Mycoses Study Group (EORTC/MSG) Consensus Group. *Clin Infect Dis* 2008; 46: 1813–1821.
14. de Hoog GS, Guarro J, Gene J, Figueras MJ (eds). *Atlas of clinical fungi*, 2nd edn. Utrecht: Centraalbureau voor Schimmelcultures/Universitat Rovira i Virgili, 2000; 305–309 and 899–901.
15. National Committee for Clinical Laboratory Standards (NCCLS). *Reference method for broth dilution antifungal susceptibility testing of filamentous fungi; approved standard. NCCLS document M38-A*. Wayne, PA: NCCLS, 2002.
16. Australian Bureau of Statistics. *Population by age and sex, Australian States and Territories*, Canberra: Australian Bureau of Statistics, 2004; 3201.0.
17. Sahi H, Avery RK, Minai OA *et al.* *Scedosporium apiospermum* (*Pseudallesacheria boydii*) infection in lung transplant recipients. *J Heart Lung Transplant* 2007; 26: 350–356.
18. Symoens F, Knoop C, Schrooyen M *et al.* Disseminated *Scedosporium apiospermum* infection in a cystic fibrosis patient after double-lung transplantation. *J Heart Lung Transplant* 2006; 25: 603–607.
19. Tamm M, Malouf M, Glanville A. Pulmonary *Scedosporium* infection following lung transplantation. *Transpl Infect Dis* 2001; 3: 189–194.
20. Gilgado F, Serena C, Cano J, Gene J, Guarro J. Antifungal susceptibilities of the species of the *Pseudallescheria boydii* complex. *Antimicrob Agents Chemother* 2006; 50: 4211–4213.
21. Gilgado F, Cano J, Gene J, Serena C, Guarro J. Different virulence of the species of the *Pseudallescheria boydii* complex. *Med Mycol* 2008; 24: 1–4.

Rhinocerebral mucormycosis in patients without predisposing medical conditions: a review of the literature

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Abstract

Rhinocerebral mucormycosis is a rare disease, affecting almost exclusively patients with known predisposing conditions such as diabetes mellitus, immunocompromised status, haemochromatosis or major trauma. Subsequent to a case of rhinocerebral mucormycosis in a 78-year-old woman without any known risk factor, we reviewed the published English-language literature and found an additional 72 cases. Reviewing all the published case series of mucormycosis involving any site, the proportion of apparently normal hosts among cases of rhinocerebral mucormycosis was found to be 9.06% (95% confidence interval 6.7–11.8). These findings suggest that rhinocerebral mucormycosis in patients without known predisposing factors is more prevalent than was previously believed.

Keywords: Immunocompetent, mucormycosis, predisposing factors, rhinocerebral

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Rhinocerebral mucormycosis, the most common presentation of mucormycosis [1–3] is limited, in most cases, to people with previously recognized risk factors such as diabetes mellitus, immunosuppression, iron overload or after trauma [1,4,5]. Subsequent to a fatal case of rhinocerebral mucormycosis in a patient without known predisposing factors, we reviewed the English-language literature for cases in apparently normal hosts. In addition, we searched for all case series of mucormycosis to determine the relative proportion of patients without previously recognized predisposing conditions among patients with rhinocerebral mucormycosis.

Case Report

A 78-year-old woman presented to the emergency room with left palate pain and somnolence. The patient's medical history was remarkable only for hypertension, treated with hydrochlorothiazide. The white blood cell count was 19 400 cells/μL, with 92% neutrophils and the serum sodium level was 106 mmol/L. A loose tooth seen in the left upper jaw was removed, intravenous normal saline and amoxicillin/clavulanic acid was started and the patient's condition improved significantly.

