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Acute Invasive Fulminant Fungal Rhinosinusitis: An Evaluation of 25 Cases

ABSTRACT

Background: Acute invasive fungal rhinosinusitis (AIFRS) is a severe infection that affects the nasal cavity and paranasal sinuses, often seen in individuals with comorbidities such as diabetes mellitus and hemato-oncological diseases. This study aims to retrospectively analyze patients diagnosed with AIFRS from 2014 to 2023.

Methods: The study was a single-center, descriptive investigation focusing on demographic details, clinical presentation, radio-pathological features, and suggested management of AIFRS patients.

Results: Of the 25 patients involved in the study, with a mean age of 48 years, hemato-oncological diseases were the most common underlying condition (44%), followed by diabetes mellitus (28%). Fungal analysis revealed *Aspergillus* species (32%) and *Mucor* (24%). The most frequently involved site was the middle turbinate (84%), while the least affected was the inferior turbinate (36%). The mortality rate was 48%, primarily due to underlying hemato-oncological diseases (32%). *Aspergillus* (16%) and *Mucor* (16%) were the most commonly encountered pathogens in fatal cases.

Conclusion: Patients with diabetes mellitus, hemato-oncological diseases, or secondary immunodeficiency undergoing steroid treatment should be vigilantly screened for AIFRS. Early diagnosis and prompt management are crucial to improve patient outcomes.

Keywords: acute invasive fungal rhinosinusitis, Aspergillus, endoscopic surgery, Mucor

INTRODUCTION

Acute invasive fungal rhinosinusitis (AIFRS) is a rapid, severe infection that primarily targets the nasal cavity and paranasal sinuses. The disease can extend to the palate, eyes, and intracranial structures.[1] It often occurs in patients with immunodeficiency, diabetes mellitus (DM), users of immunosuppressive drugs, individuals with hemato-oncological diseases, and those with AIDS. Recent reports also document instances of AIFRS in patients with coronavirus disease-2019 (COVID-19).[2,3]

The disease typically originates as a mucosal inflammation in the middle turbinate region, spreading swiftly to the paranasal sinuses. Microscopic analysis can reveal fungal hyphae within the mucosa, submucosa, bone, or intravascular structures. The most common clinical presentations include the sudden onset of facial pain, fever, nasal congestion, and foul-smelling nasal discharge. In more severe cases, patients may present with decreased visual acuity, limited gaze, diplopia, or neurological deficits and seizures, indicative of intracranial involvement.[4,5]

Aspergillus spp. is more frequently encountered in neutropenic patients, while Mucor is more common in diabetic patients.[6] Computed tomography (CT) is the preferred imaging technique to highlight changes in bone structure, whereas magnetic resonance imaging (MRI) is recommended in cases of suspected intracranial and intraorbital involvement. Management of AIFRS requires systemic antifungal therapy and critical surgical debridement, alongside addressing any contributing factors like neutropenia or high blood glucose levels. Despite these measures, mortality rates reported in various publications remain high, ranging from 18% to 80%.[5,7,8]

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Given the rare but potentially fatal nature of this disease, we aimed to present our clinic's experience with AIFRS and contribute to the literature.

MATERIAL AND METHODS

Following approval from the Hacettepe University Non-Interventional Ethics Committee (GO 22/691), we retrospectively reviewed the files of 44 patients who underwent surgery for suspected invasive fungal infections at the Hacettepe University Department of Otorhinolaryngology and Head Neck Surgery between 2014 and 2023. Biopsies were obtained from patients exhibiting clinical and radiological indications suggestive of AIFRS. All patients with a suspicion of an invasive fungal infection, based on the results of the post-biopsy pathology and/or microbiological examination, underwent surgical debridement. Patients diagnosed with AIFRS based on the results of surgical specimens were included in the study. Consequently, our study included 25 patients whose pathology results confirmed the presence of an invasive fungal infection.

