Endoscopic Surgery Outcomes in Patients With Rhino-Orbito-Sinusal Mucormycosis

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Abstract- The aim of this study is to evaluate the response to endoscopic treatment and treatment outcomes in patients with rhino-orbito-sinusal mucormycosis. In this descriptive cross-sectional study, 19 patients with rhino-orbito-sinusal mucormycosis were involved. Data such as age, gender, the 6-month survival rate of the patients, type of underlying disease, site of involvement, number of endoscopic procedures, history of exenterating of the eye, type of received systemic treatments, and the time interval between the onset of symptoms and the start of treatment were recorded and analyzed. The 6-month outcome analysis showed that 10 out of 19 patients (58.8%) survived. The results also revealed no significant difference in the 6-month survival rate according to parameters such as gender, underlying disease (57.9% of the patients had diabetes and 42.1% had cancer), age, delay in surgery, site of involvement, and the number of surgeries (P>0.05). However, there was a significant difference in the 6-month survival rates of patients with respect to exenterating of the eye (P<0.05). According to our results, uncontrolled diabetes is the most common underlying cause of rhino-orbito-sinusal mucormycosis. It also seems that exenterating of the eye affects the survival rate of patients. This study suggests that timely and early diagnosis as well as correct treatment, endoscopic procedure, if possible, play an important role in the prognosis of the disease and can greatly reduce the mortality rate.

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Keywords: Mucormycosis; Endoscopy; Site of involvement; Exenterating

Introduction

Rhino-orbito-cerebral mucormycosis is a fungal disease, and its diagnosis is important since late diagnosis can lead to the sufferers' death. It starts without any symptoms, so its diagnosis is difficult (1-3). Patients with rhinocerebral mucormycosis almost always complain of facial pain, headache, or both. Occasionally, fever and varying degrees of orbital cellulitis may occur. The first symptom is an inflamed or swollen nose, which is usually nonspecific and may include turbinate hypertrophy and nasal obstruction. Diagnosis at this stage requires strong clinical suspicion. In high-risk individuals, resistant rhinitis may be the first manifestation of mucormycosis (4). Primary diagnosis is based on clinical symptoms and consideration of underlying disease, and definitive diagnosis is based on biopsy. Culture, despite the aggressive nature of the disease, is worthless and often negative (5-10). The progression of the disease causes ischemia, thrombosis, necrosis of the turbinates, and bloody nasal discharge and makes the turbinates black. The disease is slowly progressing to the invasive stage, and symptoms such as ptosis, proptosis, orbital cellulitis, ophthalmoplegia, and the involvement of the fifth and seventh cranial nerves will occur. Other symptoms include decreased vision and altered consciousness (1,2). Therefore, the importance of mucormycosis is due to its high mortality, which is estimated at 75% to 80%. On the other hand, successful treatment of mucormycosis can be achieved

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by timely diagnosis, removal of underlying predisposing risk factors, adequate surgical debridement, and an effective total dose of systemic antifungal medications. Therefore, in this study, we investigated the response to endoscopic treatment and treatment outcomes in patients with mucormycosis.

Materials and Methods

After approval by the local Ethics Committee and obtaining written informed consent, in this cross-sectional study 19 patients with rhino-orbito-sinusal mucormycosis in Yazd, Iran (2017 to 2019), included. Rhino-orbito-sinusal mucormycosis was confirmed based on the CT scan and MRI findings and following pathological confirmation (smear or histopathology). Patients who did not undergo any diagnostic or therapeutic measures and those with incomplete medical records were excluded. All data such as age, gender, 6-month survival rate, type of underlying disease (diabetes and cancer), site of involvement, spread of the disease to orbit, palate, sinuses and septum, and skin, number of endoscopic procedures and the time interval between them, history of exenterating of the eye, type of received systemic treatments including Amphotericin, and the time interval between the onset of symptoms and the start of treatment were recorded and analyzed by using SPSS (version 19) and running ANOVA, T-test, and survival analysis. $P<0.05$ was considered significant.