On the fourth hospital day, right eye chemosis, ptosis and lateral gaze palsy with central retinal artery thrombosis appeared, followed by disarthria and right hemiparesis. Magnetic resonance imaging of the brain revealed pansinusitis

TABLE 1. Characteristics of patients suffering from rhinocerebral mucormycosis, with no underlying predisposing conditions (*n* = 73)

Characteristic	*n* (%)	Mortality *n* (%)
Age, mean ± SD (range)	41.5 ± 18 (0.17–82)	–
Male : female ratio	2:1	26/8 (54/33)
Country		
India	39 (53)	22 (56)
USA	15 (21)	8 (53)
Asia (other than India)	9 (12)	2 (22)
Europe and Israel	6 (8)	1 (17)
Other	4 (5)	1 (25)
Clinical presentation (applicable for 72/73; 99%)		
Isolated sinus	27 (37)	8 (30)
Sino-orbital	13 (18)	4 (31)
Rhinocerebral	32 (44)	20 (63)
Positive culture (was done for 29/73; 40%)[a]	13/29 (45)	–
Treatment (applicable for 55/73, 75%)		
Surgery + antifungal[a]	42 (76)	11 (26)
Antifungal alone[b]	8 (15)	4 (50)
Surgery alone	5 (9)	2 (40)
Total death rate	34 (47)	

[a]*Apophysomyces elegans*, *n* = 6; *Rhizopus* species, *n* = 4; *Mucor pusillus*, *Cunninghamella* and *Actinomucor elegans* were described once.
[b]Antifungal, amphothricin B 47/50 (94 %) including four liposomal amphothricin B.

and a high signal in the left parietal cortex, compatible with acute cerebral infarction. A lumbar puncture was performed. The cerebrospinal fluid contained 280 leukocytes/μL (124 neutrophils), with normal protein and glucose; the Gram stain was negative. An orbital biopsy specimen obtained during functional endoscopic sinus surgery, showed necrosis of fibroadipose tissue and hyphal elements within blood vessel walls. The hyphae were broad, branching at right angles without septations, consistent morphologically with mucormycosis. Cultures obtained at operation yielded *Pseudomonas aeruginosa* but were negative for fungal growth. Liposomal amphotericin B and cefepime were begun but the patient was comatose and expired 2 weeks later.

Literature review

We performed a MEDLINE search for articles published in the English-language literature up to December 2007. The search terms used were: zygomycosis, mucormycosis or phycomycosis, as well as one of the terms: sinusitis, rhinocerebral, rhino-orbito-cerebral or cerebral.

TABLE 2. Case series of patients with rhinocerebral mucormycosis

Author (reference)	Year[a]	Country	Years[b]	Cases	Number of patients without predisposing factors	Death rate (%)
Addlestone and Baylin [7]	1975	USA	1964–1974	9	1	3/9 (33)
Pillsbury and Fisher [25]	1977	USA	1963–1977	13	1	2/13 (15)
Marchevsky *et al.* [43]	1980	USA	1958–1978	12	0	9/12 (75)
Blitzer *et al.* [44]	1980	USA	1972–1979	9	0	4/9 (44)
Centeno *et al.* [45]	1981	USA	5 years	10	1	6/10 (60)
Kurrasch *et al.* [46]	1982	USA	1970–1982	14	2	8/14 (57)
Maniglia *et al.* [47]	1982	USA	1977–1982	8	0	2/8 (25)
Ferry and Abedi [48]	1983	USA	1959–1981	16	1	11/16 (69)
Abedi *et al.* [49]	1984	USA	1957–1982	18	0	4/16 (25)
Rangel-Guerra *et al.* [50]	1985	Mexico	1970–1985	8	0	5/8 (62)
Parfrey NA [16]	1986	USA	1941–1983	14	2	6/13 (46)
Gamba *et al.* [51]	1986	USA	6 years	10	0	5/10 (50)
Ochi *et al.* [17]	1988	USA	6 years	11	2	9/11 (82)
Ferguson *et al.* [52]	1988	USA	1969–1988	12	0	6/12 (50)
Chetchotisakd *et al.* [53]	1991	Thailand	5 years	11	0	8/11 (73)
Nussbaum and Hall [54]	1994	USA	1979–1992	11	2	7/11 (64)
Shpitzer *et al.* 55]	1995	Israel	1981–1995	10	0	8/10 (80)
Rangel-Guerra *et al.* [56]	1996	Mexico	1980–1995	22	0	7/22 (32)
Peterson *et al.* [57]	1997	USA	1955–1995	28	1	8/28 (29)
Jiang and Hsu [58]	1999	China	1985–1997	15	0	6/15 (40)
Alobid *et al.* [59]	2001	Spain	1994–1999	5	0	0/5 (0)
Sohail *et al.* [60]	2001	Oman	8 years	9	0	3/9 (33)
Chakrabarti *et al.* [61]	2001	India	1990–1999	34	8	10/34 (29)
Talmi *et al.* [62]	2002	Israel	5 years	19	0	10/19 (53)
Petrikkos *et al.*[63]	2003	Greece	1993–2002	11	0	7/11 (64)
Nithyanandam *et al.* [64]	2003	India	1992–2000	34	0	16/34 (47)
Khor *et al.* [65]	2003	Taiwan	1988–2000	21	1	5/21 (24)
Dhiwakar *et al.* [33]	2003	India	1997–2000	8	1	6/8 (75)
Hosseini and Borghei[66]	2005	Iran	2000–2004	10	0	4/10 (40)
Safar *et al.* [67]	2005	Canada	1998–2003	7	0	4/7 (57)
Sundaram *et al.* [37]	2005	India	1971–2001	56	17	50/56 (89)
Al-Ajam *et al.* [68]	2006	Lebanon	1981–1999	12	0	7/12 (58)
Mohindra *et al.* [42]	2007	India	1997–2005	27	7	9/27 (33)
Cheema and Amin [69]	2007	Pakistan	4 years	5	0	2/5 (40)
Total				519	47[c]	257/519 (49.5)