We collected data on the patients' demographic characteristics, comorbidities, neutrophil levels, and HbA1C levels in the case of those with DM. We then evaluated the initial intranasal sites of involvement, the number of surgical treatments performed, and any additional surgical treatments—such as maxillectomy and orbital exenteration—that were carried out in addition to endoscopic debridement. Finally, we assessed the status of microorganism growth in tissue fungal cultures, angioinvasion in the pathology specimens, necrosis, and the mortality rates among the patients. The Kaplan–Meier estimate was used for survival analysis.

RESULTS

Our cohort consisted of 25 patients, comprising 13 males and 12 females. The median age was 46, with a range from 10 months to 74 years. Nasal obstruction was the predominant symptom, followed by fever, facial pain, headache, and facial swelling. Seven patients (28%) had DM, one of whom presented to the emergency department with ophthalmoplegia and diabetic ketoacidosis. Surgical debridement and maxillectomy were performed within 24 hours of an AIFRS diagnosis, provided the patient was hemodynamically stable. Comorbidities of the study are given in Table 1.

Mortality occurred in 4 (16%) out of 8 patients (32%) with *Aspergillus flavus* growth in tissue culture, 4 (16%) out of 6 patients (24%) with *Mucorales* class fungi, 1 patient with *Fusarium proliferatum* growth, and 3 (12%) out of 8 patients (32%) with unspecified growth in tissue cultures. *Candida krusei* and *Blastomonas ursincola* were each found in 1 patient, with no mortality observed (Table 2). Mortality was also documented in relation to additional diseases: 8 (32%) out of 11 patients (44%) with hemato-oncological diseases, 2 (8%) patients with DM, 1 (4%) patient with focal segmental glomerulosclerosis (FSGS), and 1 (4%) renal transplant patient (Table 2). The 1-year survival rate was 96.2%, dropping to 60% over 5 years, highlighting long-term mortality due to morbidities (Figure 1).

In the initial endoscopic examination of the patients, indications of invasive fungal infection were detected based on necrotic tissue, mucosal discoloration, and tissue blood supply (Figure 2). Nine patients (36%) had inferior turbinate involvement, 21 (84%) had middle turbinate involvement, 14 (56%) had septum involvement, and 15 (60%) had paranasal sinus involvement. Notably, middle turbinate involvement was present in all patients with *Mucorales* growth in tissue culture, and a wide range of intranasal structures was involved in a single patient with *C. krusei* growth. In the patient with *B. ursincola* growth, only septum involvement was detected, while only middle turbinate involvement was

Table 1. Demographic Findings, Comorbidities, Tissue Culture, and Surgical Treatment Data of the Patients

	Count	(%)
Age (median, minimum–maximum)	46 (10 months-74 years)	
Sex		
Male	13	52
Female	12	48
Comorbidities		
Diabetes mellitus	7	28
Hemato-oncological diseases	11	44
Primary immunodeficiency	2	8
Renal transplantations	2	8
Intracranial mass	1	4
Sarcoidosis	1	4
Focal segmental glomerulosclerosis	1	4
Species		
Mucorales	6	24
Aspergillus flavus	8	32
Candida krusei	1	4
Blastomonas ursincola	1	4
Fusairum prolifetarum	1	4
Not specified	8	32
Surgical treatment		
Only debridement	12	48
Debridement + orbital exenteration	2	8
Debridement + maxillectomy	7	28
Debridement + maxillectomy + orbital exenteration	4	16
Total cases	25	100

MAIN POINTS

- Acute Invasive Fungal Rhinosinusitis (AIFRS) has high rate of mortality, severe infection that primarily targets the nasal cavity and paranasal sinuses.
- Patients with diabetes mellitus, hematological malignancies, and immunosuppression should be alert for AIFRS.
- Early diagnosis and prompt management are crucial to improve patient outcomes.

