CASE REPORT

Deadly Orbital Mucormycosis, Rare Yet Possible Infection

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ABSTRACT

An adult male patient presented with right eye (RE) proptosis. After history and investigations a working diagnosis of orbital pseudotumour was made. The patient presented without any identifiable risk factors of mucormycosis. Biopsy results confirmed the diagnosis of mucormycosis.

CASE SCENARIO:

A 39 year old man presented to the University Teaching Hospital (UTH) eye clinic with complaints of right sided headache, poor vision right eye (RE) for 2 months, tearing RE, numbness right brow and right side of face for 1 month. Left eye (LE) was fine and patient had no complaints concerning it.

In the past medical history patient had been seen at a private hospital three days earlier and was started on 30mg oral prednisolone of which patient noticed some improvement. Family History was unremarkable and drug history was as above.

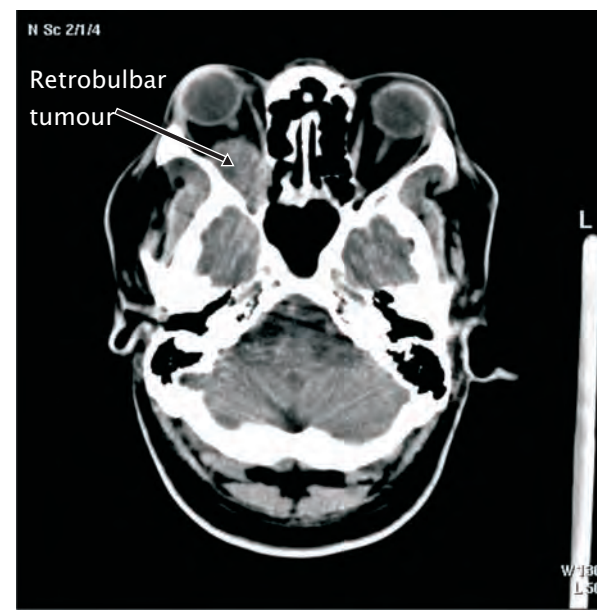
Ocular examination showed Visual Acuity (VA), RE 6/60 and LE 6/6, Near Vision RE 24 LE 5 and Colour Vision was abnormal for RE. RE Proptosis measured by Hartel's was RE 25mm and LE 18mm giving 7mm difference. The Extraocular motility was restricted laterally RE and there was Relative Afferent Pupillary Defect (RAPD) whereas the LE pupil was normal. Systemic examination was unremarkable.

Provisional diagnosis of Orbital Pseudo-tumour RE was made. Full Blood Count and Erythrocyte Sedimentation Rate (ESR) were normal.

The CT Scan performed reported a tumour measuring 35 x 23 mm in the retro-bulbar space and anterior temporal lobe. The tumour was displacing the optic nerve superiorly and encasing lateral and medial recti muscles. The conclusion reached was orbital pseudo-tumour RE with a differential diagnosis of lymphoma.

The CT Scan film below shows the retro-bulbar tumour described in the report

Other investigations done were fasting Blood Sugar which was normal (5.1 mmol/L), retroviral test, (non-reactive), and the peripheral smear was non-revealing.



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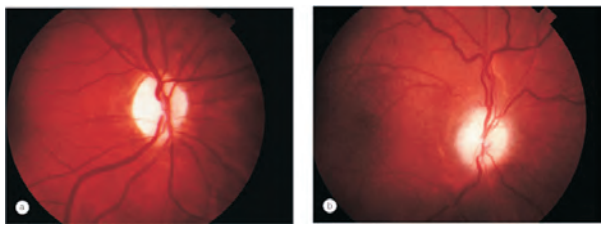
The patient was put on high dose oral prednisolone starting with 80mg then tapered by 5mg on every third day until the drug was stopped.

Ptosis and ophthalmoplegia developed in both eyes. The optic nerve disc / head became pale as shown in the picture below.



Neurosurgeon was urgently consulted and noted the similar findings. Craniotomy, orbital roof decompression and biopsy was done. The biopsy results revealed fungal elements isolated; with a conclusion of mucormycosis.

The patient was commenced on Amphotericin B, 50 mg IV for 21 days then once per week for 6 weeks. Following this treatment the RE pain reduced, proptosis reduced but VA was still NPL. Follow up CT Scans showed a shrunk tumour, though sinuses were still involved. The patient is currently on fluconazole 200mg once per day for life.

Patient also received carbamazepine in the retro-bulbar space to reduce the pain of the RE. Repeat biopsy done at the University Teaching Hospital (UTH) by the Ear Nose and Throat (ENT) surgeons also revealed mucormycosis.

