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Research Article

Reconstructive Modalities in the Management of Rhino-Orbito Maxillary Mucormycosis

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Abstract

Background: Mucormycosis is considered as a medical emergency due to its rapid fatal nature. After aggressive surgical excision of facial mucormycosis, extensive defects with facial disfigurement are left behind which remain challenging for reconstructive surgeons.

Objective: Our study aimed to demonstrate different surgical modalities for reconstruction of rhino-orbito-maxillary mucormycosis.

Methodology: This retrospective study was carried out in Plastic Surgery Department of Shifa International Hospital from 1st January 2018 till 31st December 2023. A total of 14 patients were reported with mucormycosis of the head and neck region. Diagnosis was based on fungal potassium hydroxide and histopathology. Computed tomography or magnetic resonance imaging was performed to evaluate the extent of infection. After getting disease clearance by radical debridement and concomitant use of I/V amphotericin B, resultant defects were reconstructed by either padicle flap or free flap.

Results: There were 42.8% females and 57.1 % males with mean age of 47.7 years. The predisposing factors were diabetes in 8 (57.1%) patients, 3 (21.4%) patients were post-covid, 1 (7.1%) was post renal transplant, 1 (7.1%) was post-acute lymphocytic leukemia, whereas 1 (7.1%) had post RTA defect with no known co-morbid. Reconstruction was done by regional flaps in 14.2% and free flaps in 35.7% cases. The mean follow-up period was 17.8 months, with no recurrence of disease or flap failure.

Conclusion: Mucormycosis is a lethal disease, and its diagnosis requires high index of suspicion. Proper disease eradication is necessary for reconstruction with different autologous flaps to achieve good functional and aesthetic results.

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Introduction

Mucormycosis is considered to be the 3rd commonest opportunistic fungal infection after candidiasis and aspergillosis.[1] Facial mucormycosis is a rare entity that causes a rapidly advancing, destructive and perilous infection.[2] It gains entry through the respiratory tract via nose and spreads into the nasal cavity and paranasal sinuses from where it enters the orbit through direct or hematogenous route with possible further progression into intracranial region as rhino-orbital-cerebral mucormycosis which is the most common type of mucormycosis.[2,3] It mostly attacks immunocompromised hosts with poorly controlled diabetes mellitus or diabetic ketoacidosis, immunosuppressive therapy from chronic steroids, history of organ transplant, hematologic malignancies and hemochromatosis.[3]

Invasive Mucormycosis is categorized as rhino-orbital-cerebral, pulmonary, cutaneous, gastrointestinal, disseminated, and miscellaneous.[4,8] Mucormycosis was recognized as a lethal and untreatable disease until the

advent of amphotericin as a cure in 1960.[5] Recognition of disease requires high index of suspicion. Prompt diagnosis should be made on fungal KOH and histopathology.[6]

Management of mucormycosis is complex and challenging. This study highlights the effectiveness of multidisciplinary approach for complete eradication and reconstruction of defect. With recent medical and surgical advances, it has become possible to (i) treat the underlying comorbidity (ii) early commencement of antifungal therapy, (iii) aggressive surgical resection of the affected tissues, (iv) reliable reconstruction and proper rehabilitation.[7]

Methodology:

This retrospective study was approved by institutional review board and conducted in department of plastic surgery, Shifa International Hospital, Islamabad over a period of 6 years from 1st January 2018 till 31st December 2023. All patients who underwent treatment for mucor-

Table 1: *Summary of demographic and clinical characteristics and management of patients*

S. No	Age / Sex	Predisposing Factors	De-Bridements (No)	Surgical Resection	Flap Type	Compli-cation	Follow Up (M)	Secondary Procedures
1	40/F	Diabetic	10	right maxilla, nasal side wall, palate	temporalis flap, cheek rotation flap and forehead flap	Nil	36	Scar revision, fat grafting, alar readjustment
2	45/M	Diabetic	4	left orbital exenteration with left total maxillectomy + palatal defect	ALTF	Nil	16	Flap debulking
3	64/M	Diabetic	6	B/L subtotal maxillectomy with >50% palatal defect	ALTF	Nil	13	Nil
4	39/M	RTA (trauma)	4	cutaneous mucormycosis of left side of face + forehead sparing left eye	ALTF + Skin graft for forehead	Nil	24	Flap debulking, FTSG for lower eyelid
5	9/F	post ALL (Acute lymphocytic leukemia)	5	left nasal defect, maxilla and left orbital exenteration	Myocutaneous latissimus dorsi flap	Nil	30	Flap debulking, Nasal augmentation with rib graft, socket creation
6	52/F	post renal transplant	4	B/L maxillary, upper alveolar process, palatal defect	Osteocutaneous fibula flap	Nil	16	Nil
7	51/M	post covid	7	left orbital exenteration with left total maxillectomy+ palatal defect	ALTF	palatal fistula	25	fistula repair
8	47/F	post covid	4	Left subtotal maxillectomy + >50% palate	ALTF	Nil	14	Nil
9	52/F	post covid	4	Left hemi palatal defect	temporalis flap	Nil	13	Nil
10	49/F	Diabetic	5	Right orbital exenteration	free radial artery forearm flap	Nil	12	Scar revision
11	50/M	Diabetic	7	B/L maxillary, upper alveolar process, palatal defect	osteocutaneous fibula flap	Nil	18	Nil
12	54/M	Diabetic	5	Right hemifacial skin resection + subtotal maxillectomy	free radial artery forearm flap	Nil	21	Scar revision
13	57/M	Diabetic	6	left subtotal maxillectomy orbital exenteration	free radial artery forearm flap	Nil	10	Nil
14	55/M	Diabetic	5	left orbital exenteration with left maxillectomy+ palatal defect	ALTF	Nil	9	Flap debulking

