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Original Research Article

Clinical Profile of Mucormycosis: A Study from Teaching Hospital in North Karnataka, India

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ABSTRACT

Background and objectives: Mucormycosis is a relatively rare opportunistic fungal infection. It is one of the devastating infections of immunocompromised host. Though several studies were done in India and elsewhere on Mucormycosis, it has not been extensively studied of late. The objective of the study is to study the clinical profile of Mucormycosis in the northern part of Karnataka.

Materials and Methods: Our series compromised of 14 cases seen over a period of 5 years. Detailed history, clinical examination, laboratory investigations were carried out in all the cases.

Results: The study group consisted of 10 males and 4 females aged 20 – 70 years (mean 50 years). Most of the patients in the study group had evident blackish nasal eschar and sinus disease. Cultures were positive for Mucorales in 08 cases. 11 patients were treated with amphotericin B in the doses ranging from 0.5 – 1.0 mg/kg up to a total of 2.6 grams, and duration of the treatment varied from 1 – 31 days.

Conclusions: Mucormycosis is a rare opportunistic fungal infection with rapidly progressive and fulminant course with often fatal outcome. A strong suspicion, prompt diagnosis with pathological confirmation and aggressive surgical treatment gives a better outcome.

KEY WORDS: Mucormycosis, Fungal, Amphotericin.

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INTRODUCTION

Mucormycosis is an uncommon opportunistic infection, which represents the third most common angio-invasive fungal infection after candidiasis and aspergillosis and is considered as one of the most important medical complications in immunocompromised patients [1,2].

Even though it is extremely rare, it has been reported from all corners of the world [1,3]. The majority of cases reported were either isolated communications or small, retrospective series [4]. Management of this devastating infection is still big challenge and is based on different strategies which include a rapid diagnosis, reduction of risk factors and rapid and aggressive antifungal agents with or without surgical debridement [5].

We report 14 cases of Mucormycosis retrospectively reviewing medical records of such patients and have made attempt to define clinical features, risk factors, diagnosis and treatment of such patients.

MATERIALS AND METHODS

Our series compromised of 14 cases seen over a period of 5 years. Data studied were patient age, gender, underlying disorders, clinical features, risk factors, diagnostic procedures and treatment including side effects and outcome. Microbiological studies were performed on tissue biopsies. Samples were examined microscopically in a 20% KOH mount and fungal culture was done in most cases. Histological studies included paraffin embedded H & E, PAS and methenamine silver stained slides.

Statistical methods: Descriptive analyses were used to study the parameters. Microsoft word and excel have been used to generate the graphs and tables.

RESULTS

The study group consisted of 10 males and 4 females aged 20-70 years (mean 50 years). Almost all patients except one had at least one recognised underlying disorder (Table 1), of whom 13 had diabetes mellitus. Four patients had more than one risk factor.

Presenting symptoms and signs are listed in Table 2. Most of the patients in the study group had evident blackish nasal eschar and sinus disease was demonstrated in most of them (08), where neuroimaging was done (Table 3); this includes computed tomography scanning (07) and magnetic resonance imaging (01).

All patients underwent biopsies. Broad, non septate, branching hyphe were seen in all cases in KOH smears and in 14 histologic specimens showing tissue invasion. Cultures were positive for Mucorales in 08 cases, all of them showing rhizoids and collapsed columellae compatible with Rhizopus species. Mixed fungal infection was seen in one patient (Aspergillosis + candidal infection).

09 patients underwent surgical debridement procedures. 02 patients had an orbital exenteration. 08 patients were alive, 4 dead, 1 was referred to other centre and 1 was discharged against medical advice.

11 patients were treated with amphotericin B in the doses ranging from 0.5 – 1.0 mg/kg up to a total of 2.6 grams, and duration of the treatment varied from 1 – 31 days. Incidence and severity of adverse effects of treatment are recorded in table 1. Reaction varied from mild to severe and was intolerable in 2 cases. These patients were treated with liposomal form of the drug-Ambisome. 07 cases had hypokalemia and 02 cases had renal dysfunction.