DISCUSSION

Mucormycosis is the term used to describe fungal infections caused by fungi in the order Mucorales,[1] and *Mucor, Rhizopus, Absidia,* and *Cunninghamella* species are most frequently implicated. Mucormycosis is also known as Zygomycosis. Mucormycosis is caused by common fungi frequently found in the soil and in decaying vegetation. Most individuals are exposed to these fungi on a daily basis, but people with immune disorders may be more susceptible to infection.[2]

Conditions most commonly associated with mucormycosis include diabetes (usually poorly controlled diabetes), chronic steroid use, metabolic acidosis, organ transplantation, leukemia/lymphoma, treatment with deferoxamine, and HIV/AIDS.[3] Mucormycosis frequently involves the sinuses, brain, or lungs as the sites of infection. While oral or cerebral Mucormycosis are the most common types of the disease, this infection can also manifest in the gastrointestinal tract, skin, and in other organ systems.[4] In rare cases, the maxilla may be affected by Mucormycosis.[5]

The rich vascularity of maxillofacial areas usually prevents fungal infections, although more prevalent fungi, such as those responsible for Mucormycosis, can often overcome this difficulty.[5] Trauma and the use of contaminated medical supplies over wounds are associated with cutaneous mucormycosis. In addition, patients with burns and those who use intravenous drugs are at a higher risk. Some patients with mucormycosis have no identifiable risk factors.

Manifestation of mucormycosis

There are several ways mucormycosis can manifest. One such manifestation is direct fungal invasion into the vascular network which results in thrombosis and death of surrounding tissue by loss of blood supply.[6] If the disease involves the brain then one would present with one sided headache behind the eyes, facial pain, fevers, nasal stuffiness that progresses to black discharge, and acute sinusitis along with swelling of the eye.[7] Affected skin may appear relatively normal during the earliest stages of infection. This skin quickly progresses to an erythmic (reddening, occasionally with oedema) stage, before eventually turning black due to necrosis.[7]

Rhinocerebral disease may manifest as unilateral, retro-orbital headache, facial pain, numbness, fever, and nasal stuffiness that progress to black discharge. Initially, mucormycosis may mimic sinusitis.[4] Late symptoms that indicate invasion of the orbital nerves and vessels include diplopia and visual loss. These late symptoms indicate a poor prognosis and are usually followed by reduced consciousness. The clinical findings one may get would be:

- Orbital swelling and facial cellulitis are progressive. Black pus discharges from the necrotic palatine or nasal eschars.

- Proptosis, ptosis, chemosis, and ophthalmoplegias indicate retro-orbital extension. Cranial nerves V and VII are the most commonly affected. Loss of vision can occur with retinal artery thrombosis.
- A reduced conscious state denotes brain involvement.[4]

Our patient presented classically with rhinocerebral disease and had the symptoms and signs fitting with the same disease pattern. Its interesting to note that the patient presented with no risk factors at all.

Other forms of mucormycosis can occur depending of which part of the body is affected.

1. This would include lung (pulmonary) mucormycosis which could present with:
   - Persistent cough (occasionally bloody)
   - Fever
   - Shortness of breath.[4]

Most patients with pulmonary disease have malignancies and a history of neutropenia. Lung examination may reveal decreased breath sounds and riles.[4]

2. Gastrointestinal (GI) mucormycosis usually affects severely malnourished individuals. This may manifest with:

Abdominal pain and/or mass
Haematamesis
Bloody stool.[4]

3. Symptoms of kidney (renal) mucormycosis include:
   - Fever
   - Flank (side) pain
   - Renal failure.[4]

4. Symptoms of skin (cutaneous) mucormycosis include a single painful hardened area of skin that may have a blackened center.[4]

5. Central Nervous System (CNS) disease manifests as headache, decreasing consciousness, and focal neurologic symptoms. Patients with CNS involvement may have a history of open head trauma, drug use, or malignancy.[5]

Mortality/Morbidity

Mucormycosis carries a very high mortality rate (60-95%).[4] Pulmonary and GI diseases carry an even higher mortality rate because these forms are typically diagnosed late in the disease course. Rhinocerebral disease causes significant morbidity in patients who survive because treatment usually requires extensive, and often disfiguring, facial surgery.[6]

Race

There are no racial factors that predispose people to mucormycosis.[6]

Sex

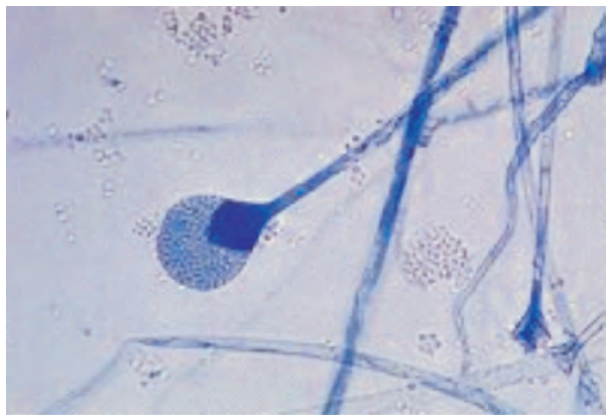
Sex is not likely to affect the occurrence of mucormycosis because the underlying conditions are the major predisposing factors. Reviews of cases from single institutions show an equal sex distribution. However, a recent review of all published cases of pulmonary mucormycosis performed by Lee et al (1999) showed a male-to-female ratio of 3:1[3]

Age

Mucormycosis is found in patients of a wide age range.[4]

EXAMS, TESTS AND DIAGNOSIS

Mucormycosis should be suspected if symptoms appear in individuals with immune disorders such as diabetes, HIV/AIDS or those with weakened immune systems such as transplant recipients. Depending on where the symptoms are, CT scans or MRIs may be done. Evaluation by specialist is recommended as dictated by the part of the body suspected to be involvement. A tissue specimen must be taken and analyzed in order to make a definitive diagnosis of mucormycosis. As swabs of tissue or discharge are generally unreliable, the diagnosis of Mucormycosis tends to be established by a biopsy specimen of the involved tissue.[9]



This photomicrograph reveals a mature sporangium of a Mucor species fungus, which can be responsible for Mucormycosis.

