

CASE REPORT

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Fungal Sphenoiditis in a Patient With ANCA-associated Vasculitis

Maria A. Shumikhina, Tatyana A. Shirokikh, Pavel V. Azarov

City Clinical Hospital No. 52, Moscow, Russia

ABSTRACT

Fungal sinusitis comprises a heterogeneous group of diseases differing in etiology, clinical presentation, and pathogenesis. One such form is a *mycetoma*, a noninvasive form characterized by the accumulation of fungal hyphae and debris within a sinus cavity, without invasion of the mucosa. Isolated sphenoid sinus mycetoma is relatively rare, and its pathophysiology remains incompletely understood. The patient's immune status plays a critical role in the pathogenesis of fungal sinusitis, as immunosuppression is a major risk factor for the transformation of noninvasive mycetoma into an invasive form, potentially resulting in severe complications. Therefore, immune status assessment in patients with noninvasive fungal sinusitis, particularly in the presence of comorbidities and immunosuppressive therapy, is essential for determining optimal treatment strategies. This article presents a clinical case of *fungal sphenoiditis* in a female patient with granulomatosis with polyangiitis (*ANCA-associated vasculitis*) undergoing immunosuppressive therapy. The case is notable for the combination of noninvasive fungal sphenoiditis with a high risk of invasive disease due to immunosuppression. Given the elevated risk, the patient underwent endoscopic sphenoidectomy followed by systemic antifungal therapy. This case highlights the importance of early surgical intervention and appropriate systemic antifungal treatment in preventing infection progression and complications in patients with noninvasive fungal sinusitis, especially in the context of immunosuppression.

Keywords: fungal rhinosinusitis; mycetoma; fungal sphenoiditis; *Aspergillus* spp.; ANCA-associated vasculitis; functional endoscopic sinus surgery; endoscopic nasal sphenoidectomy.

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КЛИНИЧЕСКИЙ СЛУЧАЙ

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Грибковый сфеноидит у пациента с АНЦА-ассоциированным васкулитом

М.А. Шумихина, Т.А. Широких, П.В. Азаров

Городская клиническая больница № 52, Москва, Россия

АННОТАЦИЯ

Грибковые синуситы представляют собой гетерогенную группу заболеваний, различающихся по этиологии, клиническим проявлениям и патогенезу. Среди них выделяют мицетому — неинвазивную форму, характеризующуюся скоплением грибковых гиф и детрита в пазухе, без поражения слизистой оболочки. Изолированная мицетомы клиновидной пазухи появляется относительно редко, и патофизиология ее развития остается до конца не изученной. Важную роль в патогенезе грибковых синуситов играет иммунный статус пациента, поскольку иммуносупрессия — это значимый фактор риска трансформации неинвазивной мицетомы в инвазивную форму, что может приводить к серьезным осложнениям. Следовательно, оценка иммунного статуса у пациентов с неинвазивной формой грибкового синусита, особенно при наличии сопутствующих заболеваний и иммуносупрессивной терапии, приобретает решающее значение для выбора оптимальной тактики лечения. В настоящей статье представлен клинический случай грибкового сфеноидита у пациентки с гранулематозом с полиангиитом (АНЦА-ассоциированным васкулитом), получавшей иммуносупрессивную терапию. Особенность данного случая — сочетание неинвазивного грибкового сфеноидита и высокого риска развития инвазивного процесса в условиях иммуносупрессии. Учитывая это, пациентке была выполнена эндоскопическая сфеноэтомидэктомия с последующей системной противогрибковой терапией. Данный пример подчеркивает важность раннего хирургического вмешательства и адекватной системной антимикотической терапии для предотвращения прогрессирования инфекции и развития осложнений у пациентов с неинвазивным грибковым синуситом, особенно при наличии факторов риска иммуносупрессии.

Ключевые слова: грибковый риносинусит; мицетомы; грибковый сфеноидит; *Aspergillus* spp.; ANCA-ассоциированный васкулит; функциональная эндоскопическая хирургия носовых пазух; эндоскопическая назальная сфеноэтомидэктомия.

Как цитировать

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INTRODUCTION

Fungal sinusitis is a heterogeneous group of diseases characterized by a wide variety of etiologies, causative agents, clinical manifestations, microscopic and macroscopic features, treatment options, and prognoses. The histological diagnostic criteria proposed by DeShazo classify allergic, chronic non-invasive (mycetoma), chronic invasive, granulomatous invasive, and acute fulminant invasive fungal sinusitis [1, 2]. The pathogenesis of fungal sinusitis depends on the patient's immune status and comorbidities [3].