Table 2. Mortality Rates According to Culture Results and Comorbidities

		Mortality		
		Yes (%)	No (%)	Total (%)
Species	*Aspergillus*	4 (16)	4 (16)	8 (32)
	Mucorales	4 (16)	2 (8)	6 (24)
	Candida	0 (0)	1 (4)	1 (4)
	Fusarium	1 (4)	0 (0)	1 (4)
	Blastomonas	0 (0)	1 (4)	1 (4)
	Not speficied	3 (12)	5 (20)	8 (32)
Total		12 (48)	13 (52)	25 (100)
Comorbidities	Diabetes mellitus	2 (8)	5 (20)	7 (28)
	Hemato-oncological diseases	8 (32)	3 (12)	11 (44)
	Primary immunodeficiency	0 (0)	2 (8)	2 (8)
	Renal transplantation	1 (4)	1 (4)	2 (8)
	Intracranial mass	0 (0)	1 (4)	1 (4)
	FSGS	1 (4)	0 (0)	1 (4)
	Sarcoidosis	0 (0)	1 (4)	1 (4)
Total		12 (48)	13 (52)	25 (100)

FSGS, focal segmental glomerulosclerosis.

found in the patient with *F. prolifetarum* growth. *A. flavus* overgrowth was most commonly associated with middle turbinate involvement (Table 3).

DISCUSSION

Acute invasive fungal rhinosinusitis is a potentially life-threatening clinical condition requiring quick diagnosis and timely medical and surgical treatment. It predominantly affects patients with hemato-oncological diseases, DM, and primary and secondary immunodeficiencies. In diabetic patients, the chronic hyperglycemic state impacts the cell-mediated immune system, impairing chemotaxis, phagocytosis, and macrophage cytokine secretion.[9] With the ongoing COVID-19 pandemic, the incidence of AIFRS has increased, owing to the impairment of T lymphocyte, CD4+, and CD8+ T-cell functions.[10] Additionally, the use of glucocorticoids, a standard treatment for COVID-19, raises the risk due to their anti-inflammatory and immunosuppressive properties. Eker et al[11] have reported that orbital and cavernous sinus involvement is more common in patients with COVID-19-associated mucormycosis. In our cohort of 25 cases, 1 patient diagnosed with acute myeloid leukemia and concurrent COVID-19 developed AIFRS in the first week and passed away on the 33rd day. A study by Kurşun et al[12] found that the most common underlying clinical conditions in their series were DM, hemato-oncological diseases, and chronic renal failure, respectively. Another study of 18 cases reported that 50% of patients had DM, and 44% had leukemia.[13] Two additional studies also found DM to be the most common predisposing factor and concurrent disease leading to AIFRS.[14,15] Unlike these studies, our

