
Rhinocerebral Mucormycosis

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Background

Rhinocerebral mucormycosis is a relatively rare opportunistic fungal infection, usually affect patient with DM, renal failure, organ transplant, desferal user&rarely in healthy person^{5, 7, 8,9,18}. We try to look how frequent this disease is prevalent in the cases admitted to our hospital & what is the outcome of our treatment.

Method

A prospective study done in Al-Hussein General Hospital-Karbala/Iraq in the period June 2001-August 2005, to examine all patients with DM, CRF who have unexplained headache, facial edema, ophthalmoplgia or disturbed conscious for rhinocerebral mucormycosis.Diagnosis based on clinical suspicion , The presence of necrotic tissues in nasal cavity, radiological exam including CT- scan whenever available &fungal detection on of nasal swab &scraping..

Result

We diagnosed ten patients. Eight treated surgically &with amphotricin B (0.5mg/kg/d for six weeks). Two were treated with amphotricin B&local cleaning only. Seven of those treated patients were cured; three died, those who died were presented late with ophthalmoplegia with or without disturbed conscious.

Conclusion

Rhinocerebral mucormycosis which is relatively rare disease actually is present in our patients especially those who have DM with or without renal failure or patient with CRF on dialysis^{3,13,16}. It is a killing disease yet if we carry high index of suspicion in those cases who is presented with headache, dirty nasal discharge, fever &facial edema. We can diagnose them earlier &start treatment to control of the underlying condition, with aggressive surgical interventions combined with amphotricin B, we may safe many patients life.

Keywords: Rhinocerebral, mucormycosis, fungus, diabetes, chronic renal failure

Introduction

Organisms of the class Zygomycetes were first noted to cause

disease in humans in publications from the 1800's. Platauf is credited with the first description of zygomycosis in humans in his paper entitled Mycosis Mucorina ⁷.

Zygomycosis disease caused by the fungus of the class Zygomycetes. There are two orders of Zygomycetes containing organisms that cause human disease, the Mucorales and the Entomophthorales. The majority of human illness is caused by the Mucorales. That is why the term Mucormycosis is used. While disease is most commonly linked to *Rhizopus* spp., other organisms are also associated with human infection, including *Mucor*, *Rhizomucor*, *Absidia*, *Apophysomyces*, *Saksenaia*, *Cunninghamella*, *Cokeromyces*, and *Syncephalastrum* spp.^{7, 8}

Mucorales is a saprophytic fungus found in decayed vegetations in earth. The main categories of human disease with the Mucorales are sinusitis/rhinocerebral, pulmonary, cutaneous/ subcutaneous, gastro-intestinal, and disseminated zygomycosis. Other disease states occur with a much lower frequency and include cystitis, vaginal or gastrointestinal colonization, external otitis, and allergic disease. The spores from these molds are transmitted by inhalation, via a variety of percutaneous routes, or by ingestion of spores.

Human zygomycosis caused by the Mucorales generally cannot flourish in the normal healthy person but only if there is underlying disease or in immune-compromised hosts i.e. it is opportunistic

infections. Host risk factors include diabetes mellitus, neutropenia, sustained immunosuppressive therapy, chronic prednisone use, iron chelating therapy, broad-spectrum antibiotic use, severe malnutrition, and primary breakdown in the integrity of the cutaneous barrier such as trauma, surgical wounds, needle sticks, or burns. Zygomycosis occurs only rarely in immunocompetent hosts^{7, 9, 10, 11,16,17}

The disease manifestations reflect the mode of transmission; with rhinocerebral Mucormycosis which is an acute and often fatal infection caused by inhalation of airborne spores. of a fungus is the most common^{7,8}, the spore germinate to broad, nonseptate hyphae which invade the nasal mucosa, the nasal sinuses & may spread to the orbit or the intracranial space either by direct extension or using the its unique angiopathic capability of spreading along vascular walls, leaving the bony structure intact¹¹

High index of suspicion lead to early diagnosis & treatment with antifungal & surgical treatment will save a lot of patients^{13, 23}.