Abbreviations: ALTF=anterolateral thigh flap, B/L= bilateral, RTA=road traffic accident, FTSG=full thickness skin grafting

mycosis of the head and neck region were included in the study. Patient's demographics such as age, sex, predisposing factor, area of defect, flap type, complications, follow-up, and recurrence were noted.

Inclusion criteria was patients having facial mucormycosis involving disease in maxillary and naso-orbital areas who had undergone surgical excision and reconstruction with flaps. Exclusion criteria was patients having intracranial extension and mucormycosis involving other than head and neck region such as limbs or trunk. A multidisciplinary approach was established, and patients were evaluated by head and neck surgeon, plastic surgeon, medical specialist, infectious disease, histopathologist, radiologist. Prompt diagnosis was made, based on fungal KOH and histopathology. Computed tomography or magnetic resonance imaging was performed to evaluate the extent of disease. All patients were treated initially by head and neck surgeon and multiple sessions of surgical debridement were done until clearance was achieved. Meanwhile injectable amphotericin B was given to patients for 3-4 weeks that was later switched to oral Posaconazole 300 mg BD on day 1 followed by 300 mg OD for the next 45 days. Follow-up protocol included monitoring of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) along with renal function tests.

After complete resolution of infection, when the patients were considered disease free by head and neck surgeon, they were referred to plastic surgery. Defect sizes were assessed and reconstruction with autologous tissue was done in the form of local, regional, or free flaps. Timing of reconstruction was considered immediate if done after first debridement, Early if done within 2 weeks of serial debridement and delayed if done after 4 weeks. Patients were assessed for complications and recurrence in their follow-ups postoperatively for 1 year.

Results:

A total of 14 patients in our institution were diagnosed with facial mucormycosis out of which 13 (92.8%) were rhino-orbito-maxillary whereas as 1 (7.1%) was diagnosed with cutaneous mucormycosis. There were 42.8% females (6/14) and 57.1 % males (8/14). Mean age was 47.7 ranging from 9 -68 years. The predisposing factors were diabetes in 8 (57.1%) patients, 3 (21.4%) patients were post-covid, 1 (7.1%) had road traffic accident with no known co-morbid, 1 (7.1%) was post renal transplant and 1(7.1%) was post-acute lymphocytic leukemia chemotherapy. Twelve (85.7%) cases were diagnosed and treated primarily in our hospital whereas 2 (14.2%) cases with established diagnosis of mucormycosis came to us for further treatment. One case of cutaneous mucormycosis was treated in outside facility for coverage with pectoralis major flap and presented to us with recurrence for revision. In each individual case after completion of the medical management with I/V amphotericin B for 3-4 weeks and a mean of 5.4 surgical debridements, we established a disease-free status with repeat biopsy and fungal KOH from the previously infected areas. After thorough debridement we came across defects of variable sizes and depth. Their respective surgical resections are mentioned in (Table 1).

For these variety of defects different surgical modalities were used. Reconstruction was planned according to the defect (Figure1-3). Delayed reconstruction was done in all cases. Two (14.2%) patients were reconstructed with regional flaps including temporalis muscle flap, cheek rotation flap and forehead flap whereas in 12 (85.7%) cases reconstruction was done with free flaps. In our study, Anterolateral thigh flap was used 6 (42.8%) patients, osteocutaneous free fibula in 2 (14.2%) patients, radial forearm free flap in 3 (21.4%) patients and myo-cutaneous LD flap in 1 (7.1%) patient.