TREATMENT

Prompt amphotericin B (50mg once per day) therapy should be administered due to the rapid spread and mortality rate of the disease.[4,8,10] Amphotericin B works by damaging the cell walls of the fungi and is administered for a further 4–6 weeks after initial therapy begins to ensure eradication of the infection. Posaconazole has been shown to be effective against Mucormycosis, perhaps more so than amphotericin B, but has not yet replaced it as the standard of care.[8,10]

After administration of either amphotericin B or Posaconazole, surgical removal of the "fungus ball" may be indicated. The disease must be monitored carefully for any signs of reemergence.[4,8]

Surgical therapy can be very drastic, and in some cases of Rhinocerebral disease removal of infected brain tissue may be required. In some cases surgery may be disfiguring because it may involve removal of the palate, nasal cavity, or eye structures.[7] Surgery may be extended to more than one operation.[4] It has been hypothesised that hyperbaric oxygen may be beneficial as an adjunctive therapy because higher oxygen pressure increases the ability of neutrophils to kill the organism.[6,10]

Mucormycosis may be treated right away with surgery to remove all dead and infected tissue, along with intravenous (directly into a vein) antifungal therapy. Surgical removal of infected tissue may be disfiguring because it may involve removal of the palate, parts of the nose, or parts of the eye. Without his aggressive surgery, however, chances of survival are greatly decreased.

PROGNOSIS

In most cases, the prognosis of Mucormycosis is poor and has varied mortality rates depending on its form and severity. In the rhinocerebral form, the mortality rate is between 30% and 70%, whereas disseminated Mucormycosis presents with the highest mortality rate in an otherwise healthy patient, with a mortality rate of up to 90%.[6] Patients with AIDS have a mortality rate of almost 100%.[8]

Possible complications of Mucormycosis include the partial loss of neurological function, blindness and clotting of brain or lung vessels.[7] Mucormycosis has an extremely high mortality rate even with aggressive surgical intervention. Death rates range from 25 - 90% depending on the body area involved and the individual's underlying immune problems.

PREVENTION

Because the fungi that cause mucormycosis are widespread, the most appropriate preventive measures involve improved control of the underlying illnesses associated with mucormycosis.

REFERRENCES

1. James, William D.; Berger, Timothy G.; et al. (2006). Andrews' Diseases of the Skin: clinical Dermatology. Saunders Elsevier. ISBN 0-7216-2921-0.
2. Rinaldi M.G. (1989). "Zygomycosis". *Infect Dis Clin North Am* 3: 19–41.
3. Lee F.Y.; Mossad S.B.; Adal K.A. (1999). "Pulmonary mucormycosis: the last 30 years". *Arch Intern Med* 159: 1301–9.
4. Nancy F Crum-Cianflone, MD MPH. "Mucormycosis". eMedicine. http://www.emedicine.com/med/topic1513.htm. Retrieved 2008-05-19.
5. Auluck A (2007). "Maxillary necrosis by mucormycosis. a case report and literature

review" (PDF). Med Oral Patol Oral Cir Bucal 12 (5): E360–4. PMID 17767099. http://www.medicinaoral.com/medoralfree01/v12i5/medoralv12i5p360.pdf. Retrieved 2008-05-19.

6. Spellberg B, Edwards J, Ibrahim A (2005). "Novel perspectives on mucormycosis: pathophysiology, presentation, and management". *Clin. Microbiol*. Rev. 18 (3): 556–69. doi:10.1128/CMR.18.3.556-569.2005. PMID 16020690. http://cmr.asm.org/cgi/content/full/18/3/556. Full text at PMC: 1195964
7. "MedlinePlus Medical Encyclopedia: Mucormycosis". http://www.nlm.nih.gov/medlineplus/ency/article/000649.htm. Retrieved 2008-05-19.
8. Rebecca J. Frey, PhD. "Mucormycosis". Health A to Z. http://www.healthatoz.com/healthatoz/Atoz/clients/haz/general/custom/default.jsp. Retrieved 2008-05-19
9. Roden MM, Zaoutis TE, Buchanan WL, et al (September 2005). "Epidemiology and outcome of Mucormycosis: a review of 929 reported cases". *Clin. Infect. Dis*. 41 (5): 634–53. doi:10.1086/432579. PMID 16080086.http://www.journals.uchicago.edu/doi/abs/10.1086/432579. Retrieved 2008-05-19.
10. Stevens DA. Aspergillosis. In: Goldman L, Ausiello D, eds. Cecil Medicine. 23rd ed. Philadelphia, Pa: Saunders Elsevier; 2007: chap 360.