[a]Year of publication.
[b]Inclusion period.
[c]The proportion of patients without predisposing factor is 9.06% (95% confidence interval 6.7–11.8).

All cases of patients with no predisposing factors (diabetes mellitus; immune suppression; intravenous drug abuse; iron overload or deferoxamine treatment; s/p trauma recently in the same area of mucormycosis infection): Cases included were those with acute mucormycosis infection in the rhinocerebral region diagnosed by histology with or without a positive culture, when no known predisposing conditions for rhinocerebral mucormycosis were reported and data regarding outcome were available. Our search yielded a total of 73 cases including the present case [2,3,6–42] (Table 1).

Patients with no predisposing factors from case series: Our search was limited to case series of all consecutive proven mucormycosis infections in a defined period, which included cases of the rhinocerebral type. Series pertaining to oncological medical centres only, were excluded. Our search yielded 34 case series meeting our criteria that included 519 patients with rhinocerebral mucormycosis [7,16,17,25,33,37,42–69] (Table 2). The overall mortality rate in these cases was 49.5% (49.3% in cases with predisposing factors). Forty-seven out of 519 cases of rhinocerebral mucormycosis from these case series (9.06%, 95% confidence interval 6.7–11.8) were found in patients without known underlying conditions for mucormycosis.

Discussion

The agents of mucormycosis rarely cause disease as a result of their low virulence potential. Undefined defects of macrophages and neutrophils present in diabetic and steroid-treated patients, and deferoxamine treatment, allow replication of this mould [70]. The diagnosis was delayed in our case of rhinocerebral mucormycosis because of the lack of any known predisposing factors. Moreover, rhinocerebral mucormycosis can occur without noticeable sinus involvement, a presentation that could further delay the diagnosis. Because a combination of urgent surgery and early administration of an antifungal drug are crucial for possible cure, delayed diagnosis frequently results in death.

In a literature review of 929 cases of all sites mucormycosis, 9.6% were found to have no predisposing factors, although the data were not stratified according to the site of body involved [1]. Most of the cases without risk factors in that review (50%) were of the cutaneous form. In a 30-year literature review for pulmonary mucormycosis, 87 cases were found, with 13% of them having no apparent underlying illness [71]. In the current case series review, we found that in rhinocerebral mucormycosis, the proportion of patients without recognized predisposing factors is 9.06% (95% confidence interval 6.7–11.8). This is an unexpected high proportion but it is consistent with the data of pulmonary mucormycosis [71]. Although this proportion was extracted from reported case series and could reflect a publication bias, and no doubt case series are not representative of true prevalence and incidence, rhinocerebral mucormycosis is not common enough for adequate study designs and our estimate is probably the best proxy available.