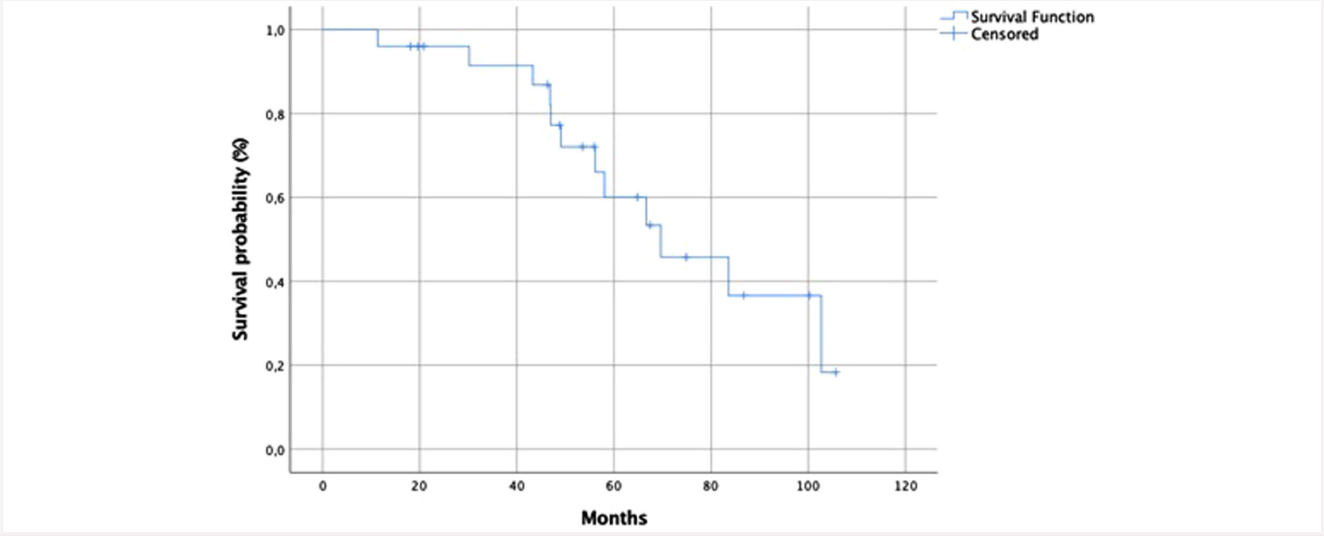

Figure 1. One-year and 5-year overall survival rates of patients.

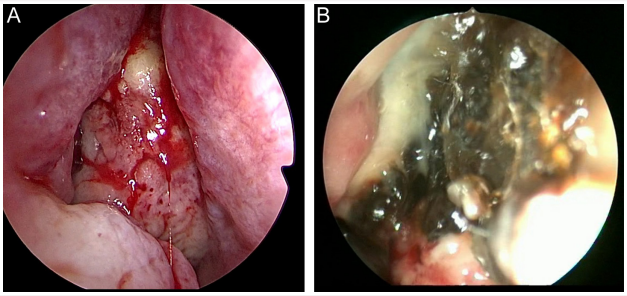

Figure 2. (A) Impaired blood supply in the middle turbinate and (B) necrotic involvement in the anterior nasal septum.

research found that hemato-oncological diseases was the most common clinical condition in 11 (44%) of AIFRS patients, followed by DM in 7 (28%) patients. The reason for the discrepancy could be the large number of hemato-oncological patients treated at our institution.

Radiological imaging plays a critical role in patients suspected of having AIFRS. While bone destruction and effacement of the periantral fat planes can be observed in CT scans, MRI provides a detailed evaluation of intracranial and orbital involvement (Figure 3). In our study, 13 patients (52%) were highly suspected of AIFRS based on radiological findings. In a previous case series of 19 patients from our clinic, AIFRS was diagnosed in patients who lacked radiological evidence of invasive fungal infection but exhibited high suspicion in endoscopic examination.[16] This highlights the importance of conducting repeat diagnostic nasal endoscopies due to the potential for a false-negative diagnosis in radiology. Del Gaudio et al[17] observed mucosal thickening in 21 (91%) of 23 patients as an early sign of CT. Howell and Ramadan, however, suggest that patients suspected of AIFRS should be evaluated with MRI if early CT scans yield no specific findings.[18]

We documented the regions with invasive fungal infection involvement at the time of patients' initial diagnosis. Middle turbinate involvement was the most common, seen in 21 (84%) out of 25 patients. Inferior turbinate involvement was found only in 9 (36%) patients. A case series from our clinic in 2006 showed the most common site of involvement to be the septum (12 patients, 63.2%), followed by the middle turbinate (11 patients, 57.9%), and the inferior turbinate (8 patients, 43%).[16] The superior blood supply of the inferior turbinate may account for its resistance to infection. A study by Gillespie et al[7] found a similar pattern, with the most common mucosal abnormalities in the middle turbinate (67%), followed by the septum (24%), hard palate (19%), and inferior turbinate (10%). Furthermore, our pathology results show that more than one intranasal structure is involved in patients with *Mucorales*-type growth in tissue culture. Despite invasive and widespread involvement seen in our patient with *C. krusei* growth in tissue culture, we were unable to make a reliable interpretation due to the limited number of patients.

