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Degree of Orbital Affections in Cases of Nasal Mucormycosis Associated with COVID-19

Ezzeddin Mohamed El Sheikh, Hani Mohamed Ali El Shamy, Manar Muhammad Abdel Rehim*, Mohammed Elsayed Elmaghawry, Tarek Gamal Ahmed El Naggar

Department of Oto-Rhino-Laryngology, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Manar Muhammad Abdel Rehim, **Mobile:** (+20) 01122828262,

E-mail: manarmohamed445@gmail.com

ABSTRACT

Background: The incidence of acute invasive fungal sinusitis (AIFS) increased without obvious cause in the COVID-19 era subsequently there is a burden on the health care system.

Objective: In our study, we attend to find the best assessment for orbital affections in patients with AIFS and decrease morbidity rates. Therefore, the present study aimed to assess the functional outcome of endoscopic debridement and medical treatment in cases of orbital affection.

Patients and methods: A one-arm interventional study was conducted in Orhinolaryngology, Head and Neck Surgery Department, Zagazig University Hospitals. The study included 19 patients, aged between 31 and 65 years, who had orbital symptoms associated with nasal mucormycosis with history of COVID-19 infection. Patients have undergone endoscopic debridement surgery, under general anesthesia.

Results: The endoscopic assessment performed intraoperatively revealed that a significant percentage of cases had septal necrosis (31.6%), superior turbinate necrosis (10.5%) and inferior turbinate necrosis (47.4%). Furthermore, all cases showed middle turbinate necrosis which is considered to be the classical sign of nasal mucormycosis by endoscopic examination. Regarding prognosis and mortality, most cases (78.9%) showed improvement while 21.1% of cases died.

Conclusion: Early combined medical and surgical treatment of AIFS can save the lives and salvage the eyes.

Keywords: Mucormycosis, Head and Neck, COVID-19, Rhinosinusitis, Intervention study, Zagazig University.

INTRODUCTION

Mucormycosis is an invasive, potentially lethal fungus belonging to the Mucorales order, including the species Rhizopus species, Mucor species, and Rhizomucor species belong [(1)].

Nasal mucormycosis in immunocompromised hosts begins with sporangiospore inhalation, direct extension to the paranasal sinuses, and hyphae angioinvasion. This leads to necrotizing vasculitis, fungal thrombi, and tissue infarctions later on [(2)]. Vascular invasion, occurs by occluding ophthalmic vessels, while direct invasion through the superior orbital fissure, or cribriform plate. Perineural invasion or the carotid artery can potentially induce intracranial involvement [(3)].

There are four types of mucormycosis involvement in the head and neck: isolated nasal, Sino-nasal, rhino-orbital, and rhino-orbital-cerebral [(4)]. When spores are inhaled or come into direct contact with wounds, mucormycosis can result in invasive infections that advance rapidly, especially in immunocompromised people. The diagnosis of this condition is dependent on the clinical symptoms, pathological criteria, and imaging findings [(5)]. Broad-spectrum antibiotics, monoclonal antibodies, and frequent use of steroids might cause a preexisting fungal illness to develop or worsen. Physicians should be aware that patients with COVID-19 infection may develop secondary, invasive fungal infections [(6)].

Diagnostic work-up is frequently put off due to the rarity of the occurrence and the possibility of vague initial symptoms. But for a curative therapy involving rigorous surgical debridement and high-dose antimycotic medication to be possible, a prompt, early and accurate diagnosis is necessary [(5)]. Thus, the present study aimed to assess the functional outcome of endoscopic debridement and medical treatment in cases of orbital affection.

PATIENTS AND METHODS

A one-arm interventional study was conducted in Orhinolaryngology, Head and Neck Surgery Department, Zagazig University Hospitals, in the period from July 2022 to December 2022.

The study included 19 patients, aged between 31 and 65 years, who had orbital symptoms associated with nasal mucormycosis with history of COVID-19 infection.

We excluded patients with positive polymerase chain reaction (PCR) for COVID-19, chronic granulomatous fungal sinusitis, MRI incompatible devices.

Patients included in study were subjected to full clinical history taking, detailed ophthalmological examination fundus examination, visual acuity (VA), assess EOM (extra ocular movement), diagnostic nasal endoscopy under local anesthesia, CT scan and MRI (T1 with gadollinum, T2 with fat suppression, diffusion

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weighted imaging (DWI) of the nose and paranasal sinuses. Chest consultation for pulmonary infection was done for all participants, together with routine preoperative laboratory investigations. Thereafter, patients have undergone endoscopic debridement surgery, under general anesthesia.