Results

Out of 19 patients, 11 (57.9%) were males, and 8 (42.1%) were females. A 6-month survival study of rhino-orbito-sinusal mucormycosis disease revealed that ten patients (58.8%) survived. The mean of 6-month survival was (4.7±0.63) months in males and (3.8±0.63) months in females ($P=0.35$). The results showed that about 57.9% of the patients had diabetes, and 42.1% had cancer and were under chemotherapy, but there were no significant differences between underlying disease and mean of 6-month survival ($P=0.32$). The mean of 6-month survival in patients according to other variables such as age ($P=0.17$), delay in surgery ($P=0.207$), site of involvement ($P=0.13$), and the number of surgeries ($P=0.96$) showed no significant differences, but a significant difference between the mean of 6-month survival rate and history of exenterating of the eye was detected ($P=0.03$) (32% of the patients underwent exenterating of the eye. Also, the 6-month survival rate was (2.8±0.7) months in patients who underwent exenterating of the eye, and it was (5.1±0.5) months in the group who did not undergo exenterating of the eye) (Table 1).

Table 1. Survival rate according to different variables.

Variables		Survival rate	*P*
Gender	**F**	42.1%	0.35
	M	57.9%	
Age	**Less than 50**	47.4%	0.17
	More than 50	56.2%	
Underlying disease	**Cancer**	57.9%	0.32
	Diabetes mellitus	42.1%	
Site of involvement	**Sinus and cornea and septum**	52.6%	0.13
	Orbit and sinus	42.1%	
Delay in surgery	**≥3 days**	47.4%	0.20
	≤2 days	52.6%	
Exenterating of the eye	**Yes**	31.6%	0.03
	No	68.4%	
Number of surgeries	**≥3 times**	36.8%	0.96
	≤2 times	63.1%	

Discussion

Fungal infections such as mucormycosis are increasingly growing due to an increase in the number of immune-compromised patients, patients undergoing chemotherapy treatments, patients with uncontrolled diabetes, and so on. Mucormycosis is known as one of the most deadly fungal infections in humans. Success in treating patients with mucormycosis depends on factors such as early detection, treatment of underlying disease, and type of medicine therapy (11-14). The aim of this study is to evaluate the response to endoscopic treatment and treatment outcomes in patients with rhino-orbito-sinusal mucormycosis. Our results showed that about 57.9% of the patients had diabetes, and 42.1% had cancer and were under chemotherapy, but no significant