Table 1: Characteristics of mucormycosis patients.

Patient	Age (yrs)	Gender	Underlying disorder	Infecting organism	Medical treatment Ampho B (mg/day), Cumulative dose (mg)	Duration of treatment (days)	Adv effects of Ampho B	Surgery (no of procedures)	Outcome
1	64	Male	DM, severe anemia	M	-	-	-	-	Alive
2	55	Female	DM	M	50 (50)	1	NR	Db	Alive
3	38	Male	DM, Pul.Koch	R	50 (600)	12	NR	Db	Dead
4	45	Male	DM	R	50 (50)	1	None	-	Dead
5	60	Male	DM, Steroids	R	50 (1675), lipos	31	++++	Db + E	Alive
6	52	Female	DM, CKD	R + A+ C	50 (750)	16	++	Db	Dead
7	20	Male	DM	R	25 (225)	9	+	Db	Alive
8	65	Male	DM	R	50 (2600),lipo	29	++++	Db + E	Alive
9	70	Male	DM	R	25 (300)	12	++	Db	Alive
10	25	Male	AML	M	-	-	-	-	Referred
11	60	Female	DM	M	50 (1150)	15	++	Db	Dead
12	35	Female	-	R	-	-	-	-	DAMA
13	50	Male	DM	M	25 (500)	20	++	Db	Alive
14	63	Male	DM	M	50 (800)	17	NR	-	Alive

DM- diabetes mellitus, CKD- chronic kidney disease, M-mucor racemosus, R-rhizopus, A-aspergillus, C-candida, NR-not recorded,+-mild, ++- moderate,++++-severe, Db- debridement, E-orbital exenteration, DAMA- discharge against medical advice.

Table 2: Clinical profile of patients.

Patient	Black nasal eschar	Malaise	Chemosis	Periorbital cellulilitis	Nasal discharge	Proptosis	ophthalmoplegia	Decreased vision	Fever	headache	Altered sensori	Palatal palsy
1	-	+	-	-	-	-	-	-	+	+	-	-
2	-	+	-	-	+	-	IC	+	+	+	-	-
3	+	-	+	+	-	+	-	-	+	-	-	-
4	-	-	-	+	+	-	IC	+	-	-	-	-
5	+	+	+	-	-	+	C	+	-	-	-	-
6	+	-	-	-	-	-	C	+	-	+	+	-
7	+	-	-	-	+	-	-	+	-	-	-	-
8	+	+	-	+	-	+	IC	+	+	+	-	-
9	+	-	-	-	-	-	-	-	+	-	-	-
10	-	+	-	-	-	-	-	-	+	-	-	-
11	+	+	-	+	+	+	IC	-	+	-	+	-
12	+	-	+	+	-	+	C	+	+	+	-	-
13	-	+	-	-	-	-	-	-	-	+	-	-
14	-	-	+	+	-	+	IC	-	-	-	-	-

