Diagnosis and Management of Sphenoid and Ethmoid Fungal Sinusitis

Komang Tri Parama Arthika^{1*}, I N Wartawan²

THT-Departemen Kepala dan Leher RSUD Wangaya, Indonesia

Email: tryparama1993@gmail.com

*Correspondence

ABSTRACT

e-ISSN: 2798-5210

p-ISSN: 2798-5652

Rhinosinusitis is a common disorder affecting 20% of the population. Chronic sinus infections unresponsive to antibiotics should raise suspicion for fungal rhinosinusitis. Various types of fungi cause inflammation of the sinus mucosa. Sinusitis is an inflammation of the mucosa of the paranasal sinuses that can be caused by viruses, bacteria, parasites, or fungi. Fungal sinusitis is the rarest form of sinusitis. Fungal sinusitis can be classified based on the severity into invasive and non-invasive types. The severity of fungal sinusitis depends on the patient's immune status. Consequently, invasive fungal sinusitis often occurs in patients with chronic diseases that impair the immune system, such as diabetes mellitus (DM). This condition can lead to dangerous complications, including the rapid spread of the fungus to the eyes, brain, and surrounding tissues. Therefore, the diagnosis and management of invasive fungal sinusitis should be conducted promptly and accurately. The incidence of fungal sinusitis is rarely encountered; however, in recent decades, the incidence has been reported to be increasing. In Asia, the incidence of fungal sinusitis accounts for 42% of all rhinosinusitis cases. Symptoms vary depending on the patient's immune status. CT scan is one of the imaging methods that can be used to assist in the diagnosis of invasive fungal sinusitis and provide important information for appropriate management, leading to more accurate and rapid treatment. Fungal sinusitis occurs when airborne fungi adhere to the mucous membrane of the nasal cavity and sinuses through respiratory inhalation. Fungal sinusitis manifests in various forms, ranging from simple irritation of the sinus mucosa to life-threatening disease. Fungal sinusitis may be asymptomatic, but common symptoms include purulent rhinorrhea, facial pain, and postnasal drip. Diagnosing fungal sinusitis through nasal endoscopy is challenging. In computed tomography (CT), fungal sinusitis is characterized by observations such as calcifications, heterogeneous soft tissue density lesions, and periosteal thickening. The treatment involves endoscopic removal of fungal masses, which fully widen the sinus ostium8.

Keywords: Sinusitis Sphenoid, Etmoid, Fungal, FESS.

INTRODUCTION

Rhinosinusitis is a common disorder affecting 20% of the population. Chronic sinus infections that are resistant to antibiotics should raise suspicion for fungal rhinosinusitis (Gowthame et al., 2024). Various types of fungi can cause inflammation of the sinus mucosa. Sinusitis is an inflammation of the mucosa of the paranasal sinuses, which can be caused by viruses, bacteria, parasites, or fungi. Fungal sinusitis is the least common form of sinusitis (Yuliyanti et al., 2025). Fungal sinusitis can be classified based on its severity into invasive and non-invasive fungal sinusitis. The severity of fungal sinusitis depends on the patient's immune status. Therefore, invasive fungal sinusitis is more commonly seen in patients with chronic immunocompromised conditions such as diabetes mellitus (DM) (Shah & Bhalodiya, 2014).

This condition can lead to dangerous complications, such as the rapid spread of the fungus to the eyes, brain, and surrounding tissues. As such, the diagnosis and management of invasive fungal sinusitis should be prompt and accurate (Suresh et al., 2016). Although fungal sinusitis is rare, its incidence has

reportedly increased over the past few decades. The incidence of fungal sinusitis in Asia accounts for 42% of all rhinosinusitis cases. Symptoms of fungal sinusitis vary depending on the patient's immune status. A CT scan is one of the imaging methods that can be used to help diagnose invasive fungal sinusitis and provide important information for appropriate management to improve treatment outcomes (Monga et al., 2022).

Fungal sinusitis occurs when airborne fungi adhere to the mucous membrane of the nasal cavity and sinuses through inhalation. Fungal sinusitis manifests in a variety of forms, ranging from mild irritation of the sinus mucosa to life-threatening conditions (Chaganti et al., 2020). Fungal sinusitis may be asymptomatic, but common symptoms include purulent rhinorrhea, facial pain, and postnasal drip. Diagnosing fungal sinusitis through nasal endoscopy can be challenging. On computed tomography (CT), fungal sinusitis is characterized by findings such as calcification, heterogeneous soft tissue density lesions, and periosteal thickening (Swain, 2022).