Patient and Method

We carried a prospective study in Al-Hussein general hospital during the period June 2001 to August 2005. It is a

combined work between medical department & ENT department to study the cases with DM with or without renal failure, patient with CRF on conservative treatment or on dialysis program & also in patient who have no underlying illness who have suspicious complaint of frontal headache of unexplained cause, facial edema, resistant sinusitis, ophthalmoplegia or mental deterioration. We diagnosed fifteen patients, Six were males & nine were females (M/F ratio is 2/3), Their age is 27-83 yr mean age is (57yr) .nine has DM,(three has DM only, Six has DM&CRF),Five has CRF only &one patient has no underlying cause Five of those cases (two females & Three males) who are initially diagnosed on clinical ground only i.e. they have black necrotic tissue on nasal & or palatal tissue, were left the hospital before completing their diagnostic&therapeutic measures . They left to other hospital or their families took them home because of their advanced underlying diseases&denial to expose them to surgery, three has CRF on irregular program of dialysis &two has DM& Renal failure. On follow up (through personal information) all died.We conducted our study on those ten patients

who continued in our hospital, of those ten patients seven were female &three were male, Six had DM (two of them had renal failure as well) Three had CRF (two were on Intermittent HD & one did PD once one year ago). We had one patient who has no immunological or metabolic abnormality.(All these information are depicted in table No, 3)

The diagnosis is done on the following criteria:

Any patient presented to the hospital departments whether to the consultation clinic or he was admitted to the hospital with facial infection as facial cellulites , orbital edema of unexplained cause or even severe unexplained headache in patient with DM or CRF is referred to the ENT surgeon to examine him looking for the possibility of fungal infection of the nasofacial tissues. All patients who are diagnosed clinically were admitted to the hospital, full history is taken &physical examination is done by senior physician and senior ENT surgeonand their clinical presentations is studied as depicted in table No. 1.

Investigation done including CBP,BU,FBS,GUE,CXR,PNS X-Ray,CT-Scan the brain whenever it was feasible of (done for seven Pt.).Nasal swab study for fungus i.e. direct staining examination was done in five Pt. The results at admission are enlisted in the table

Table- 1 the sign & symptom at first twenty four hours of patient presentation according to their frequency

Symptom	No	Sign	No
Headache	6	Dusky nasal mucosa	10
Decreasing vision	6	Nasal bridge&facial anesthesia	7
Periorbital &facial edema	5	Orbital edema&or cellulites	5
Orbital pain	5	Ophthalmoplegia	5
Nasal discharge	5	Nasal discharge	3
Deterioration of conscious	5	Palatal necrosis&gangrene	3
Nasal discharge&stuffness	3		
Fever	2		
Epistaxis	2		

Table – 2 Results of investigations

case No.	HB	WBC	RBS Swab	BU Nasal For fungus		PNS X-RAY	CT-SCAN
1	10.3g/dl	7.100/cmm	Over350mg/dl	20mg/dl	+ive	clear	Not done
2	10.5g/dl		Over350mg/dl	35mg/dl	+ive		Cerebellar &brainstem infarction
3	10 g/dl	6.000/cmm	157mg/dl	116mg/dl	--ive	HazzyRt .frontal& ethmodial sinuses	Rt.ethmoi.Hazziness Rt.Max.Involved
4	8.3 g/dl	14.000/cm m	110mg/dl	180mg/dl	Not done	Not done	Not done
5	12 g/dl	8.000/cmm	300mg/dl	30mg/dl	Not done	Lt.eth., Front. &Max. sinuses Haziness	Lt.eth.,front.,& Max. sinuses Haziness
6	8.0 g/dl	6.600/cmm	105mg/dl	140mg/dl	Not done	Not done	Rt.Nasal cavity fullness, Rt.Max. &Ethmoid. Only are involved
7	9.2gm/dl		374mg/dl	95gm/dl	+ive	Normal	Not done
8	7.0 g/dl	9000/cmm	500mg/dl	116mg/dl	Not done	Lt.eth., &Max. sinuses Haziness	Lt.eth., & Max. sinuse infiltration
9	11.3gm/dl	11.000/cm m	104mg/dl	45mg/dl	--ive	Not done	Thickened mucosa of Lt. max. &Eth. , sinuses
10	9.0gm/dl	7.000/cmm	95gm/dl	260mg/dl	--ive		Rt. max. &Eth. Sinuses haziness