Mycetoma, also known as aspergilloma, is described as a non-invasive dense conglomerate of fungal hyphae, typically *Aspergillus* spp. This condition is characterized by the gradual accumulation of hardened fungal debris and mucus in the sinuses without the involvement of mucous membranes, blood vessels, or bony structures [4, 5].

Isolated sphenoid sinus mycetoma is rare, accounting for only 1%–3% of cases of rhinosinusitis [6, 7]. The pathophysiology of an isolated sphenoid sinus mycetoma is not fully understood. For example, a maxillary sinus mycetoma has some predisposing factors, one of which is an odontogenic origin. The calcium salts (zinc oxide) in the filling material act as a catalyst for mycetoma development [8]. This assumption is difficult to apply to the sphenoid sinus due to its anatomical location. The trigger for a fungal ball in the sphenoid sinus is still unclear.

There are some theories about the pathogenesis of non-invasive fungal sphenoiditis. The aerogenic theory claims that inhaled fungal spores may become pathogenic [4, 9]. Additional triggers are necessary to activate the pathological process. The trigger foreign agent theory claims that certain anatomical features on the affected side allow foreign substances to enter the unobstructed sphenoid sinus. A unilateral excess air space in the nasal cavity is the predisposing factor, providing freer and wider access to the anterior wall of the sphenoid sinus. Forced nasal inhalation can cause a relatively small foreign body to enter the nasal cavity. A wide sphenoid ostium allows a foreign body to freely penetrate the sphenoid sinus. These features increase the likelihood that a foreign body will penetrate the sphenoid sinus and trigger mycetoma formation [10].

Computed tomography visualizes mycetoma as a hyperdense lesion caused by tangled fungal hyphae. This lesion is typically confined to a single sinus and have linear or punctate calcifications at its center [11, 12]. Although there are no signs of invasion, erosive lesions

in bone structures may be present due to necrosis caused by pressure from the fungal body [13, 14]. Systemic or local antifungal therapy is ineffective because the fungal lesions are non-invasive [15]. Surgery involves removing the fungal ball and dilating the sphenoid ostium to ensure adequate outflow [4, 8, 16]. The removed fungal ball is sent for histopathological verification. A diagnosis largely depends on these results [17] because fungal cultures often yield negative results due to the low viability of hyphae [8].

CASE DESCRIPTION

In 2017, a 61-year-old woman was diagnosed with granulomatosis with polyangiitis, a systemic antineutrophil cytoplasmic antibody (ANCA)-associated¹-vasculitis with hyperproduction of anti-proteinase 3 (PR3) antibodies, involving the ears and sinuses (bilateral otitis and pansinusitis), kidneys (rapidly progressive glomerulonephritis), and lungs (hemorrhagic bronchitis). In 2023, she was admitted to the Nephrology Department for inpatient treatment and pathogenetic therapy due to complaints of fever, general weakness, and difficulty nasal breathing. The patient's condition was considered severe due to receiving immunosuppressive therapy (glucocorticoids, cyclophosphamide, rituximab), progression of acute kidney injury in addition to Stage 3b chronic kidney disease (glomerular filtration rate of 42 mL/min according to the CKD-EPI equation), and systemic inflammatory response with C-reactive protein of 31.9 mg/L and procalcitonin of 2.42 ng/mL (Fig. 1). The anti-PR3 antibody level was negative at 9.65 relative units/mL. A multispiral computed tomography of the paranasal sinuses was performed to identify the site of infection because systemic inflammatory response was progressing (Fig. 2). A fungal infection of the right sphenoid sinus was detected, so it was decided that the mycetoma should be surgically removed (Figs. 3 and 4). The material was sent for histopathological examination.

Microscopically, small fragments appeared as intertwined threads of hyphal mycelium with signs of dystrophy and necrosis and small calcium salt deposits. The patient received non-surgical treatment. Due to acute kidney injury, the patient was switched from amphotericin B to voriconazole (400 mg twice a day at 12-hour intervals, followed by 200 mg twice a day for 9 days), co-trimoxazole (480 mg twice a day for 5 days), metronidazole (500 mg three times a day for 6 days), and methylprednisolone (4 mg for 10 days). Non-surgical treatment for acute kidney injury was also provided. Positive changes were observed during the treatment, including the normalization

¹ Antineutrophil Cytoplasmic Antibody-Associated Vasculitis.