The treatment involves endoscopic removal of the fungal ball and full widening of the sinus ostium. The sphenoid sinus, which is the paranasal structure closest to the skull base, requires special attention due to its proximity to vital structures such as the internal carotid artery and optic nerve (Lahdji & Primasari, 2017). Preoperative imaging and careful surgical planning should be performed before treatment involving the sphenoid sinus. Several fungal species have been found to involve the paranasal sinuses, with the most common being Aspergillus, Alternaria, Mucor, and Rhizopus. These fungi may affect one or multiple sinuses. The four types of fungal sinus infections are.

1. Fungal Ball

This occurs when fungi implant into a healthy sinus, and on CT, it appears as a hyperdense area without evidence of bone erosion or expansion. The maxillary sinus is the most commonly affected, followed by the sphenoid, ethmoid, and frontal sinuses, in that order. Treatment involves endoscopic removal of the fungal ball and adequate sinus drainage. Antifungal therapy is not required.

2. Allergic Fungal Sinusitis

This is an allergic reaction to the causative fungi, presenting with sinonasal polyposis and mucus that contains eosinophils, Charcot-Leyden crystals, and fungal hyphae. There is no fungal invasion of the sinus mucosa. Typically, more than one sinus is involved on one or both sides. A CT scan shows mucosal thickening with hyperdense areas. There may be sinus expansion or bone erosion due to pressure, but no fungal invasion. The treatment consists of endoscopic sinus cleaning with drainage and ventilation, combined with pre-and post-operative systemic steroids (Oretti et al., 2019).

3. Chronic Invasive Sinusitis

Here, the fungus invades the sinus mucosa, and bone erosion occurs due to fungal infiltration. Patients present with chronic rhinosinusitis. A CT scan shows thickened mucosa, sinus opacity, and bone erosion. Patients may experience intracranial or intraorbital invasion. Histopathology reveals submucosal fungal invasion and a granulomatous reaction with multinucleated giant cells. Treatment involves the surgical removal of affected mucosa, bone, and soft tissue, followed by appropriate antifungal therapy. With antifungal therapy using intravenous amphotericin B, up to a total of 2-3 grams, combined with itraconazole therapy for 12 months or longer, monitored by serial CT scans or MRI.

4. Fulminant Fungal Sinusitis

This is an acute condition most commonly observed in immunocompromised individuals or those with diabetes. The fungal species commonly involved are Mucor or Aspergillus.

- a. Mucor spp. Causes rhinocerebral disease. Due to vascular invasion, Mucor fungi lead to ischemic necrosis, which appears as a black eschar, involving the inferior turbinate, palate, or sinuses, and spreading to the face, eyes, skull base, and brain. Treatment involves debridement of necrotic tissue and intravenous amphotericin B^{3,5}.
- b. Aspergillus spp. can also cause fulminant acute sinusitis with tissue invasion. These patients present with acute sinusitis that progresses to sepsis and other sinus-related complications. Unlike Mucor infections, there is no black eschar. Treatment includes antifungal therapy and surgical intervention^{3,5}.

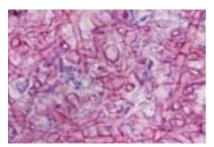


Figure 1 Histopathology finding: Aspergillosis Aspergillosis features the characteristic tangled and septated fungal hyphae, branched at 4503

Clasification Fungal sinusitis

Table T1	
Acute	
Acute Fulminant	Invasive
Chronic	
Chronic Indolent	Invasive
Fungal Ball	Non Invasive
Allergic Fungal Sinusitis	Non Invasive

This disease progresses slowly, resulting in chronic granulomatous inflammation and possible expansion of the sinus wall with polyps. The condition has been compared to an aggressive local neoplasm. Plasma cells and eosinophils can be found in the sinus mucosa, which is also seen in Allergic Fungal Sinusitis (AFS). Many of these patients have a history of allergies, making it difficult to differentiate from AFS. Fungi must be visualized microscopically in the sinus tissue to distinguish this entity from the two forms of non-invasive fungal sinusitis. Aspergillus species and the dematiaceous family are common causative organisms (Lahdji & Primasari, 2017). Chronic invasive fungal sinusitis is almost endemic in certain regions, such as Sudan and northern India. Reports of this disease have significantly decreased in the United States over the past decade. We have not seen any cases since 1980 and believe this disease is quite rare, certainly the rarest form of fungal sinus infection. When pathological examination confirms fungal invasion, the physician is obligated to treat the patient aggressively. Complete surgical excision with extensive exposure and significant bone removal is

indicated. Extensive antifungal therapy, guided by in vitro fungal culture sensitivity, should also be used. Although recurrence is common, some patients achieve full recovery, and the prognosis is much better than that of acute fungal sinusitis (Hardjoprawito et al., 2024).