Treatment:

A-Medical Treatment

General supportive treatment including fluid replacement, antibiotic cover when needed. The underlying metabolic disturbances was managed so diabetic patients were treated with soluble insulin according to their blood sugar level measured six hourly. Peritoneal dialysis also was done for patients with CRF who needed it (case No. 4 dialyzed for one time & case No. 6 for three times.). All the patients were treated with heparin 6000 I.U. 6 hrly. Amphotricin B. was given in a dose of 0.5 mg/kg.B.Wt./day for six weeks.

B-Surgical treatment: Eight of our ten patients undergo surgical intervention; the other two patients got local cleaning only. The surgery is in three of them in the form of external frontoethmoidectomy, intranasal debridement & antrostomy with orbital decompression. One with lateral rhinostomy, partial maxillatotomy with orbital decompression, and one case underwent two surgeries in the form of intranasal debridement & partial maxillatotomy with palatal fenestration .one got intranasal polypectomy-inferior meatus antrostomy frequent antral lavage. & the last two underwent intranasal ethmoidectomy with orbital

decompression & large antrostomy The case N0.6 dialyzed once before surgery & twice thereafter. Most of the cases reached with advance disease with disturbed conscious or massive facial edema found to have excessive tissues necrosis & deserve massive excision. The type of surgical interference is depicted in table three

Results

Of those ten patients who continued under our care seven were female & three were male, six has DM (two of them had renal failure a swell) Three had CRF only & one has no underlying illness. Seven out of those ten survived & three died (Survival rate 70%).

Two cases (N07 & 10) of the survived seven were females one has DM & one has CRF, both had mild disease, early presented to us, with no neurological involvement & they did not get surgical interference treated conservatively & were saved. The remaining eight patients all were treated surgically as well to medical treatment, five survived & three died. Five of the other eight cases who undergo surgery were saved (N01, 3 & 4 & 5 & 9) three of them have no neurological involvement at presentation; two had eye

involvement with ophthalmoplegia & visual deterioration. The remaining three cases who were presented late with advance disease with severe tissue destruction & facial edema. Two of them № 2&6 had disturbed consciousness with Ophthalmoplegia as all died.

Most of the cases reached with advance disease with disturbed conscious or massive facial edema found to have excessive tissues necrosis & deserve massive excision

Table – 3 the patients presentation, surgical interference & fate

Case№	Age	Sex	Disease	clinical presentation	Surgical interference	Fate
1(R.M.K)	27y	M	IDDM	conscious, fever, headache, & bloody nasal discharge	1-Surgical debridement of the septum, latt. nasal wall, 2-rt cauldwalldloc operation, Sphenoidectomy 7rt.intranasal ethmoidectomy	live
2(F.SH.N.)	61y	F	NIDDM	Proptosis, disturbed conscious, visual deterioration	1-lt external. frontoethmoidectomy through Lynch-Howarth incision 2-orbital decompression	Died from intracerebral hemorrhage
3(Z.A.A.)	75y	F	No underlying disease	conscious, headache, nasal pain Proptosis	1-Rt. external. frontoethmoidectomy 2-Rt. inferior antrostomy	Live
4(Ch.H.A.)	47y	F	CRF	Conscious, swollen. LT. eye, Ophthalmoplegia and visual deterioration	1-lt external. frontoethmoidectomy 2-Lt. intranasal debridement+inferior antrostomy 3-cleaning of posterior orbit (He refuse to remove the eye)	Live
5(S.T.I.)	40y	F	NIDDM	Conscious, bilateral periorbital & facial edema	1-polypectomy, 2-Infero-left antrostomy 3-frequent A.W.O.	live
6(A.M.,A)	65y	M	CRF	semiconscious, facial & Rt. eye swelling, visual deterioration	1-Rt. latt. rhinostomy=removal of all turbinates 2-partial Rt. maxillatotomy 3-Rt. intranasal ethmoidectomy 4-palatal fenestration, 5-Nasal septum cleaning	Died from uremia & pul. edema
7(F,S.)	55y	F	DM&CRF	conscious, headache, lt. eye & cheek swelling, cellulites & low grade fever	nasal cleaning only	live
8(S.H)	50y	M	DM&CRF	conscious, lt. eye swelling, ophthalmoplegia, visual loss, black nasal turbinate, gray soft palate	1-intranasal ethmoidectomy+orbital cleaning, 2-Partial maxillatotomy, Inferor antrostomy+cleaning of maxillary sinuses	Died
9(N,W.)	65y	F	NIDDM	conscious, flu like illness, orbital & cheek edema, & dirty nasal discharge	Intranasal debridement (partial maxillatotomy)	live
10(H.--)	85y	F	CRf	Conscious, headache, periorbital edema & erythemia	No surgical interference	Live