The mortality rate in the 73 patients with rhinocerebral mucormycosis and without apparent known predisposing conditions (47%) was similar to that found in the case series review of overall rhinocerebral mucormycosis (49.5%). The mortality rate was significantly higher when the central nervous system was involved compared to sinus or sino-orbital involvement only (63% vs. 30% and 31%, respectively), as also reported by others [1].

Seven patients in our review suffered from chronic sinusitis or nasal polyps [6,15,19,27,30,39]. Four of these underwent a nasal or sinus procedure prior to their illness and two additional patients underwent recent tooth extraction (four and present case). These data might suggest that chronic sinusitis and local surgery are additional risk factors for rhinocerebral mucormycosis. The finding that the majority of cases occurred in developing countries suggests that there may be other predisposing conditions, such as malnutrition.

In summary, our review suggests that a considerable proportion of rhinocerebral mucormycosis cases occur in patients without previously recognized predisposing factors. The characteristics and outcome of these patients are similar to those occurring in patients with the known underlying conditions. Whenever compatible clinical features for rhinocerebral mucormycosis are encountered, the absence of predisposing factors should not be used to exclude this dreadful disease, and maintaining a high index of suspicion may lead to timely diagnosis and therapy.

Transparency Declaration

All authors had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. There are no conflicts of interest and no financial support to declare.

References

1. Roden MM, Zaoutis TE, Buchanan WL *et al.* Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis* 2005; 41: 634–653.
2. Watson DF, Stern BJ, Levin ML, Dutta D. Isolated cerebral phycomycosis presenting as focal encephalitis. *Arch Neurol* 1985; 42: 922–923.