Fungal Ball

The old name for this form of non-invasive chronic fungal sinusitis includes mycetoma and aspergilloma. This disease typically affects immunocompetent, non-atopic patients and usually causes no symptoms or only mild pressure sensations. It can affect any sinus but typically involves a single sinus, most often the maxillary antrum, without causing bone erosion or mucosal invasion. The fungal proliferation results in a dense, tangled mass with a clay-like appearance. The absence of sinus inflammation distinguishes this condition from other forms of chronic fungal sinusitis. The etiological organism is almost always Aspergillus fumigatus. Treatment consists of fungal removal and sinus aeration, with a healing rate approaching 100%. In our recent review of 20 consecutive cases of chronic fungal sinusitis, 2 cases had a fungal ball, which corresponds to an incidence of 10%. This is in contrast to experiences in Europe, where it appears to be the most common form of fungal sinusitis.

Pathophysiology

Sinus health is influenced by the patency of the sinus ostia and the efficiency of mucociliary clearance within the ostiomeatal complex (OMC). Mucus also contains antimicrobial substances and other compounds that serve as defense mechanisms against pathogens that enter with inhaled air. The structures that make up the OMC are anatomically close to each other, and when edema occurs, the opposing mucosal surfaces may come into contact, preventing the cilia from moving and causing obstruction of the Ostia. As a result, negative pressure develops within the sinus cavity, leading to transudation, initially serous. This condition may be considered non-bacterial rhinosinusitis and often resolves within a few days without treatment.

However, if this condition persists, the secretions that accumulate within the sinus create an ideal medium for the growth and multiplication of bacteria, turning the secretions purulent. This progression is referred to as acute bacterial rhinosinusitis and requires antibiotic therapy. If treatment fails (for example, due to predisposing factors), inflammation continues, hypoxia develops, and anaerobic bacteria proliferate. The mucosa becomes more swollen, creating a feedback cycle that eventually leads to chronic changes in the mucosa, including hypertrophy, polypoid formation, or the development of polyps and cysts. In this state, surgical intervention may be required (Kanodia et al., 2021).

Diagnosis

Physicians must maintain a high index of suspicion for Allergic Fungal Sinusitis (AFS) to avoid overlooking the diagnosis. AFS can easily be mistaken for chronic bacterial sinusitis or non-allergic fungal sinusitis, both of which require vastly different treatments and have different prognoses. Without sufficient awareness, rhinologists may miss the diagnosis of AFS and become frustrated by unexplained recurrences in patients with "chronic sinusitis." Additionally, the presence of extra mucosal fungal hyphae may be misinterpreted as acute, potentially life-threatening fungal sinusitis, leading to inappropriate use of radical surgery or intravenous antifungal therapy. To clarify the diagnosis of AFS, we prospectively evaluated 15 consecutive patients with confirmed AFS⁵.

Treatment

Most otolaryngologists are now familiar with Allergic fungusitis (AFS), but increased recognition has not yet led to significant advances in treatment. Most experts agree that Functional Endoscopic Sinus Surgery (FESS) with total removal of the fungal mass and any trapped debris is

indicated. The extent of surgery correlates with the amount of pathology present. FESS allows for the removal of all non-diseased tissue, and external or obliterative surgery is contraindicated in uncomplicated AFS. In any form of surgery, microscopic fungal contamination in the sinus may persist, which could serve as a source of recurrent disease. Patients generally experience remarkable benefits from surgery, but unfortunately, improvement is often temporary (Kim & Jung, n.d.).