differences were detected between underlying disease and mean of 6-month survival, which may be due to the small size of the statistical population in this study. Tavanaee *et al.*, conducted a study on patients with rhino-orbito-cerebral mucormycosis and reported diabetes as the most common risk factor for this disease, which is in line with our findings (15). In another study, Javadi and Mohammadi *et al.*, investigated the underlying causes of patients with mucormycosis and reported that 55.5% of those patients had diabetes mellitus and 22.2% had leukemia (16). A study by Pinto et al. showed that 88.2% of patients with rhino-orbito-cerebral mucormycosis had diabetes mellitus and 53.3% had diabetic ketoacidosis (17). Bakhshaee *et al*., performed a study on patients with rhino-orbito-cerebral mucormycosis and yielded that the most common underlying disease was diabetes (50%) and then leukemia (44%) (18). In another study, Kashkouli et al. investigated the underlying causes of mucormycosis and reported that the most common underlying cause of mucormycosis was diabetes mellitus with a prevalence of 68.3% (19). According to all of the above mentioned studies and also according to our results, it can be concluded that diabetes is the most common risk factor for mucormycosis, which is probably related to increased blood sugar and acidosis in diabetic patients with poor control. In the present study 32% of patients with rhino-orbito-sinusal mucormycosis underwent exenterating of the eye and a significant difference between the mean of 6-month survival rate and history of exenterating of the eye was detected (P=0.03) (survival rate was (2.8±0.7) months in patients who underwent exenterating of the eye and (5.1±0.5) months in the group that did not undergo exenterating of the eye). In Javadi´s *et al*., study, exenterating of the eye was 33% that is in line with our study (16). In Tumer *et al*.,'s study, exenterating of the eye was performed for 20% of patients with mucormycosis (20). In another study, Bakhshaee *et al*., studied patients with rhino-orbito-sinusal mucormycosis and reported that the incidence of exenterating of the eye was 11.1%, which is also lower than that in our study (18). Saed *et al*., investigated endoscopic therapy in patients with mucormycosis and reported that all patients with rhino-orbito-cerebral mucormycosis who had exenterating of the eye died (9). This high mortality rate in cases with ocular involvement indicates the importance of timely exenterating of the eye to prevent pathogens invasion to the brain in these patients. In a study of patients with mucormycosis, Kashkol *et al*., demonstrated that exenterating of the eye had no effect on survival rate (19), which is inconsistent with the results of our study. In the present study, no relationship was detected between age and survival rate among patients with mucormycosis. Tavanaee *et al*., evaluated the clinical presentation and therapeutic outcomes of rhino-orbito-cerebral mucormycosis, and similarly concluded that the age of patients with mucormycosis had no effect on their survival (15). Fata *et al*., also yielded that mucormycosis can occur at any age and that people of all ages are at risk of this disease (21). Accordingly, it seems that the survival of patients with mucormycosis is not affected by age. However, more studies with a larger statistical population are needed to confirm this finding.

Our results showed that about 58% of patients were male, and there was no relationship between the patients' survival rate and gender. In a study by Khodabakhshi *et al.*, they detected no relationship between the survival of patients and gender, which is consistent with our study (22). Fata *et al*., also reported similar findings (21). So it seems that gender has no effect on the survival rate of patients with mucormycosis. In the present study, the results showed that there was no relationship between the mean of 6-month survival and the mean number of surgeries, which may be due to the small size of the statistical population. Tavanaee *et al*., evaluated clinical manifestations and treatment outcomes in patients with rhino-orbito-cerebral mucormycosis and found that lack of surgical intervention was associated with 100% mortality. Nevertheless, patients who received standard surgical treatment along with amphotericin had a survival rate of 37.5% in their study (15). According to Javadi's *et al*., study, patients who did not undergo surgery had a lower survival rate (16). The results of the aforementioned studies indicate surgical intervention in these patients. In addition, the results of the present study showed that surgical delay was associated with a decrease in the survival rate of patients; however, it was not statistically significant. In Javadi *et al*., study, patients with mucormycosis who underwent late surgery died (16), so it can be concluded that intervention in these patients should be performed as soon as possible. In a study on 24 patients with mucormycosis, Jeong *et al*., revealed that late diagnosis was associated with increased mortality in these patients (23). Javadi *et al*., found that diabetic patients with a delayed presentation did not survive despite therapeutic interventions (16). Therefore, early diagnosis and early intervention in this disease will lead to successful management of this highly fatal disease. Brad *et al*., in their study, concluded that endoscopic surgery was a pre favorable technique in the treatment of patients with mucormycosis (24) also

James *et al*., investigated mucormycosis disease using external surgery and reported high mortality (82%) in these patients despite rapid diagnosis, external surgery and treatment with amphotericin (25). The results of these studies indicate the superiority of the endoscopic surgery method over the open surgical method.

Uncontrolled diabetes is the most common underlying cause of rhino-orbito-sinusal mucormycosis. It also seems that exenterating of the eye affects the survival rate of patients. This study suggests that timely and early diagnosis as well as correct treatment, endoscopic procedure if possible, play an important role in the prognosis of the disease and can greatly reduce the mortality rate. In the absence of eye involvement and necrosis of the skin and in cases in which we are not obligated to do an open surgical treatment, endoscopic surgery is a good method for treating patients with rhino-orbito-sinusal mucormycosis because it has lower morbidity and higher accuracy.

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