Numerous fungal species such as *Rhizopus*, *Mucor*, and *Aspergillus* can cause AIFRS. In our series, *Aspergillus* was found to be the most common microorganism in 8 (32%) patients, followed by *Mucorales* in 6 (24%) patients. *Mucor* has been reported as the most common microorganism in many studies.[12,15,19-21] In AIFRS cases secondary to COVID-19, Ismaiel et al[22] reported that *Rhizopus* (44.4%) and *Aspergillus fumigatus* (33.3%) are common microorganisms, but El-Kholy et al[21] reported *Mucor* (77.8%) is more common. In our study, *F. proliferatum* was found in AIFRS secondary to COVID-19 disease, a rare occurrence. However, a weakness of our study is the lack of specific identification in tissue cultures of 8 (32%) patients. The pathology reports of these patients noted invasive fungal hyphae but could not specify the type, possibly due to colonization, transport conditions, and time in tissue culture.

Effective treatment of AIFRS requires multidisciplinary management, including otolaryngology, infectious diseases, ophthalmology, and neurosurgery. Intravenous antifungal therapy, surgical debridement, and management of underlying diseases form the cornerstone of treatment. Aggressive and repeated debridements should be performed to remove all ischemic, necrotic tissue. In our study, all patients underwent debridement, 6 (24%) patients underwent orbital exenteration, and 11 (44%) patients had maxillectomy. In a literature review by Turner et al,[23] the rate of orbital exenteration was approximately 20%. Rates of endoscopic debridement alone were reported as 61.90%,[24] 66.7%,[21] and 67.6%[25] in different series. Our series found a rate of 48% (12 patients). Gode et al[25] associated palate involvement with a poor prognosis, while orbital involvement was not linked to a poor prognosis. Liposomal amphotericin B is the first-line medical treatment and should be initiated as

Table 3. Involvement of Intranasal Structures According to Culture Results (N: number)

		Species						
		Mucorales	*Aspergillus*	*Candida*	*Blastomonas*	*Fusarium*	No Bacterial Growth	Total
Inferior turbinate involvement	N	1	3	1	0	0	4	9
	%	4	12	4	0	0	16	36
Middle turbinate involvement	N	6	6	1	0	1	7	21
	%	24	24	4	0	4	28	84
Septum involvement	N	5	3	1	1	0	4	14
	%	20	12	4	4	0	16	56
Paranasal sinus involvement	N	5	3	1	0	0	6	15
	%	20	12	4	0	0	24	60

N, number.

Figure 3. (A) Bone erosion in the posterior wall of the maxillary sinus on the left side and increased density in the periantral region on CT. (B) MRI of a patient with orbital exenteration.

soon as clinical suspicion arises. In patients undergoing treatment with liposomal amphotericin B, regular monitoring of renal function is essential. Additionally, several studies have demonstrated the efficacy of local amphotericin B as a treatment modality.[26,27,28] However, local amphotericin B was not employed in any of the patients in this study. The duration of antifungal therapy should be determined in accordance with the recommendations of infectious disease specialists. Each patient was administered intravenous antifungal therapy for a minimum of 6 weeks at our clinic.

Despite rapid diagnosis and treatment, AIFRS has overall survival rates ranging from 20% to 80%.[7,12,29,30] The mortality rate in the 807 case series by Turner et al was 50.3%, closely matched by our series with 48%. A prior study from our clinic reported a mortality rate of 68.4%; the decrease in the mortality rate is noteworthy.[16] Orbital and intracranial extensions are known to increase mortality risk[31], and in our series, 2 (33%) out of 6 patients who underwent orbital exenteration died.

The limitations of our study include its retrospective nature and a relatively small patient population. Furthermore, we lack sufficient long-term information on the duration of medical treatment and drug dosages.