Steroids are used to reduce the abnormal immune response, and their use has increased postoperatively to help control inflammation and prevent recurrence. Our recent retrospective analysis of 26 patients showed that steroids effectively reduce inflammation and help maintain periods of disease-free intervals. However, the disease recurred when steroid treatment was discontinued, and patients treated with steroids did not show a clear benefit in long-term outcomes with extended follow-up (mean follow-up = 12.5 months). Despite the lack of strong data supporting the efficacy of steroids, we still recommend their use postoperatively to prolong remission. We recommend oral prednisone postoperatively (0.4-0.6 mg/kg/day), gradually tapering by 0.1 mg/kg/day every 4 days until reaching 0.2 mg/kg/day. Patient symptoms and objective signs should guide the subsequent steroid titration. The appropriate duration of steroid therapy is not well established. An alternative regimen involves prednisone at 0.5 mg/kg/day for 3 months, after which a gradual taper should be considered5.

Some clinicians reserve steroids for recurrent disease, given their known side effects, including premature epiphyseal closure in children, gastric ulcers, weight gain, mood changes, and immunosuppression (which may increase the risk of fungal invasion). Other studies argue that the understanding of AFS as a hypersensitivity reaction rather than an invasive process supports the use of systemic steroids. Our experience has shown that all patients who are not treated with steroids will eventually experience recurrence. Preoperative use of steroids may also be considered, but the potential benefits must be weighed against the known risks and the lack of extensive clinical experience. Essentially, steroids work by dampening the pathological hypersensitivity to fungal antigens, but they do not permanently reverse the disease process, highlighting the need for other forms of therapy. Topical steroids can be used for local immune modulation without the risk of systemic complications. However, steroids are not significantly effective in AFS, possibly because nasal sprays reach the nasal cavity but not the sinuses themselves. Systemic antifungals, such as amphotericin B, are not effective in AFS5.

We have had anecdotal success with less aggressive systemic antifungals like itraconazole or ketoconazole, but, in general, they have not proven to be helpful. Theoretically, systemic antifungals should not be effective against fungi that are located outside the mucosa, beyond the reach of the drug's circulation. For antifungals to be effective, they would need to be secreted into the sinus mucus, a phenomenon that has not been supported by research and may not occur. A more realistic approach might be the future use of topical antifungals, which could hypothetically reduce the antigen load in the sinus and help modulate the immune response more directly within the affected area. Treatments for AFS may be serial endpoint titration (SET) or allergen desensitization. Desensitizing patients to the fungal antigens that trigger their abnormal Type I immune response holds therapeutic potential. If fungi act more as allergens than as infectious agents, successful treatment will likely depend on clearing each patient's sinuses of fungal antigens and modifying the pathological immune response. Many allergists express skepticism about desensitizing AFS patients, believing that the formation of IgG-blocking antibodies could worsen Type III immune responses and exacerbate the disease. We have anecdotal experience with SET yielding positive outcomes, but it has not yet been used routinely. Recent data presented by Mabry et al. suggests that immunotherapy may be both safe and effective. In a prospective

study of 10 AFS patients treated with immunotherapy, there was a "significant reduction in nasal congestion, a minimum recurrence of polypoid mucosa, and a decrease or absence of the need for steroids (both systemic and topical) in most of these patients." With this initial data, further studies on immunotherapy could be pursued with greater confidence and diligence5.

METHOD

A patient visited the ENT outpatient clinic at Wangaya Regional General Hospital on September 17, 2024, with the initials NLG/P/50 years old. The patient complained of pain in both eyeballs, a blocked nose, frequent nasal discharge in the morning, and difficulty breathing. The patient reported that these symptoms occurred almost every morning for approximately the past year. The patient had previously only consulted a general practitioner, but as the symptoms gradually worsened, the general practitioner referred the patient for a head CT scan.

The patient has a history of polyp surgery 2 years ago and reports a history of controlled hypertension, for which they regularly take Amlodipine 5 mg orally once a day. The patient denies any other systemic illnesses.

On general examination, the patient's vital signs were as follows: blood pressure 120/90 mmHg, pulse 82 beats per minute, respiratory rate 22 breaths per minute, axillary temperature 36.7°C, and SpO2 99%. On local examination of the ENT, no abnormalities were noted. However, the patient brought a CT scan result from the BE Primary Clinic, which showed mucosal thickening in the walls of the right and left ethmoidal sinuses, as well as the right sphenoid sinus, while other structures were within normal limits.