3. Chopra H, Dua K, Malhotra V, Gupta RP, Puri H. Invasive fungal sinusitis of isolated sphenoid sinus in immunocompetent subjects. *Mycoses* 2006; 49: 30–36.
4. Prabhu RM, Patel R. Mucormycosis and entomophthoramycosis: a review of the clinical manifestations, diagnosis and treatment. *Clin Microbiol Infect* 2004; 10 (suppl 1): 31–47.
5. Garcia-Covarrubias L, Bartlett R, Barratt DM, Wassermann RJ. Rhino-orbitocerebral mucormycosis attributable to *Apophysomyces elegans* in an immunocompetent individual: case report and review of the literature. *J Trauma* 2001; 50: 353–357.
6. Blodi FC, Hannah FT, Wadsworth JA. Lethal orbito-cerebral phycomycosis in otherwise healthy children. *Am J Ophthalmol* 1969; 67: 698–705.
7. Addlestone RB, Baylin GJ. Rhinocerebral mucormycosis. *Radiology* 1975; 115: 113–117.
8. Castelli JB, Pallin JL. Lethal rhinocerebral phycomycosis in a healthy adult: a case report and review of the literature. *Otolaryngology* 1978; 86: ORL-696–ORL-703.
9. Rao VR, Pillai SM, Mathews G, Radhakrishnan VV. Cerebral mucormycosis – a case report. *Neuroradiology* 1978; 15: 291–293.
10. Sweeney PJ, Hahn JF, McHenry MC, Mitsumoto H. Mucormycosis presenting as positional nystagmus and hydrocephalus. Case report. *J Neurosurg* 1980; 52: 270–272.
11. Grigoriu D, Bambule J, Delacretaz J, Savary M. Pseudo-tumoral form of fungal frontal sinusitis. *J Dermatol* 1980; 7: 285–287.
12. Dhir SP, Munjal VP, Gupta A, Jain IS. Rhino-orbito-cerebral, mucormycosis. *Indian J Ophthalmol* 1983; 31: 425–427.
13. Kohn R, Hepler R. Management of limited rhino-orbital mucormycosis without exenteration. *Ophthalmology* 1985; 92: 1440–1444.
14. Zak SM, Katz B. Successfully treated spheno-orbital mucormycosis in an otherwise healthy adult. *Ann Ophthalmol* 1985; 17: 344–348.
15. Pennisi AK, Parenti DM, Stevens A, Guest S, Simon GL, Wilson WR. Paranasal sinus mucormycosis in an immunologically competent host. *Am J Otolaryngol* 1985; 6: 471–473.
16. Parfrey NA. Improved diagnosis and prognosis of mucormycosis. A clinicopathologic study of 33 cases. *Medicine* 1986; 65: 113–123.
17. Ochi JW, Harris JP, Feldman JI, Press GA. Rhinocerebral mucormycosis: results of aggressive surgical debridement and amphotericin B. *Laryngoscope* 1988; 98: 1339–1342.
18. Hauman CH, Raubenheimer EJ. Orofacial mucormycosis. *Oral Surg Oral Med Oral Pathol* 1989; 68: 624–627.
19. de Biscop J, Mondie JM, Venries de la Guillaumie B, Peri G. Mucormycosis in an apparently normal host. Case study and literature review. *J Craniomaxillofac Surg* 1991; 19: 275–278.
20. Akpunonu BE, Ansel G, Kaurich JD, Savolaine ER, Campbell EW Jr, Myles JL. Zygomycosis mimicking paranasal malignancy. *Am J Trop Med Hyg* 1991; 45: 390–398.
21. Bhattacharyya AK, Deshpande AR, Nayak SR, Kirtane MV, Ingle MV, Vora IM. Rhinocerebral mucormycosis: an unusual case presentation. *J Laryngol Otol* 1992; 106: 48–49.
22. MacArthur CJ, Lindbeck E, Jones DT. Paranasal phycomycosis in the immunocompetent host. *Otolaryngol Head Neck Surg* 1992; 107: 460–462.
23. Ishida M, Taya N, Noiri T *et al.* Five cases of mucormycosis in paranasal sinuses. *Acta Otolaryngol* 1993; 501: 92–96.
24. Del Valle Zapico A, Rubio Suarez A, Mellado Encinas P, Morales Angulo C, Cabrera Pozuelo E. Mucormycosis of the sphenoid sinus in an otherwise healthy patient. Case report and literature review. *J Laryngol Otol* 1996; 110: 471–473.
25. Pillsbury HC, Fischer ND. Rhinocerebral mucormycosis. *Arch Otolaryngol* 1977; 103: 600–604.
26. Saltoglu N, Tasova Y, Zorludemir S, Dundar IH. Rhinocerebral zygomycosis treated with liposomal amphotericin B and surgery. *Mycoses* 1998; 41: 45–49.