Operative procedure: The procedure started by endoscopic overview to assess necrosed tissues to be removed. Removing septum, inferior or middle turbinates if necrosed, open all sinuses in the affected side, open pterygopalatine fossa and infratemporal fossa if affected and removal of lamina paprecia with orbital clearance if there is an orbital invasion. An anterior nasal pack socked in amphotricin B was inserted. Intra operative recording on DVD was used.

Postoperative care: Operated patients were taken from the operating room and placed in a recovery room for observation after the procedure. They stayed there for two to four hours, until their vital signs had stabilized. Then, patients were taken to the ward or ICU depending on their overall condition after leaving the recovery room.

Postoperative care, follow up: Removing the pack was done after 48 hours. Good antibiotic coverage for one week. Parentral amphotericin B was administrated for 2 weeks until appearance of the culture with monitoring of renal function. Analgesics were used, as needed. Nasal irrigation with betadine diluted with normal saline. Close observation for headache, periorbital swelling. Follow up was done weekly for the first month, then monthly for the following six months and include clinical examination and endoscopic examination.

Ethical Consideration:

This study was ethically approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Zagazig University. Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 20 for windows. Qualitative data were defined as numbers and percentages. Quantitative data was described as mean and standard deviation (SD).

RESULTS

Table 1 summarizes the basic demographic and clinical characteristics of the studied patients.

Table (1): Characteristics of the studied group (n=19).

Characteristic	Study group (n=19)		
Age			
Mean ±SD **Range**	51.58 ± 10.91 (31-70)		
Category		**No.**	**%**
Sex	Female	13	68.4
	Male	6	31.6
COVID-19	Negative	0	0
	Positive	19	100
Comorbidity	Uncontrolled DM	19	100

Pre and post-operative eye evaluations are illustrated in **Table 2**.

Table (2): Clinical pre-operative and post-operative examination of effected eye to the studied group.

Characteristic	Category	Study group (n=19)	
		No.	**%**
Pre-operative			
Affected eye	**Left**	9	47.4
	Right	10	52.6
EOM	**Full**	2	10.5
	Restricted	7	36.8
	Complete ophthalmoplegia	10	52.6
Proptosis	**No**	3	15.8
	Mild	4	21.1
	Moderate	6	31.6
	Severe	6	31.6
Post-operative			
EOM	**Full**	4	26.7
	Restricted	4	26.7
	Complete ophthalmoplegia	7	46.7
Proptosis	**No**	6	40
	Mild	5	33.3
	Severe	4	26.7

EOM= Extraocular movement

Endoscopic diagnosis of studied patients is summarized in **Table 3**.

Table (3): Pre-operative endoscopic diagnosis of the studied group.

Characteristic	Category	Study group (n=19)	
		No.	%
Septal necrosis	**Yes**	6	31.6
	No	13	68.4
Superior turbinate necrosis	**Yes**	2	10.5
	No	17	89.5
Middle turbinate necrosis	**Yes**	19	100
Inferior turbinate	**Yes**	9	47.4
	No	10	52.6

Table 4 showed that most cases showed improvement while 21.1% of cases died.

Table (4): Prognosis of the studied group cases.

Characteristic	Category	Study group (n=19)	
		No.	%
Prognosis	**Died**	4	21.1
	Improved	15	78.9

Table 5 summarizes the clinical post-operative eye examination of the studied patients.

Table (5): Clinical post-operative eye examination of the studied group.

Characteristic	Category	Study group (n=15)	
		No.	%
Pupil right	**RRR**	10	66.7
	Abnormal (dilated fixed)	5	33.3
Pupil left	**RRR**	8	53.3
	Abnormal (dilated fixed)	7	46.7
Fundus right	**No optic atrophy**	2	13.3
	Optic atrophy	6	40
Fundus left	**No optic atrophy**	2	13.3
	Optic atrophy	5	33.3
Excentration	**No (improved)**	12	80
	Yes (right side)	2	13.3
	Yes (left side)	1	6.6

RRR= round in shape, Regular and reacting to light
EOM= Extraocular movement

Table 6 shows pre-operative diagnosis to affected right visual acuity test and fundus examination.

Table (6): Pre-operative visual acuity (bedside) and fundus examination of affected right eye within the studied group.

Characteristic	Category	Study group (N=10)	
		No.	%
Visual acuity test	**No pl**	7	70
	HM	1	10
	2/60	2	20
Fundus	**No optic atrophy**	2	20
	Optic atrophy	8	80

Hand movements (HM), perception of light (PL).

Post-operative diagnoses to affected right visual acuity test and fundus examination are summarized in **Table 7**.

Table (7): Post-operative visual acuity and fundus examination affected right eye within the studied group.