On September 17, 2024, the patient underwent an anterior nasal endoscopy, which revealed secretions in both nostrils and a leftward septal deviation, with other findings still within normal limits. The patient was then scheduled for a CT scan of the nose and paranasal sinuses at Wangaya Regional General Hospital to confirm the presence of sinusitis. The patient was prescribed cefixime 200 mg orally twice daily, Avamys nasal spray 2 puffs once daily, and advised to return for a follow-up visit on September 27, 2024.

The patient was later informed of the CT scan results, which indicated chronic right and left ethmoidal sinusitis, right sphenoid sinusitis, a patent stomatal complex, minimal leftward septal deviation, and hypertrophy of the inferior turbinates on both sides and the right medial turbinate.



Figure 2 Ct. Scan sinus Ethmoidalis



Figure 3
Ct. Scan sinus Sphenoid

After receiving the results, the patient was scheduled for Functional Endoscopic Sinus Surgery (FESS). The patient was then referred to the Internal Medicine and Anesthesia departments for an assessment of the operability and suitability for surgery. On October 5, 2024, the patient underwent a chest X-ray and a complete blood count (CBC) while awaiting readiness for the surgical procedure.

On October 6, 2024, the patient underwent surgery, with FESS, under general anesthesia via endotracheal intubation (GA-OTT).



Figure 4
Fungus Ball at Sinus Sphenoid
before operation



Figure 5 Sinus Sphenoid with FESS After operation

After the surgical procedure, the patient reported post-operative pain. There was no diplopia (-), and the movement of the eyeballs was normal (+/+) on examination. On the ENT examination, the nasal cavity appeared to have tampons in place, making it difficult to evaluate the mucosa, turbinates, secretions, and septum. The patient was treated with intravenous fluid (IVFD RL 20 tpm), ceftriaxone 1 gram intravenously twice daily, methylprednisolone 8 mg orally twice daily, omeprazole 20 mg twice daily, pain relief as per anesthesia protocol, and was scheduled for tampon removal on October 07, 2024, at the ENT clinic.

On October 07, 2024, the patient underwent tampon removal. The patient still complained of minimal post-operative pain, described as throbbing at the surgical site. The patient was allowed to go home with the following medications: ciprofloxacin 500 mg orally twice daily, methylprednisolone 8 mg orally three times a day, omeprazole 20 mg orally twice daily, ketoconazole 200 mg orally twice daily, paracetamol 500 mg orally three times a day, and a follow-up scheduled for October 14, 2024.

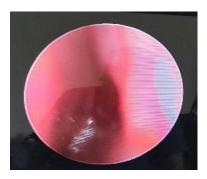


Figure 6 days post fess

On October 14, 2024, the post-operative pain had decreased. The ENT examination revealed crusting in the left nostril, with other findings within normal limits. The patient was continued on the same medication regimen and scheduled for a follow-up visit on October 21, 2024.



Figure 7 days post FESS

On October 21, 2024, the patient reported further improvement and a nasoendoscopy was performed, which showed that the nasal cavity appeared normal according to the images.



Figure 8
Days post FESS

The patient was also prescribed additional therapy of nasal irrigation with a 0.9% NaCl solution (morning and evening) and advised to follow up if any more complaints.

RESULTS AND DISCUSSION

A case of fungal sinusitis, specifically sphenoid fungal ball, has been reported in a 50-year-old female patient who underwent excision of fungal tissue from the right sphenoid sinus. Comparing this case with the established theory, the symptoms observed are consistent with those of fungal sinusitis, which typically include purulent rhinorrhea, facial pain, and post-nasal drip. These symptoms were also reported by the patient.

In terms of diagnostic support, the literature recommends a paranasal sinus CT scan to evaluate fungal sinusitis, and in this case, the patient also underwent a CT scan, which is in line with the standard procedure.

Regarding treatment, the literature suggests the use of corticosteroids (either nasal or oral) and antifungal medications, which is consistent with the management provided to the patient. The patient was given oral methylprednisolone, Avamys nasal spray, and oral ketoconazole, which align with the recommended therapeutic approach for fungal sinusitis.

In this case, the patient underwent Functional Endoscopic Sinus Surgery (FESS) with excision of the fungal mass. This is by the theory, as FESS is considered the most favored surgical procedure by many otolaryngologists. FESS is minimally invasive, offers faster recovery, ensures complete removal of the fungal mass and debris trapped in the sinus cavity, and allows the patient to return home and recover without further complications. The procedure was successful, and the patient showed significant improvement, confirming the appropriateness of the approach.