27. Brown SR, Shah IA, Grinstead M. Rhinocerebral mucormycosis caused by *Apophysomyces elegans*. *Am J Rhinol* 1998; 12: 289–292.
28. Sharma RR, Pawar SJ, Delmendo A, Lad SD, Athale SD. Fatal rhino-orbito-cerebral mucormycosis in an apparently normal host: case report and literature review. *J Clin Neurosci* 2001; 8: 583–586.
29. Davel G, Featherston P, Fernandez A *et al.* Maxillary sinusitis caused by *Actinomucor elegans*. *J Clin Microbiol* 2001; 39: 740–742.
30. Ruoppi P, Dietz A, Nikanne E, Seppa J, Markkanen H, Nuutinen J. Paranasal sinus mucormycosis: a report of two cases. *Acta Otolaryngol* 2001; 121: 948–952.
31. Larsen K, von Buchwald C, Ellefsen B, Francis D. Unexpected expansive paranasal sinus mucormycosis. *ORL J Otorhinolaryngol Relat Spec* 2003; 65: 57–60.
32. Chakrabarti A, Ghosh A, Prasad GS *et al. Apophysomyces elegans*: an emerging zygomycete in India. *J Clin Microbiol* 2003; 41: 783–788.
33. Dhiwakar M, Thakar A, Bahadur S. Improving outcomes in rhinocerebral mucormycosis – early diagnostic pointers and prognostic factors. *J Laryngol Otol* 2003; 117: 861–865.
34. Scharf JL, Soliman AM. Chronic rhizopus invasive fungal rhinosinusitis in an immunocompetent host. *Laryngoscope* 2004; 114: 1533–1535.
35. Ketenci I, Unlu Y, Senturk M, Tuncer E. Indolent mucormycosis of the sphenoid sinus. *Otolaryngol Head Neck Surg* 2005; 132: 341–342.
36. Sridhara SR, Paragache G, Panda NK, Chakrabarti A. Mucormycosis in immunocompetent individuals: an increasing trend. *J Otolaryngol* 2005; 34: 402–406.
37. Sundaram C, Mahadevan A, Laxmi V *et al.* Cerebral zygomycosis. *Mycoses* 2005; 48: 396–407.
38. Park SK, Jung H, Kang MS. Localized bilateral paranasal mucormycosis: a case in an immunocompetent patient. *Acta Otolaryngol* 2006; 126: 1339–1341.
39. Deboni MC, Pozzani VR, Lisboa T, Hiraki K, Viplich R, Naclerio-Homem MG. Mucormycosis in an immunocompetent patient: follow-up of 1 year after treatment. *Acta Otolaryngol* 2006; 126: 993–996.
40. Schutz P, Behbehani JH, Khan ZU, Ahmad S, Kazem MA, Dhar R *et al.* Fatal rhino-orbito-cerebral zygomycosis caused by *Apophysomyces elegans* in a healthy patient. *J Oral Maxillofac Surg* 2006; 64: 1795–1802.
41. Jayasuriya NS, Tilakaratne WM, Amaratunga EA, Ekanayake MK. An unusual presentation of rhinofacial zygomycosis due to *Cunninghamella* sp. in an immunocompetent patient: a case report and literature review. *Oral Dis* 2006; 12: 67–69.
42. Mohindra S, Mohindra S, Gupta R, Bakshi J, Gupta SK. Rhinocerebral mucormycosis: the disease spectrum in 27 patients. *Mycoses* 2007; 50: 290–296.
43. Marchevsky AM, Bottone EJ, Geller SA, Giger DK. The changing spectrum of disease, etiology, and diagnosis of mucormycosis. *Hum Pathol* 1980; 11: 457–464.
44. Blitzer A, Lawson W, Meyers BR, Biller HF. Patient survival factors in paranasal sinus mucormycosis. *Laryngoscope* 1980; 90: 635–648.
45. Centeno RS, Bentson JR, Mancuso AA. CT scanning in rhinocerebral mucormycosis and aspergillosis. *Radiology* 1981; 140: 383–389.
46. Kurrasch M, Beumer J 3rd, Kagawa T. Mucormycosis: oral and prosthodontic implications. A report of 14 patients. *J Prosthet Dent* 1982; 47: 422–429.
47. Maniglia AJ, Mintz DH, Novak S. Cephalic phycomycosis: a report of eight cases. *Laryngoscope* 1982; 92: 755–760.
48. Ferry AP, Abedi S. Diagnosis and management of rhino-orbitocerebral mucormycosis (phycomycosis). A report of 16 personally observed cases. *Ophthalmology* 1983; 90: 1096–1104.
49. Abedi E, Sismanis A, Choi K, Pastore P. Twenty-five years' experience treating cerebro-rhino-orbital mucormycosis. *Laryngoscope* 1984; 94: 1060–1062.