+-present, -absent, IC-incomplete, C-complete

Patient	Neuroimaging findings	Involved sites	Predisposing local conditions
1	-	-	-
2	-	-	-
3	CT (PNS): Abnormal soft tissue mucosal thickening/ fluid involving maxillary, ethmoid, frontal and sphenoid sinuses. CT (brain): large ill defined hypodense area involving left basifrontal, frontal, corpus callosum with mild mass effect over ventral horn of left lateral ventricle.	Left maxillary, ethmoid, frontal and sphenoid sinus	Chronic sinusitis
4	-	-	-
5	MRI: fluid collection in right sphenoid, ethmoid, maxillary sinus. Small intracranial, extraaxial extension in right medial temporal region with partial thrombosis of right cavernous sinus.	Right sphenoid, ethmoid, maxillary sinus.	Chronic sinusitis
6	CT (PNS): soft tissue swelling in the nasal cavity. Inflammatory soft tissue tissue in bilateral maxillary, ethmoid and focal sphenoid sinus.	Bilateral maxillary, ethmoid and focal sphenoid sinus.	Chronic sinusitis
7	CT (PNS): Abnormal soft tissue mucosal thickening/ fluid involving right maxillary, ethmoid sinus with cellulitis.	Right maxillary, ethmoid sinus.	Chronic sinusitis
8	CT (PNS): Inflammatory soft tissue tissue in bilateral maxillary, frontal, anterior ethmoid and sphenoid sinus with erosion of medial wall of left orbit.	Bilateral maxillary, frontal, anterior ethmoid and sphenoid sinus.	Chronic sinusitis
9	CT (PNS): abnormal soft tissue with hypodense contents involving right premaxillary, retromaxillary and inframaxillary regions	Right maxillary sinus.	Chronic sinusitis
10	-	-	-
11	CT (PNS): Abnormal soft tissue mucosal thickening/ fluid involving right maxillary.	Right maxillary sinus.	Chronic sinusitis
12	CT (PNS): Inflammatory soft tissue tissue in bilateral maxillary, frontal, anterior ethmoid and sphenoid sinus with erosion of medial wall of left orbit.	Bilateral maxillary, frontal, anterior ethmoid and sphenoid sinus.	Chronic sinusitis
13	-	-	-
14	-	-	-

Table 3: Neuroimaging findings.

DISCUSSION

Mucormycosis is a devastating infection of immunocompromised hosts. The different forms of mucormycosis are rhino-orbital-cerebral, pulmonary, disseminated, cutaneous, gastro-intestinal and miscellaneous [6-8].

The mucoraceae are ubiquitous in nature [6-8]. This fungi gain entry to the body through the respiratory tract. They have affinity for arteries

and grow along the internal elastic lamina, causing thrombosis and infarction. Progression of the disease from the nose and sinuses is either direct or leads to the vascular occlusion of the orbital contents. Intracranial involvement occurs also from the invasion by the way of the superior orbital fissure, ophthalmic vessels and cribriform plate, through the carotid artery, or possibly via a perineural route.

Due to the rarity of this infection, it is difficult to calculate accurately its incidence. In 2011 Mignogna et.al [5] reported in their study the annual incidence of mucormycosis in United States is approximately 500 cases per year.

The mean age of the patients was 50 years in our study. Talmi et.al [4] in their study reported mean age of the patients was 50 years. Commonly, Mucormycosis has shown an equal sex distribution. But in our there is slightly male predominance with ratio of male: female is 2.5:1.

Uncontrolled diabetes mellitus was the most common underlying predisposing disease in our series. While Talmi et.al [4] reported hematological malignancies as most common underlying disease.

Orbital and nasal findings are the most common presenting clinical features. Orbital involvement ranges from 58 to 100% of cases in our series. Similar findings were also observed by Talmi et.al [4] in their study (66-100%). Orbital symptoms include loss of function of the 2nd, 3rd, and 6th cranial nerves with proptosis, ptosis, Chemosis, orbital pain, central retinal artery occlusion, conjunctival hyperaemia, dilated pupil and visual loss. Invasion of the eye globe is uncommon and was noted in only one of our cases.

Cultures were positive in 8 of 14 our cases, of which one case had mixed fungal infections. Talmi et.al reported similar findings in their study. Rhizopus was the most common infective agent in our study.

The treatment of Mucormycosis is mainly medical treatment with amphotericin B (amph B) and surgical debridement. 11 received the treatment, 8 were treated with conventional amph B and 3 were treated with liposomal amph B and it is not widely used because of its cost.

Recognised side effects of amph B noted in our study are fever, chills, headache, nausea, vomiting, thromboplebitis, hypokalemia and azotemia.

Survival in mucormycosis patients dependent on multiple factors and early initiation of treatment is an important element. More than 60% of the patients survived in our study.

CONCLUSION

Mucormycosis is a rare opportunistic fungal infection with rapidly progressive and fulminant course with often fatal outcome. A strong suspicion, prompt diagnosis with pathological confirmation and aggressive surgical treatment gives a better outcome.

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