Characteristic	Category	Study group (n=10)	
		No.	%
Died		2	20
Visual acuity (N=8)	**No pl**	6	75
	3/60	2	25
Fundus (N=8)	**No optic atrophy**	2	25
	Optic atrophy	6	75

Perception of light (PL).

Pre and post-operative diagnoses to affected left visual acuity test and fundus examination are summarized in **Table 8**.

Table (8): Pre-operative and Post-operative visual acuity and fundus examination of affected left eye within the studied group:

Characteristic	Category	Study group (N=9)	
		No.	%
Pre-operative			
visual acuity left	**No pl**	5	55.5
	HM	1	11.1
	1/60	2	22.2
	2/60	1	11.1
Fundus	**No optic atrophy**	4	44.4
	Optic atrophy	5	55.5
Post-operative			
Died (no pl + optic atrophy)		2	22.2
visual acuity (N=7)	**No pl**	4	57.1
	Pl	1	14.2
	2/60	1	14.2
	6/36	1	14.2
Fundus (N=7)	**No optic atrophy**	2	28.5
	Optic atrophy	5	71.4

DISCUSSION

Regarding Gender of patients, our study found that more than half of cases (68.4) were females similar to Western India study **Mishra *et al.*** [7], and **Ebrahim *et al.*** [8] study as 52.3% of studied patients were women, unlike most of previous studies which found that male gender represented the majority of cases [9-11].

The demographic profile in our study was consistent with **Baghel *et al.*** [12] study, with a mean age of 51.7 years however, they showed a male predominance of 70.2% patients. Also similar to our findings, **El-Hameed *et al.*** [13], showed that mean age of studied patients was 58.8±9.6 years, about 60% of them were females.

Due to diminished chemotaxis and phagocytosis by macrophages, monocytes, and neutrophils, as well as an environment of hyperglycemia, ketosis, and low oxygen tension, individuals with diabetes have immune function impairment, which creates an ideal atmosphere for the fungus to proliferate [14].

Diabetes increase the risk of mucormycosis by 7.5 times compared to the general population [15]. In our study, all cases (100%) had diabetes mellitus which is similar to **El-Hameed *et al.*** [13] who recorded that all patients had diabetes (29 individuals with post-COVID-19 new onset and 43 patients with preexisting diabetes). In a study conducted in India in 2021 by **Mishra *et al.*** [7], diabetes was linked to cases of COVID-19 associated mucormycosis in 87.5% of cases.

The literature assessment of the available global data by **Singh *et al.*** [16] revealed that 80% of instances are caused by patients with diabetes. Additionally, data from 2022 (Baghel) showed that 88/104 (84.6%) of the 104 diabetics had uncontrolled diabetes.

Since the REMAP (randomized, embedded, multi-factorial, adaptive platform) trial showed that dexamethasone is the treatment of choice in treatment of COVID-19 pneumonia with hypoxia as it lowers the mortality, it has become the treatment of choice [17].

Since then, there has been a dramatic rise in steroid use. This prepares the environment for opportunistic infections to occur. As COVID-19 infections increase, more cases of other opportunistic diseases, including candidiasis, aspergilloma, and mucormycosis, are being documented. Unknown at this time causes of the prevalence and risks of mucormycosis in COVID-19 patients. Global cases of mucormycosis during the pre-pandemic period ranged from 0.005 to 1.7 per million people [18].

Similar to prior research, those who underwent combined medical and surgical care had a noticeably superior outcome [19]. Antifungal medications probably penetrate necrosed tissue more effectively after surgical debridement, leading to good results. The majority of patients with rhino-orbital mucormycosis needed surgery [9].

Recent research indicates that orbital exenteration is an essential component of therapy in severely affected orbit, halting future deterioration [20-22]. However, a retrospective investigation revealed that patients who underwent orbital exenteration had a significant mortality rate (88.9%) [24]. It can be difficult to determine when orbital exenteration is necessary [20].

Comparable operations were carried out by **Dhwani *et al.*** [24] who found that 3 patients (or 25%) needed FESS with exenteration, out of which 2 had involvement of the Central Nervous System.

Pre-operative diagnosis in right affected eye revealed that 70% of cases had no light perception, while 20% recorded visual acuity at 2/60 and the remaining 10% responded to hand movement. Fundus examination indicated optic atrophy in approximately (80%). Post-operative diagnosis showed that for affected right visual acuity test results, a majority (75%) could not record perception of light, while the rest (25%) demonstrated a score of 3/60. Again, fundus examination confirmed optic atrophy in about three-quarters (75%).