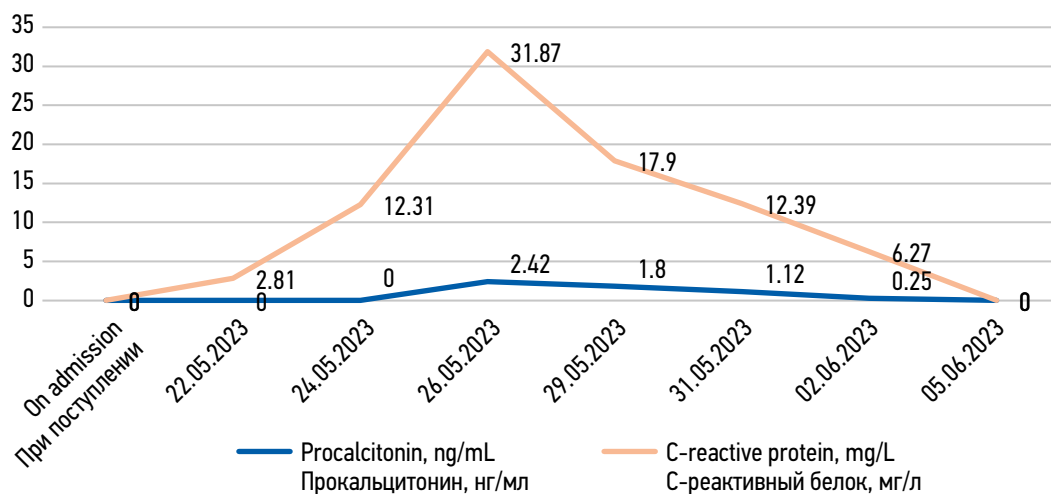


Fig. 1. Temporal changes in inflammatory markers (C-reactive protein, procalcitonin).

Рис. 1. Динамика маркеров воспалительного процесса (С-реактивный белок, прокальцитонин).

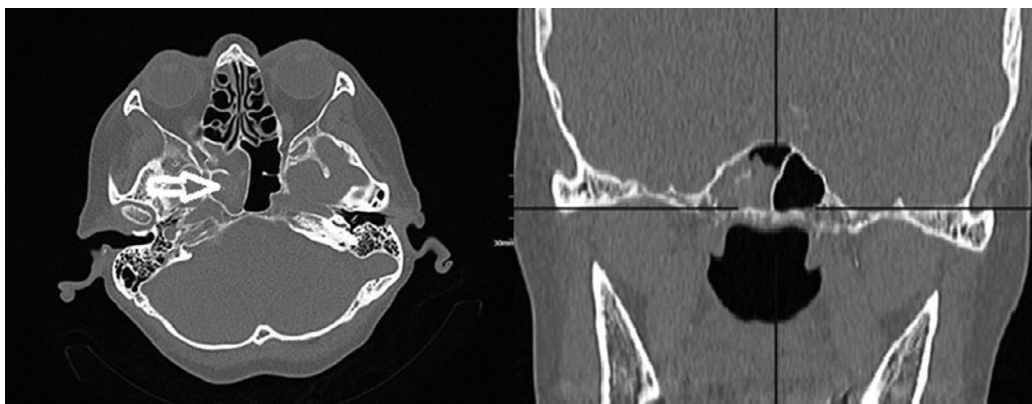


Fig. 2. Multislice computed tomography of the paranasal sinuses (2023), sagittal and coronal views. A hyperdense lesion with a solid component (*fungal ball*) and an area of calcification (*arrow*) is observed in the right sphenoid sinus, which is characteristic of a mycetoma. No signs of bony destruction are detected.

Рис. 2. Мультиспиральная компьютерная томограмма придаточных пазух от 2023 г. в сагиттальной и коронарной проекциях. На сагиттальной проекции в правой клиновидной пазухе определено гиперденсивное образование с плотным компонентом (грибковое тело) с участком кальцификации (указано стрелкой), что характерно для мицетомы. Деструктивных изменений костных структур не выявлено.