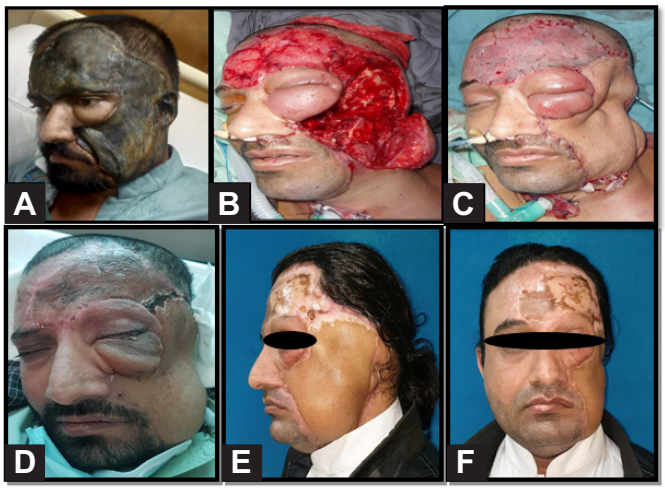

Figure1: ***A)*** *case of cutaneous mucormycosis in which skin changes occurred 5 days after RTA.* ***B)*** *intraoperative picture showing debrided part of previously done pectoralis major flap and final defect.* ***C)*** *coverage done with Anterolateral thigh flap and split thickness skin graft for forehead.* ***D)*** *early follow-up at 1 month. E,F) follow-up at 1 year after flap debulking and lower lid full thickness skin grafting.*

Secondary procedures were done in 8(57.1%) patients for aesthetic improvement which included flap debul-

king, scar revision, fat grafting, alar readjustment, nasal augmentation. Among the patients included in our study, there was no mortality and survival rate of all flaps was 100% with no free flap failure. All patients were closely followed after discharge and none of the cases had a recurrence.

Only 1 (7.1%) patient had a complication of palatal fistula identified at 5th month for which fistula repair was done. The mean follow-up was 17.8 ranging from 9 to 36 months.

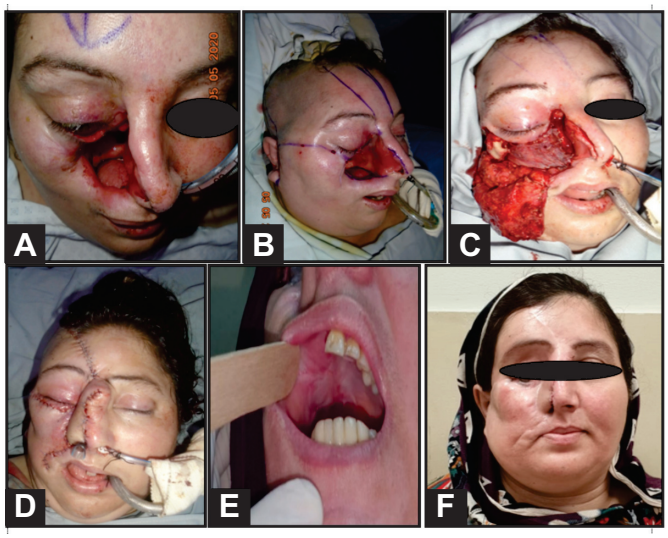

Figure 2: ***A)*** *Young lady with large defect of right cheek, nasal dorsum, and palate with visible tongue at base.* ***B)*** *Markings for forehead fap, temporalis muscle fap and cheek rotation advancement faps.* ***C)*** *Temporalis muscle fap inset done to reconstruct palate and fill the dead space.* ***D)*** *Per-operative pic showing inset of forehead and cheek faps.* ***E)*** *Intra-oral view showing good mucosalization of temporalis muscle.* ***F)*** *Frontal view of follow up at 6 months.*

Discussion:

Mucormycosis is an angio-invasive fungal infection that forms intraluminal thrombosis that eventually leads to tissue necrosis by restricting delivery and penetration of drugs into infected hypovascularized tissues.[10] Rhino-orbital-cerebral mucormycosis is the most common presentation of disease after which cutaneous form is the next in line.[8,10] The mean age of our patients is comparable to studies of Rao et al[16] and Ojha et al.[18] The most frequent initial manifestation of mucormycosis is sinusitis, orbital cellulitis, eye or facial pain/ swelling and facial numbness[9] which was also seen in our patients. Due to vascular thrombosis and tissue necrosis black dusky eschars are formed on the nasal mucosa or palate that are pathognomonic of mucormycosis. This ulceration of the hard palate stipulates disease progression beyond maxillary sinuses[7,10].