50. Rangel-Guerra R, Martinez HR, Saenz C. Mucormycosis. Report of 11 cases. *Arch Neurol* 1985; 42: 578–581.
51. Gamba JL, Woodruff WW, Djang WT, Yeates AE. Craniofacial mucormycosis: assessment with CT. *Radiology* 1986; 160: 207–212.
52. Ferguson BJ, Mitchell TG, Moon R, Camporesi EM, Farmer J. Adjunctive hyperbaric oxygen for treatment of rhinocerebral mucormycosis. *Rev Infect Dis* 1988; 10: 551–559.
53. Chetchotisakd P, Boonma P, Sookpranee M, Pairojkul C. Rhinocerebral mucormycosis: a report of eleven cases. *Southeast Asian J Trop Med Public Health* 1991; 22: 268–273.
54. Nussbaum ES, Hall WA. Rhinocerebral mucormycosis: changing patterns of disease. *Surg Neurol* 1994; 41: 152–156.
55. Shpitzer T, Stern Y, Anavi Y, Segal K, Feinmesser R. Mucormycosis: experience with 10 patients. *Clin Otolaryngol Allied Sci* 1995; 20: 374–379.
56. Rangel-Guerra RA, Martinez HR, Saenz C, Bosques-Padilla F, Estrada-Bellmann I. Rhinocerebral and systemic mucormycosis. Clinical experience with 36 cases. *J Neurol Sci* 1996; 143: 19–30.
57. Peterson KL, Wang M, Canalis RF, Abemayor E. Rhinocerebral mucormycosis: evolution of the disease and treatment options. *Laryngoscope* 1997; 107: 855–862.
58. Jiang RS, Hsu CY. Endoscopic sinus surgery for rhinocerebral mucormycosis. *Am J Rhinol* 1999; 13: 105–109.
59. Alobid I, Bernal M, Calvo C, Vilaseca I, Berenguer J, Alos L. Treatment of rhinocerebral mucormycosis by combination of endoscopic sinus debridement and amphotericin B. *Am J Rhinol* 2001; 15: 327–331.
60. Sohail MA, Al Khabori M, Hyder J, Verma A. Acute fulminant fungal sinusitis: clinical presentation, radiological findings and treatment. *Acta Trop* 2001; 80: 177–185.
61. Chakrabarti A, Das A, Sharma A *et al.* Ten years' experience in zygomycosis at a tertiary care centre in India. *J Infect* 2001; 42: 261–266.
62. Talmi YP, Goldschmied-Reouven A, Bakon M *et al.* Rhino-orbital and rhino-orbito-cerebral mucormycosis. *Otolaryngol Head Neck Surg* 2002; 127: 22–31.
63. Petrikkos G, Skiada A, Sambatakou H *et al.* Mucormycosis: ten-year experience at a tertiary-care center in Greece. *Eur J Clin Microbiol Infect Dis* 2003; 22: 753–756.
64. Nithyanandam S, Jacob MS, Battu RR, Thomas RK, Correa MA, D'Souza O. Rhino-orbito-cerebral mucormycosis. A retrospective analysis of clinical features and treatment outcomes. *Indian J Ophthalmol* 2003; 51: 231–236.
65. Khor BS, Lee MH, Leu HS, Liu JW. Rhinocerebral mucormycosis in Taiwan. *J Microbiol Immunol Infect* 2003; 36: 266–269.
66. Hosseini SM, Borghei P. Rhinocerebral mucormycosis: pathways of spread. *Eur Arch Otorhinolaryngol* 2005; 262: 932–938.
67. Safar A, Marsan J, Marglani O, Al-Sebeih K, Al-Harbi J, Valvoda M. Early identification of rhinocerebral mucormycosis. *J Otolaryngol* 2005; 34: 166–171.
68. Al-Ajam MR, Bizri AR, Mokhbat J, Weedon J, Lutwick L. Mucormycosis in the Eastern Mediterranean: a seasonal disease. *Epidemiol Infect* 2006; 134: 341–346.
69. Cheema SA, Amin F. Five cases of rhinocerebral mucormycosis. *Br J Oral Maxillofac Surg* 2007; 45: 161–162.
70. Ribes JA, Vanover-Sams CL, Baker DJ. Zygomycetes in human disease. *Clin Microbiol Rev* 2000; 13: 236–301.
71. Lee FY, Mossad SB, Adal KA. Pulmonary mucormycosis: the last 30 years. *Arch Intern Med* 1999; 159: 1301–1309.