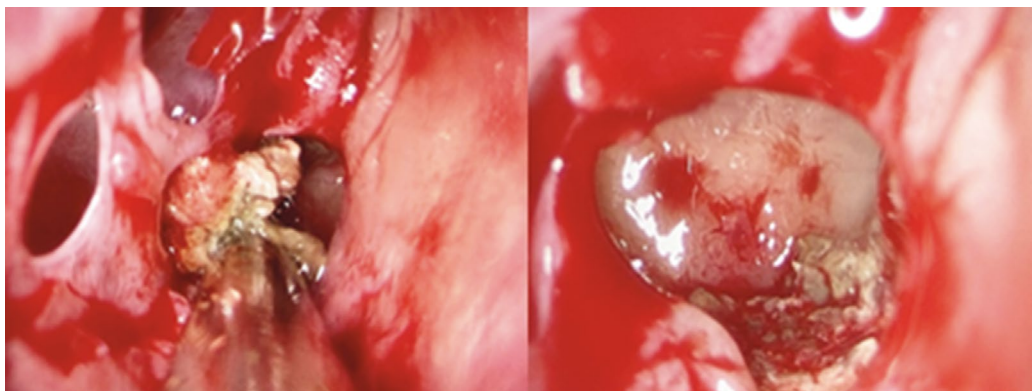


Fig. 3. Intraoperative endoscopic view. Endoscopic transnasal sphenoidectomy was performed on the right side. A fungal ball occupying the lower third of the right sphenoid sinus was visualized.

Рис. 3. Интраоперативная эндоскопическая картина. Была выполнена эндоскопическая трансназальная сфеноэтмоидэктомия справа. При эндоскопии в правой основной пазухе определено грибковое тело, полностью занимающее нижнюю треть пазухи.

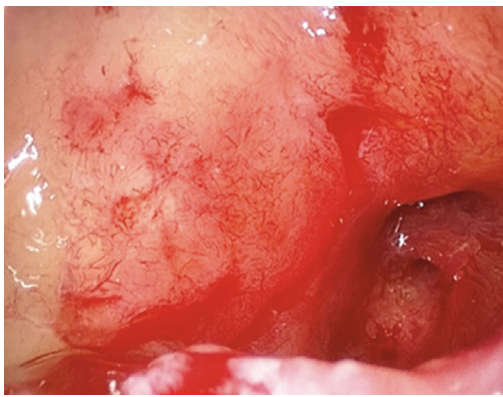


Fig. 4. Intraoperative endoscopic view after removal of the fungal ball. The sinus was irrigated with an antiseptic solution and 0.9% sodium chloride. No residual fungal material was detected on inspection with 30° and 70° endoscopes; the mucosa appeared edematous.

Рис. 4. Интраоперационный эндоскопический обзор после удаления грибкового тела. Пазуха промыта раствором антисептика и 0,9% раствором натрия хлорида. При осмотре пазухи 30° и 70° эндоскопом данных о наличии грибкового тела нет, слизистая оболочка отечна.

of systemic inflammatory response markers, such as C-reactive protein (0 mg/L) and procalcitonin (0.25 ng/mL). The patient was discharged from the hospital under the supervision of a local nephrologist and was prescribed antifungal therapy with voriconazole for 3 months at 400 mg/day.

In 2024, multispiral computed tomography of the paranasal sinuses (Fig. 5) and exploratory endoscopy of the sphenoid sinus (Fig. 6) were performed.

DISCUSSION

Although mycetoma is noninvasive, there are some reports that suggest it can progress to an invasive form in immunocompromised patients [8, 18, 19]. Some authors recommend additional systemic antifungal therapy, such as itraconazole, for immunocompromised patients with non-invasive sinusitis because sphenoid sinus mycetoma may progress to an invasive form after surgery [8, 20, 21]. Clinicians should remain alert for potential serious complications of sphenoid sinus mycetoma. Even if the *Aspergilli* are non-invasive, as demonstrated by negative mucosal biopsy, the fungal ball can serve as a site for subsequent bacterial attachment, leading to bacterial sinusitis, meningitis, and subdural empyema [22].

One article compares two groups of patients, with and without risk factors for invasive fungal sinusitis. Each group was diagnosed with paranasal sinus mycetoma [23, 24]. The authors concluded that the following predisposing factors increase the likelihood of mycetoma affecting the deep sinuses, such as the sphenoid



Fig. 5. Multislice computed tomography of the paranasal sinuses (2024), coronal and sagittal views. A wide communication between the right sphenoid sinus and the ethmoid air cells remains along the anterior wall, up to 7 mm. No mucosal thickening or sinus contents are observed. No bony destruction is noted.