In conclusion, the management of this case, including diagnostic evaluation, therapeutic approach, and surgical intervention, is consistent with the current standards for fungal sinusitis and has resulted in a favorable outcome for the patient.

CONCLUSION

Fungal sinusitis, specifically sphenoid fungal ball, is a rare condition but can lead to serious complications if not treated properly. Case studies in this journal show that the main symptoms experienced by patients, such as purulent rhinorrhea, facial pain, and postnasal drip, correspond to the clinical manifestations of fungal sinusitis that have been reported in the literature. The diagnosis carried out using a CT scan of the paranasal sinuses has confirmed the presence of a fungal infection, which is also the standard procedure in the identification of fungal sinusitis. In this case, the patient underwent Functional Endoscopic Sinus Surgery (FESS) as the primary intervention method, which is a minimally invasive surgical technique and is effective in the management of fungal sinusitis.

The therapy given, including the use of corticosteroids and antifungal drugs such as ketoconazole, is also in line with treatment recommendations in various previous studies. Postoperatively, patients show significant improvement, signaling the success of the diagnosis and treatment strategies applied. Overall, this study confirms the importance of early diagnosis and proper management in cases of fungal sinusitis to prevent further complications. An evidence-based approach involving imaging, pharmacological therapy, and surgical intervention provides optimal outcomes for patients.

DAFTAR PUSTAKA

- Chaganti, P. D., Rao, N. B., Devi, K. M., Janani, B., Vihar, P. V, & Neelima, G. (2020). Study of fungal rhinosinusitis. *Journal of Dr. YSR University of Health Sciences*, 9(2), 103–106.
- Gowthame, K., Prabakaran, S., Namasivaya Navin, R. B., Rajasekaran, S., Muthukumar, R., Balaji, D., Sarath Kumar, B., & Lakshana, R. (2024). Prevalence of Fungal Sinusitis in Cases of Allergic Rhinitis: A Cross-Sectional Study. *Indian Journal of Otolaryngology and Head & Neck Surgery*, 1–4.
- Hardjoprawito, T. J. A., Poerbonegoro, N. L., Priyono, H., Tamin, S., Bramantyo, B., Alviandi, W., Zizlavsky, S., Reksodiputro, M. H., Wardani, R. S., & Yunizaf, R. (2024). *Buku Pendidikan Dasar Ilmu Kesehatan Telinga Hidung Tenggorok-Bedah Kepala Leher*.
- Kanodia, A., Verma, H., Jain, A., Kalsotra, G., Kumari, S., Agrawal, S. K., Gautam, H., Kaushal, D., Gugliani, A., & Lodha, J. (2021). Prevention and management of complications. *Essentials of Rhinology*, 277–307.
- Kim, J. K., & Jung, S. J. (n.d.). A Case of the Sphenoid Fungal Sinusitis Under Local Anesthesia. *World J Surg Surgical Res.* 2024; 7, 1548.
- Lahdji, A., & Primasari, A. (2017). Buku Ajar Sistem Telinga, Hidung dan Tenggorokkan. Unimus Press.
- Monga, S., Malik, J. N., Sharma, A., Agarwal, D., Priya, R., & Naseeruddin, K. (2022). Management of fungal rhinosinusitis: experience from a tertiary care centre in North India. *Cureus*, *14*(4).
- Oretti, G., Castellana, G., Manuguerra, R., Silini, E. M., & Ferri, T. (2019). Isolated fronto-ethmoidal allergic fungal rhinosinusitis: case report and review of the literature. *Acta Bio Medica: Atenei Parmensis*, 90(4), 563.
- Shah, H., & Bhalodiya, N. (2014). Scenario of fungal infection of nasal cavity and paranasal sinuses in Gujarat: a retrospective study. *Gujarat Med J*, 69(2), 27–31.
- Suresh, S., Arumugam, D., Zacharias, G., Palaninathan, S., Vishwanathan, R., & Venkatraman, V. (2016). Prevalence and clinical profile of fungal rhinosinusitis. *Allergy & Rhinology*, 7(2), ar-2016.
- Swain, S. K. (2022). Management of acute invasive fungal sinusitis. *Mustansiriya Medical Journal*, 21(2), 104–110.



© 2025 by the authors. Submitted for possible open-access publication under the terms and conditions of the Creative Commons Attribution (CC BY SA) license (https://creativecommons.org/licenses/by-sa/4.0/).