Acute invasive fungal rhinosinusitis is a high mortality and morbidity clinical condition, the prevalence of which has surged in recent years due to the advent of immunosuppressive treatments, the COVID-19 pandemic, and other predisposing factors. The key to early diagnosis is a high level of suspicion in patients presenting with clinical predisposing factors. A diagnostic nasal endoscopy and biopsy should be performed promptly. To prevent mortality, it is essential to ensure a swift diagnosis, rapid commencement of empirical antifungal therapy, and early surgical intervention. The most crucial aspect, however, lies in managing the underlying predisposing factors effectively.

Ethics Committee Approval: This study was approved by the Ethics Committee of Hacettepe University (Approval no.: GO 22/691; Date: 05.07.2021).

Informed Consent: N/A.

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REFERENCES

1. Kasapoglu F, Coskun H, Ozmen OA, Akalin H, Ener B. Acute invasive fungal rhinosinusitis: evaluation of 26 patients treated with endonasal or open surgical procedures. *Otolaryngol Head Neck Surg*. 2010;143(5):614-620. [CrossRef]
2. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. *Am J Emerg Med*. 2021;42:264.e5-264.e8. [CrossRef]
3. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus*. 2020;12(9):e10726. [CrossRef]
4. Momeni AK, Roberts CC, Chew FS. Imaging of chronic and exotic sinonasal disease: review. *AJR Am J Roentgenol*. 2007;189(6 suppl):S35-S45. [CrossRef]
5. Aribandi M, McCoy VA, Bazan C. Imaging features of invasive and noninvasive fungal sinusitis: a review. *RadioGraphics*. 2007;27(5):1283-1296. [CrossRef]
6. Middlebrooks EH, Frost CJ, De Jesus RO, Massini TC, Schmalfuss IM, Mancuso AA. Acute invasive fungal rhinosinusitis: a comprehensive update of CT findings and design of an effective diagnostic imaging model. *AJNR Am J Neuroradiol*. 2015;36(8):1529-1535. [CrossRef]
7. Gillespie MB, O'Malley BW, Francis HW. An approach to fulminant invasive fungal rhinosinusitis in the immunocompromised host. *Arch Otolaryngol Head Neck Surg*. 1998;124(5):520-526. [CrossRef]
8. Parikh SL, Venkatraman G, DelGaudio JM. Invasive fungal sinusitis: a 15-year review from a single institution. *Am J Rhinol*. 2004;18(2):75-81. [CrossRef]
9. Erener S. Diabetes, infection risk and COVID-19. *Mol Metab*. 2020;39:101044. [CrossRef]
10. Moorthy A, Gaikwad R, Krishna S, et al. SARS-CoV-2, uncontrolled diabetes and corticosteroids-an unholy trinity in invasive fungal infections of the maxillofacial region? a retrospective, multi-centric analysis. *J Maxillofac Oral Surg*. 2021;20(3):418-425. [CrossRef]
11. Eker C, Tarkan O, Surmelioglu O, et al. Alternating pattern of rhino-orbital-cerebral mucormycosis with COVID-19 in diabetic patients. *Eur Arch Otorhinolaryngol*. 2023;280(1):219-226. [CrossRef]
12. Kursun E, Turunc T, Demiroglu YZ, Aliskan HE, Arslan AH. Evaluation of 28 cases of mucormycosis. *Mycoses*. 2015;58(2):82-87. [CrossRef]
13. Bakhshaee M, Bojdi A, Allahyari A, et al. Acute invasive fungal rhinosinusitis: our experience with 18 cases. *Eur Arch Otorhinolaryngol*. 2016;273(12):4281-4287. [CrossRef]
14. Ketenci I, Unlü Y, Kaya H, et al. Rhinocerebral mucormycosis: experience in 14 patients. *J Laryngol Otol*. 2011;125(8):e3. [CrossRef]
15. Mohammadi R, Meidani M, Mostafavizadeh K, et al. Case series of rhinocerebral mucormycosis occurring in diabetic patients. *Caspian J Intern Med*. 2015;6(4):243-246.
16. Süslü AE, Öğretmenoğlu O, Süslü N, Yücel ÖT, Önerci TM. Acute invasive fungal rhinosinusitis: our experience with 19 patients. *Eur Arch Otorhinolaryngol*. 2009;266(1):77-82. [CrossRef]
17. DelGaudio JM, Swain RE, Kingdom TT, Muller S, Hudgins PA. CT Wndings in patients with invasive fungal sinusitis. *Arch Otolaryngol Head Neck Surg*. 2003;129(2):236-240. [CrossRef]
18. Howells RC, Ramadan HH. Usefulness of CT and MR in fulminant invasive fungal rhinosinusitis. *Am J Rhinol*. 2001;15(4):255-261. [CrossRef]
19. Abu El-Naaj I, Leiser Y, Wolff A, Peled M. The surgical management of rhinocerebral mucormycosis. *J Craniomaxillofac Surg*. 2013;41(4):291-295. [CrossRef]
20. Bellazreg F, Hattab Z, Meksi S, et al. Outcome of mucormycosis after treatment: report of five cases. *New Microbes New Infect*. 2015;6:49-52. [CrossRef]