Рис. 5. Мультиспиральная компьютерная томограмма придаточных пазух от 2024 г. Коронарная и сагиттальная проекция компьютерной томографии околоносовых пазух. В правой половине клиновидной пазухи сохранено широкое сообщение с ячейками решетчатой кости по передней стенке пазухи до 7 мм. Утолщения слизистой оболочки и содержимого не определены. Деструктивных изменений клиновидной пазухи не выявлено.

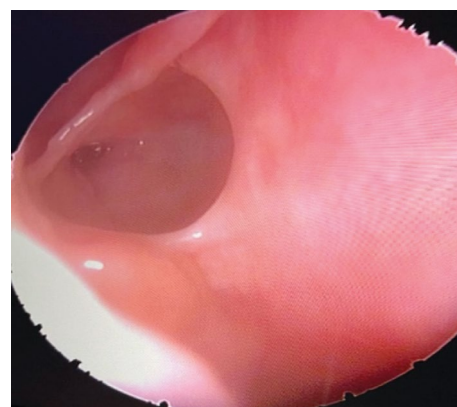


Fig. 6. Endoscopic image (2024), 0° endoscope. No sinus content is observed in the right sphenoid sinus. The mucosa appears pale pink, smooth, and glistening. The sphenoid sinus ostium remains widely patent.

Рис. 6. Эндоскопическая картина от 2024 г. Осмотр эндоскопом 0°. При эндоскопическом осмотре клиновидной пазухи справа данных о содержимом нет. Слизистая оболочка бледно-розовая, гладкая, блестящая. Сустье клиновидной пазухи широко раскрыто.

and ethmoid sinuses: immunosuppressive therapy, long-term systemic corticosteroid therapy, immunodeficiency, kidney transplantation, hematologic malignancies, and uncontrolled diabetes mellitus. All cases of mycetoma were treated surgically. For difficult-to-treat cases, antifungal therapy was administered for complete cure.

The clinical case describes an immunocompromised patient with isolated fungal sphenoiditis who received immunosuppressive, hormonal, and monoclonal antibody therapies for an underlying disease, ANCA-associated vasculitis. This is a risk factor for an invasive fungal process. In this case, fungal sphenoiditis was most likely caused by immunosuppressive therapy and prolonged hormonal therapy. Elevated procalcitonin levels should be mentioned as a sign of an increased risk for sepsis. A large retrospective study showed that, unlike bacterial sepsis, fungal sepsis is characterized by a lower increase in blood procalcitonin levels [4]. Considering all of the above factors, the authors decided to perform an endoscopic sphenoidectomy, followed by systemic antifungal therapy, to reduce the risk of complications.

CONCLUSION

It is important to differentiate between invasive and noninvasive fungal sinusitis to determine treatment strategies and predict disease outcomes. This case report emphasizes the importance of evaluating the risk of progression from non-invasive to invasive fungal sinusitis, especially in patients with immunodeficiency and those receiving immunosuppressive therapy. For patients with non-invasive fungal sinusitis who are at risk of progression to an invasive form, early surgical treatment followed by systemic antifungal therapy should be considered. Therefore, risk stratification for invasive fungal sinusitis is important for patients receiving immunosuppressive therapy and for those with primary or secondary immunodeficiencies.

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ADDITIONAL INFORMATION

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AUTHORS INFO

* **Maria A. Shumikhina**, MD;

address: 3 Pekhotnaya St., Moscow, 123182, Russia;

ORCID: 0009-0001-1557-0220;

e-mail: masha_myxa@mail.ru

Tatyana A. Shirokikh, MD;

ORCID: 0009-0000-1360-3992;

e-mail: tshirokih83@yandex.ru

Pavel V. Azarov, MD;

ORCID: 0009-0004-7408-7847;

eLibrary SPIN: 3536-5462;

e-mail: azarovp@mail.ru

ОБ АВТОРАХ

* **Шумихина Мария Артемовна**;

адрес: Россия, 123182, Москва, ул. Пехотная, д. 3;

ORCID: 0009-0001-1557-0220;

e-mail: masha_myxa@mail.ru

Широких Татьяна Анатольевна;

ORCID: 0009-0000-1360-3992;

e-mail: tshirokih83@yandex.ru

Азаров Павел Викторович;

ORCID: 0009-0004-7408-7847;

eLibrary SPIN: 3536-5462;

e-mail: azarovp@mail.ru

* Corresponding author / Автор, ответственный за переписку