CLINICAL COMMENTARY

Sinonasal mucormycosis: Case report


ENT and Head and Neck Surgery Department, La Timone Adults Hospital, 1, boulevard Jean-Moulin, 13005 Marseille, France

Available online 30 March 2010

KEYWORDS
Mucormycosis; Endoscopic treatment; Posaconazole

Summary
Objectives: To present and discuss the case of a diabetic patient admitted with acidoketotic coma, with inner canthus tumefaction due to mucormycosis.

Case study: A 38-year-old diabetic man was admitted with acidoketotic coma and poor general health status. Clinical examination found right inner canthus tumefaction and mucopurulent rhinorrhea. Endoscopy of the nasal fossae found medial meatus sphaceluses. Sinus CT scan found a bilateral ethmoid infiltrating and osteolytic infectious process. Emergency endoscopic bilateral ethmoidectomy was performed. Mucormycosis was diagnosed, and liposomal amphotericin B was administered intravenously for 1 month then replaced by posaconazole. The patient was followed up monthly; the antifungal treatment was terminated after 8 months, the disease appearing to have resolved.

Comments and conclusion: Mucormycosis is one of the most rapidly fatal fungal infections. Facial and cerebral CT scan is essential and is systematically abnormal in case of sinonasal mucormycosis. Emergency multidisciplinary treatment should address the diabetes and include rapid surgical debridement and effective antifungal medication. The reference antifungal is amphotericin B, to be administered at maximal dose (3 to 5 mg/kg per day). Posaconazole, available in Europe since July 2005, proved successful in the present case.

© 2010 Published by Elsevier Masson SAS.

Introduction
Mucormycosis is one of the most rapidly fatal fungal infections in humans. It occurs in diabetic patients in acidoketotic coma or in profound immunodepression. The most characteristic clinical feature is rhino-orbito-cerebral involvement. The present case exemplifies the therapeutic and diagnostic issues raised by this pathology.

Case study
A 38-year-old man was admitted with acidoketotic coma. Twenty days later, when his diabetic state was stabilized, painful inflammatory tumefaction appeared in the right hemiface, with deterioration of general health status and bilateral mucopurulent rhinorrhea without fever. Biological analysis found an inflammatory biological syndrome (hyperleukocytosis at 15 G/l, CRP at 12 mg/l). Facial CT scan found right ethmoid sinusitis, and the patient was transferred to ENT. Nasal fossae endoscopy found bilateral diffuse whitish filaments, which were sampled for biopsy, and an aspect of sphaceluses in the medial meatuses. CT control at 48 hours...
found an osteolytic infiltrating infectious process (bilateral ethmoid opacity and lysis of the right papyraceous lamina and lachrymal bone and osteitis of the nasal bone) (Fig. 1). Cerebral and sinus MRI confirmed the absence of brain lesion. Mucormycosis was suspected, and endonasal surgery was immediately undertaken without waiting for the biopsy results, comprising right ethmoidectomy and right medial meatomty, and left anterior ethmoidectomy with anatomopathologic, biologic and mycologic sampling. Direct examination found large mycelial filaments with a crumpled aspect associated with signs of ischemic necrosis, confirming diagnosis. IV liposomal amphotericin B (3 mg/kg per day) was initiated. Evolution was favorable as of the first week, with cessation of pain and regression of the hemifacial edema. After 1 month, the IV treatment was replaced by oral posaconazole (400 mg twice daily). At 2 months, on readmission for surveillance, the clinical symptomatology had resolved, but sinus CT found persistent lysis of the skull base, ethmoid papyraceous lamina and right lachrymal bone (Fig. 2). Endonasal samples were free of mycotic agents, and the patient therefore underwent no further complementary surgery. He was followed up monthly for 1 year (Fig. 3). Antifungal medication was withdrawn after 8 months.

Discussion

Epidemiologically, the factors predisposing to mucormycosis are acidoketosis (in diabetes or renal insufficiency) and immunodepression (organ transplant, HIV infection, corticotherapy, deferoxamine treatment, prolonged neutropenia) [1—3]. Some rare cases have been reported in patients without obvious immune deficiency [4]. Mucormycosis is most frequently sinonasal (39%), then pulmonary (24%), cutaneous (19%), cerebral (9%), gastro-intestinal (7%), other (6%) or disseminated (6%) [5]. The entry point is usually respiratory, by spore inhalation, or more rarely by digestion or percutaneous inoculation. Inter-human contamination has never been reported [6]. Incidence is increasing, and in 2006 mucormycosis ranked third among opportunistic deep fungal infections, after candidiasis and aspergillosis [3,5,7]. It is due to a ubiquitous (soil, bread mold, manure, rotting vegetables) mucoral fungus [1]. The later the diagnosis, the poorer the survival [5]. Facial and cerebral CT is the essential examination, and is systematically abnormal in rhinocerebral mucormycosis [1,8]. The most frequent radiologic signs are osteolysis, nodular thickening of the sinus mucosa and absence of sinal fluid level [1]. Other affected areas are the lateral wall of the nasal fossae, septum, maxillary sinus, palate and orbit [1,3]. CT determines lesion extension towards the orbit and brain. MRI is more effective in assessing vascular (cavernous sinus or internal carotid thrombosis) and cerebral invasion, and can screen for cerebral involvement before onset of clinical signs [2]. Without treatment, mucormycosis is generally fatal [1—3,5,7], and even with early treatment recovery is achieved in only 40% of cases [5]. Management comprises addressing predisposing factors, and rapid surgical debride-
delay in treatment initiation [5]). Among treatment options, even partial resection of necrotic and/or infected tissue is preferable to abstention, and antifungal medication is consistently more effective when associated to surgery [3,5]. The partial functional endonasal surgery performed in the present case, however, cannot be taken as a recommendation backed up by a high-level of evidence. The reference antifungal is amphotericin B, to be administered at maximal dose despite its immediate side effects (fever, lowered blood pressure, vomiting) and nephrotoxicity [3,5,7]. Clinical and biological tolerance is better with lipid formulae: liposomal (Ambisome®), colloidal (Amphocil®), or lipid complex (Abelcet®), with the drawback that these can only be administered intravenously. Despite its proven in vitro anti-mucoral action, itraconazole was judged inappropriate in 2007 [3,5]. Posaconazole, available since July 2005 [9,10], was used in oral form with success in the present case. Caspofungin would seem to potentiate amphotericin B [10], and efficacy studies are in progress. Hyperbaric oxygen therapy makes a useful contribution in case of resistance to medico-surgical treatment [3].

Conclusion

Management of patients suffering from mucormycosis should be multidisciplinary and initiated without delay. High-dose Ambisome® (3 to 5 mg/kg) should be prescribed for 1 month, with early surgery and subsequent replacement by posaconazole (800 mg/day). There is no consensus as to total treatment duration, which varies according to individual clinical evolution.

Conflict of interest statement

The authors have not communicated any conflicts of interest.

References