 100 mg every 6 hours for 5 months, a cure was effected. In the adult patient a dose of 3 g/day would keep serum levels between 0,1 - 0,5 µg/ml. Amphotericin B is very active against mucormycosis at doses between 0,01 and

0,1 mg/kg.⁴ The side-effects of amphotericin B taken orally are much less severe than with the intravenous form.

After 5 months on amphotericin B the patient developed diarrhoea that was easily controlled by discontinuing the drug. Biopsies done at this time were negative, and the amphotericin B was stopped permanently (Fig. 4).

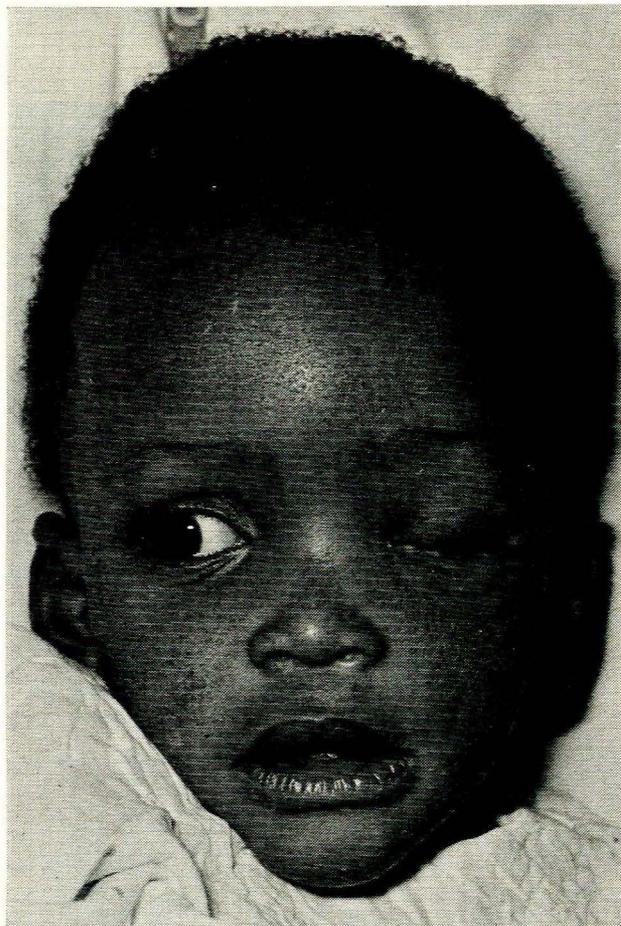


Fig. 4. The patient after 5 months of treatment, with a permanently blind left eye.

At this time the swelling of the left side of the face had disappeared completely, the eye was permanently blind and the palatal defect was closed. To date, the infant has been in good health.

DISCUSSION

Mucormycosis is an acute, frequently fatal, fungal disease, characterised by the occurrence in tissue of broad non-septate hyphae, which tend to grow into arteries and produce thrombosis and infarction. The infection nearly always develops in a person whose resistance is lowered by a metabolic disorder, blood dyscrasia, corticosteroid therapy or malnutrition.⁵

In the differential diagnosis, especially in the presence of diabetes with acidosis, *Phycomyces* should be suspected in cases of acute and rapidly spreading sinusitis, cellulitis

in orbital tissues and even in bronchial or lobar pneumonia. Isolation of the fungus should be attempted at the earliest opportunity if a diagnosis is to be made before the fatal termination of this usually fulminating disease.

The natural course of phycomycosis caused by species of *Absidia*, *Rhizopus* and *Mucor* is characterised by rapid growth in necrotic tissue. Among the 78 patients reviewed by Baker in 1968,⁵ 46% were under the age of 10 years and 82% under 21 years. Martinson and Clark⁶ found a male preponderance of 10:1. Patients complained of discomfort from swollen tissues about the face but not pain.

Rhinocerebral mucormycosis usually begins in the nasal mucosa and extends to the palate, the paranasal sinuses, orbit, face and brain. Extension from the nasal mucosa to the nasal sinuses may cause clouding of the sinuses and the appearance of a tumour due to mucosal invasion by hyphae. The causative fungus probably reaches the tissues of the orbital cavity from the nasal cavity or the paranasal sinuses, especially the ethmoid air cells.^{7,8} The infection may extend through the roof of the orbit producing mucormycosis of the brain. The fungus may invade the palate causing perforation due to infarction. Thrombosis and hyphae can be demonstrated in the blood vessels of the palate in many cases,⁹ and are the cause of a bloodless field when biopsy specimens are taken.

Diagnosis is never easy, but according to Smith and Kirchner¹⁰ the following symptoms are usual: a blood-tinged nasal discharge of short duration and facial pain on the same side; soft peri-orbital or perinasal swelling going on to discoloration, induration, and progressive vascular occlusion; ptosis of the eyelid, proptosis of the eyeball, and complete ophthalmoplegia; multiple unrelated cranial and systemic palsies, and black necrotic turbinates, easily mistaken for dried, crusted blood.

Little is known about the immunology of phycomycosis. Evidence such as its rarity, the ubiquity of spores of the fungi in a human environment, the tendency to spontaneous recovery in the subcutaneous forms and the fact that it is not infectious, all suggest that man possesses good natural resistance to this infection.

Phycomycosis infections appear to be increasing in frequency and in medical importance, and many more species of *Phycomyces* are pathogenic for man and animal than was previously thought. It should be noted that ordinary pus swabs usually give cultures for other organisms but not for *Phycomyces*. A biopsy specimen of the necrotic tissue is much more rewarding, and the disease can easily be diagnosed by means of histology and culture. It is always desirable to do cultures in order that positive identification of the specific genus can be made.

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