21. El-Kholy NA, El-Fattah AMA, Khafagy YW. Invasive fungal sinusitis in post COVID-19 patients: a new clinical entity. *Laryngoscope*. 2021;131(12):2652-2658. [CrossRef]
22. Ismaiel WF, Abdelazim MH, Eldsoky I, et al. The impact of COVID-19 outbreak on the incidence of acute invasive fungal rhinosinusitis. *Am J Otolaryngol*. 2021;42(6):103080. [CrossRef]
23. Turner JH, Soudry E, Nayak JV, Hwang PH. Survival outcomes in acute invasive fungal sinusitis: a systematic review and quantitative synthesis of published evidence. *Laryngoscope*. 2013;123(5):1112-1118. [CrossRef]
24. Dokania V, Gaikwad NS, Gite V, et al. Emergence of invasive fungal rhinosinusitis in recently recovered COVID-19 patients. *Ann Otol Rhinol Laryngol*. 2022;131(11):1202-1209. [CrossRef]
25. Gode S, Turhal G, Ozturk K, Aysel A, Midilli R, Karci B. Acute invasive fungal rhinosinusitis: survival analysis and the prognostic indicators. *Am J Rhinol Allergy*. 2015;29(6):e164-e169. [CrossRef]
26. Agarwal V, Kumia K, Gupta A, Singh V. Local injection of amphotericin B: novel use in the treatment of fungal maxillary sinusitis. *Int J Oral Maxillofac Surg*. 2023;52(12):1282-1285. [CrossRef]
27. Seiff SR, Choo PH, Carter Sr. Role of local amphotericin B therapy for sino-orbital fungal injecitons. *Opthalmşc Plast Reconstr Surg*. 1999;15(1):28-31.
28. Raj P, Vella EJ, Bickerton RC. Successful treatment of rhinocerebral mucormycosis by a combination of aggressive surgical debridement and the use of systemic liposomal amphotericin B and local therapy with nebulized amphotericin—a case report. *J Laryngol Otol*. 1998;112(4):367-370. [CrossRef]
29. Vaezi A, Moazeni M, Rahimi MT, de Hoog S, Badali H. Mucormycosis in Iran: a systematic review. *Mycoses*. 2016;59(7):402-415. [CrossRef]
30. Chen CY, Sheng WH, Cheng A, et al. Invasive fungal sinusitis in patients with hematological malignancy: 15 years experience in a single university hospital in Taiwan. *BMC Infect Dis*. 2011;11(11):250. [CrossRef]
31. Mohindra S, Mohindra S, Gupta R, Bakshi J, Gupta SK. Rhinocerebral mucormycosis: the disease spectrum in 27 patients. *Mycoses*. 2007;50(4):290-296. [CrossRef]