Urgent diagnosis with KOH smear or tissue biopsy is mandatory.[11] Biopsy is considered as gold standard in terms of recognition of wide, aseptate, ribbon like hyphal structures branching at right angles[12]. It is considered unreasonable to wait for fungal cultures in light of clear clinical signs and symptoms of mucor and one should not delay beginning of antifungal treatment to inhibit from further progression of disease.[3] Amphotericin B was reported to be drug of choice.[10,12] Nephrotoxicity was the most serious side effect of this drug due to which in 1991 a less toxic and more potent form, liposomal amphotericin was developed and used in patients with worsening renal functions[12]. In our study liposomal amphotericin was not used due to its high expense, so conventional amphotericin B has been the mainstay of antifungal treatment with satisfactory results that was later switched to oral Posaconazole with an initial dose of 300mg twice a day for 1 day followed by 300mg daily for 6 weeks.[14]

It is crucial to radically excise mucor inflicted tissues (as in malignancy) so that no residual infected area is left behind, therefore huge complex defects are created with significant functional impairment and aesthetic disfigurement that are challenging to reconstruct.[13] To achieve disease free margins in our study, all infected tissues were excised with 1 cm margin beyond the point of affected area with removal of involved part of bone which is similar to other studies.[14,15]

After confirmation of disease elimination, reconstruction is planned with the consultation of head and neck surgeon. According to the assessment of area, size and volume of defect the plastic surgeon decides whether to reconstruct using a prosthesis or autologous tissue.[7]

We believe that autologous reconstruction is superior as it brings vascularized tissue in an area of infection and combats residual infection by good blood supply, it avoids wear and tear by covering the exposed structures with the downside of being time consuming procedure that needs expertise and may require secondary procedures for better cosmesis.[7]

Anitha et al in their study used pedicled flaps after resection for primary coverage and found some complications of flap necrosis. We believe local and pedicled flaps encounter difficulty in reaching mid facial defects. Therefore, they do not provide enough tissue and adequate bulk to fill composite facial defects, in our study pedicled flaps were used in only 2 of our patients at the

time of covid wave to shorten the operative time due to hospital policy.

Figure3: ***A)*** *Mucor extension into left orbit, maxilla and palate, serial excisions showing left enucleation.* ***B)*** *left side defect shown in CT scan.* ***C)*** *final defect at the time of reconstructive surgery.* ***D)*** *reconstruction done with Anterolateral thigh flap.* ***E, F)*** *follow-up pictures at 8 months.*

Gupta,[10] Humnekar,[13] Rao[16] and Allensworth strongly suggests usage of free flaps in their studies to attain superior results in reconstruction of complex 3-D defects as compared to pedicled flaps. Free flaps have a reliable blood supply and superior coverage of complex mid facial defects. In our study we have used variety of free flaps in accordance with different composite defects showing satisfactory results.

There is also a debate on immediate reconstruction or whether to delay it. In a literature review, most of the studies 13/16 had done delayed reconstruction with an average time of 16.7 weeks (range 2-36 weeks) and immediate reconstruction was reported by two authors 3/16 only.[15] Our study also states delayed reconstruction once the disease is cured. Other authors have also reported multiple debridement to establish disease free status and undergone delayed reconstruction[12,13,17] which is not in favor of immediate reconstruction done by Gupta et al[10] and Ojha et al.[18]

In the present study there was no flap failure or recurrence of mucormycosis which is similar to studies presented by Ojha et al[18] and Gupta et al.[10]

The various complications reported in literature review by Palacios et al are oronasal fistula, naso-orbital fistula and oropharyngeal fistula, recurrent bleed, exposed meninges, CSF leak etc.[15]. In our series only 1 patient developed oronasal fistula and after fistula repair satisfying results were achieved. Our study has a mean follow up of 17.8 months compared to Parvati et al.[11] Flap survived in all patients with good wound healing and acceptable esthetic and functional results.

Conclusion

Mucormycosis is a fatal disease if not treated early, its diagnosis requires high index of suspicion. Reconstruction should be delayed until complete eradication of disease is achieved. Pedicled flaps are used to cover small, isolated defects of orbit or palate but they are found to be inadequate for extensive defects. Free flaps give freedom of design and ability to do 3-D reconstruction and found to be a reliable option for complex maxillofacial defects.

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Conflict of interest: None.

Author's contribution:

Dr. Fatima Askari: Conception and design of the study, data collection, Drafting the work, analysis and interpretation, Final approval of the version to be published and accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Dr. Saad ur Rehman: Conception and design of the study, critical revision of the article and final approval of the article to be published

Dr. Shayan Shahid Ansari: Article Editing,Manuscript Revision analysis & interpretation of data

Dr. Rehan Abbas: Data collection, Article Editing, Manuscript Revision, analysis and interpretation of data

Dr. Maira Shoaib: Study design, drafting of work, Data Collection and analysis and interpretation

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