Pre-operative diagnosis in left affected eye indicated that a majority (55.5%) of cases had no perception of light, while 11.1% and 22.2% responded to hand movements or showed visual acuity readings of 2/60 or 1/60, respectively. Fundus examination revealed optic

atrophy in around half (55.5%) of the affected individuals. Post-operation, it was found that about half (57.1%) of the cases still lacked perception for light; however, there were some improvements observed as well with approximately equal proportions showing responses to perception for light and having visual acuities recorded at either 2/60 or better levels such as being able to record a reading like "6/36". Additionally, fundus examination revealed an increase in percentage by nearly twenty percent indicating optic atrophy present in most patients now reaching up to around seventy-one percent (71.4%).

In **Dhwani *et al.*** [(24)] study, they demonstrated that All patients had unilateral ocular involvement; 5 (41.66%) patients had involvement of the right eye and 7 (58.34%) patients had involvement of the left eye. Six patients (50%) had vision between 20/40 and 20/100 while 4 (33.3%) patients had no perception of light in the damaged eye; 2 (16.7%) patients had just light perception.

Clinical examination is crucial in identifying clinical manifestations of patients with COVID-19 at moderate to greater risk of developing mucormycosis since early diagnosis is crucial for a higher likelihood of patient survival. This entails checking for sinus pain and performing an eye examination. The ocular examination includes a fundus examination, testing for extraocular abnormalities, extraocular motility, and visual acuity. Patients with mucormycosis frequently have abnormalities such ophthalmoplegia, proptosis, blepharoptosis, impaired vision up to no light perception, oedema, and necrosis [(25)].

Extraocular movement diagnosis throughout our study revealed that 52.6% of cases had complete ophthalmoplegia, 36.8% showed restricted eye movement while 10.5% showed full movement. Regarding proptosis, 31.6% of cases showed moderate proptosis, 31.6% of cases showed severe proptosis, 21.1% of cases showed mild proptosis and 15.8% showed no proptosis.

Similar to **Bilgic *et al.*** [(26)]**,** who identified ocular involvement among 21 (55%) patients, and revealed that ptosis, ophthalmoplegia, total vision loss, and orbital edema were the primary ocular symptoms in 19 (90%) patients, 18 (47%) patients, 15 (39%) patients, and 11 (29%) patients, respectively.

While in our study preoperative ophthalmoplegia was 52.6%, post-operative 46.7%, while severe proptosis (31.6%) and postoperative (26.7%). These findings suggest that the surgical intervention did not significantly improve visual outcomes, as the majority of cases remained unable to perceive light and showed persistent optic atrophy post-operatively.

Patients who first arrived with vision loss showed mild, progressive ophthalmoplegia improvement without an improvement in visual acuity, according to a report in [(27)].

In our study, the endoscopic assessment performed intraoperatively revealed that a significant percentage of cases had septal necrosis (31.6%), superior turbinate necrosis (10.5%) and inferior turbinate necrosis (47.4%). Additionally, middle turbinate necrosis, which is regarded as the hallmark indication of sinonasal mucormycosis in nasal endoscopy, was seen in all instances. When present in patients with known or suspected fungal sinus infections, this result should alert doctors to the possibility of diagnosing fulminant fungal rhinosinusitis [(28)].

In our study regarding prognosis and mortality, most cases (78.9%) showed improvement while (21.1%) of cases died.

In our study 21.1% of patients died in agreement with **Alloush *et al.*** [(29)] study in which 3 (21.4%) patients died while 11 (78.5%) patients made a full recovery and were released from the hospital. As the mortality rate of ROCM ranged from 31-49% **Prakash *et al.*** [(30)] and **Patel *et al.*** [(9)]**,** our mortality rate is regarded as low when compared to India publications. This highlights the value of an interdisciplinary multidisciplinary team composed of an otorhinolaryngologist, an ophthalmologist, and a pathologist for early diagnosis and management. Even a 6-day delay in starting treatment causes a 26% increase in 30-day mortality, from 35 to 66% [(31)].

CONCLUSION

The value of early diagnosis and treatment by a multidisciplinary team include pathologists, ophthalmologists, and otorhinolaryngologists. Even a 6-day delay in starting treatment causes a 2-fold increase in 30-day mortality, from 35 to 66%. We recommend good control to DM any other immunosuppressive agent, lowering steroids therapy in treatment of covid-19 and in case it is critical; use it with cautions and good monitoring. Early discovering mucormycosis clinically and radiologically and early surgical intervention with endoscopic debridement and antifungal treatment help no more deterioration of vision and decrease morbidity. Excentration of invaded eye after endoscopic debridement can prevent intracranial extension and secure lives.

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