Discussion

Rhinocerebral Mucormycosis is an invasive, opportunistic fungal infection usually seen in immunocompromised patients, and particularly in the setting of diabetes or chronic renal failure & immune deficiency.^{1, 2,23,24,21}

It didn't take the important concerning the term of early recognition in the daily work in the general hospital which deal with variable cases or even in sometime in special center dealing with immunocompromised. We lost few patients in the medical department. some of them are in the renal unit because of fever; facial edema disturbed conscious then coma, which led to death. They were diagnosed as bacterial cellulites, sinusitis, ethmoidites with cerebral extension & possibility of cerebral sinuses thrombosis or lately diagnosed as Rhinocerebral mucormycosis. Sometimes even there are no mucosal changes or radiological changes & diagnosis should depend on clinical suspicion & biopsy^{3, 5, 7}.

In the last decade preceding the study where the country was under cruel embargo which exhausted the medical resources for the hospital, the economic & health state of the patients with the poverty of diagnostic facilities as a good X-Ray, or laboratory personal or the availability of treatment as amphotericin –

B. Also because we as physician in Iraq not keeping fungal infection frequently in our differential diagnosis of many clinical illnesses firstly because of its rarity & second because the deficient experience or unavailability of diagnostic means

So in spite of intensive antibiotic treatment & trial to correct the underlying metabolic disturbances we lost those cases. Under religious & constitutional rules we have no postmortem study on them.

Thereafter we tried to be fully oriented to those case with diabetes, CRF on dialysis or on conservative treatment or any patient with suspicious facial infection of no explainable cause & we plan our study in that field. & New importance should be given to Rhinocerebral Mucormycosis as what was regarded uncommon is no longer so.

Conclusion

Rhinocerebral Mucormycosis which was regarded as a rare infection in our patient especially with DM with or CRF is no longer true especially if we keep the diagnosis in our mind. This is the general impression observed in also other studies.^{3,10} This raise the possibility that other form of mucormycosis as in pulmonary, gastrointestinal or cutaneous form in patient who are immune-ocompromised, debilitated or extensively burned patient may be underdiagnosed & this point deserve

special attention.¹⁶

Any patient with DM, CRF, immunocompromised immune state or even normal patient who is complaining of severe unexplained headache, dirty nasal discharge. Periorbital or facial edema or deterioration of consciousness following flu like illness should have thorough ENT examination to rule out the possibility of Rhinocerebral Mucormycosis. 11, 15

Early diagnosis of Rhinocerebral Mucormycosis before extensive tissue damage & extension to the CNS & active medical treatment to control the metabolic causes in conjunction with extensive surgical intervention to excise all dead & necrotic tissue with repeated session if needed This is combined with amphotericin _B (0.5mg/kg/day for five weeks) will cure many patients this is still the main outline of treatment 11,14, 17, although some new drugs like Caspofungin Acetate for disseminated zygomycosis used in mice 13 or New treatment options will soon exist with triazole antifungal agents 9 or hyperbaric oxygen 18

Abbreviations:CRF=chronic renal failure, DM = diabetes mellitus ENT=ear, nose&throat department

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