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Case Report

Rhino Orbital Mucormycosis in a Kidney Transplant Recipient Despite Initially Negative Sinonasal Imaging

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Abstract

Background: Rhino-orbital mucormycosis is a rapidly progressive opportunistic infection in immunocompromised patients. Early disease may lack characteristic sinonasal findings, which can delay tissue diagnosis. **Case Presentation:** A 29-year-old man with focal segmental glomerulosclerosis underwent living-donor kidney transplantation in October 2024. He received tacrolimus, mycophenolate mofetil, and corticosteroids. In February 2025, he was admitted with fever, chills, headache, and febrile neutropenia. Initial otorhinolaryngologic examination and paranasal sinus computed tomography showed no findings suggestive of mucormycosis. His prolonged hospital course was complicated by recurrent fever, pancytopenia, and multiple microbiological findings, including Candida krusei, Aspergillus flavus, cytomegalovirus, and adenovirus. When a new crusted lesion developed in the oral cavity and nasal passage, punch biopsy with intraoperative frozen-section assessment demonstrated mucormycosis. Surgical debridement and liposomal amphotericin B at 5 mg/kg/day were initiated, and immunosuppression was reduced. Subsequent contrast-enhanced magnetic resonance imaging demonstrated nasopharyngeal, orbital, and sinonasal involvement. Despite intensive antifungal therapy, surgery, and supportive care, the patient died during hospitalization. **Conclusions:** Initially normal sinonasal examination and imaging do not exclude mucormycosis in highly immunosuppressed kidney transplant recipients. Repeated examination and urgent tissue sampling are essential when fever persists without a satisfactory response to antimicrobial treatment.

Keywords: mucormycosis; kidney transplantation; rhino-orbital infection; invasive fungal infection; tissue diagnosis

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1. Introduction

Mucormycosis is an uncommon but life-threatening invasive fungal infection caused by fungi of the order *Mucorales*. Its characteristic angioinvasive behavior may result in vascular thrombosis, tissue infarction, and rapidly progressive necrosis [1–4]. Despite advances in diagnostic methods and antifungal therapy, delayed diagnosis and treatment remain associated with substantial morbidity and mortality [1,3,5].

Although classically associated with uncontrolled diabetes mellitus and hematological malignancies, mucormycosis also occurs in patients receiving corticosteroids, those with prolonged neutropenia, and individuals with trauma or burns [2–5]. Solid-organ transplant recipients are particularly vulnerable because of cumulative immunosuppression, metabolic complications, graft dysfunction, rejection therapy, renal replacement therapy,

and exposure to broad-spectrum antimicrobial agents [6,7]. In a recent systematic review of mucormycosis in solid-organ transplant recipients, kidney transplant recipients represented approximately half of reported cases, while rhino-orbital-cerebral involvement was among the most frequent disease presentations [8].

Rhino-orbital-cerebral mucormycosis may rapidly extend from the paranasal sinuses to the orbit and central nervous system through direct invasion and angioinvasion [1,4,9]. However, its early manifestations may be nonspecific, and initial endoscopic or radiological assessments can be unrevealing. Persistent or evolving sinonasal, facial, or orbital symptoms in a high-risk patient should therefore prompt serial clinical and radiological reassessment and timely tissue sampling [1,9,10]. Histopathological demonstration of tissue invasion, supported by fungal culture and molecular identification when available, remains central to diagnostic confirmation [1,10].

Here, we report rhino-orbital mucormycosis in a kidney transplant recipient whose initial sinonasal evaluation was unrevealing. Diagnosis was established only after serial reassessment and tissue sampling, highlighting the importance of sustained diagnostic vigilance when clinical suspicion persists despite initially nondiagnostic findings.

2. Case Presentation

A 29-year-old man with focal segmental glomerulosclerosis underwent living-donor kidney transplantation on 24 October 2024. He was admitted on 10 February 2025 with fever, chills, unilateral headache, myalgia, and sore throat. Initial testing showed febrile neutropenia (leukocyte count, 660/mm^3; absolute neutrophil count, 80/mm^3) and a C-reactive protein concentration of 180 mg/L. Serial blood and urine cultures, as well as thoracic imaging studies, were performed as part of the evaluation of persistent fever and respiratory symptoms.

Because of the combination of persistent fever and unilateral headache in a highly immunosuppressed kidney transplant recipient, neurologic and otorhinolaryngologic assessments were performed early during admission. There was no orbital deficit, facial asymmetry, or meningeal irritation. Initial otorhinolaryngologic examination revealed no suspicious lesion in the nasal cavity, palate, or oropharynx. Paranasal sinus computed tomography showed no pathology suggestive of invasive fungal sinusitis, although findings consistent with bacterial sinusitis were noted and cranial imaging did not demonstrate a focal intracranial process. Therefore, there was no initial clinical or radiological evidence of rhino-orbital mucormycosis.

The subsequent hospital course was prolonged and clinically complex. The hospital course was complicated by recurrent fever, persistent cytopenias, respiratory complications, and neurologic manifestations. Serial neurologic examinations and cranial computed tomography and magnetic resonance imaging did not identify a focal intracranial cause at that stage. Bronchoscopy respiratory specimens grew Candida krusei and Aspergillus flavus; these were respiratory isolates, without documented tissue evidence establishing invasive candidiasis or aspergillosis. Cytomegalovirus and adenovirus were detected by EDTA-plasma polymerase chain reaction during March 2025 (positive results were documented on 18 and 24 March); repeat testing was negative on 28 April. Mycophenolate mofetil was withheld during periods of severe infection and cytopenia, while tacrolimus exposure and corticosteroid doses were modified according to the clinical condition and drug levels. Mycophenolate mofetil (1000 mg twice daily) was withheld because of severe cytopenia. Tacrolimus and corticosteroid doses were subsequently adjusted according to his clinical status and drug levels. By 10 April 2025, his corticosteroid was methylprednisolone (Prednol), 10 mg once daily; the tacrolimus trough level was 7.6 ng/mL on that date (approximately

8 ng/mL). Severe neutropenia persisted despite granulocyte colony-stimulating factor, with no sustained neutrophil recovery documented.

The diagnostic process remained challenging because several alternative explanations for persistent fever were present throughout the admission. Profound neutropenia, multiple microbiological findings, recurrent inflammatory activity, and respiratory complications supported a broad differential diagnosis that included bacterial infection, viral reactivation, invasive candidiasis, aspergillosis, drug-related cytopenia, and other opportunistic infections. In this context, the lack of a visible sinonasal lesion at the first otorhinolaryngologic examination and the absence of suggestive findings on initial paranasal sinus imaging made invasive sinonasal mucormycosis less apparent at presentation.

Nevertheless, the patient remained at high risk for invasive mould infection because of recent kidney transplantation, multidrug immunosuppression, corticosteroid exposure, severe neutropenia, and a complicated infectious course. The clinical picture also evolved over time. Persistent or recurrent fever despite repeated reassessment and targeted antimicrobial treatment remained an important warning sign.

On 12 April 2025, persistent fever and new mucosal symptoms prompted repeat otorhinolaryngologic evaluation. Whitish lesions were identified on the left middle turbinate and within the oral cavity; however, their macroscopic appearance was not considered characteristic of mucormycosis (Figure 1A). Frozen-section examination of a biopsy showed hyphal structures compatible with mucormycosis in necrotic tissue (Figure 1B). The oral cavity lesion biopsy showed regular squamous epithelium without significant abnormality. The available pathology report did not specify special stains, detailed hyphal morphology, or explicit tissue or vascular invasion; it recommended correlation with microbiological findings. Fungal culture or molecular identification results were not documented in the available records.

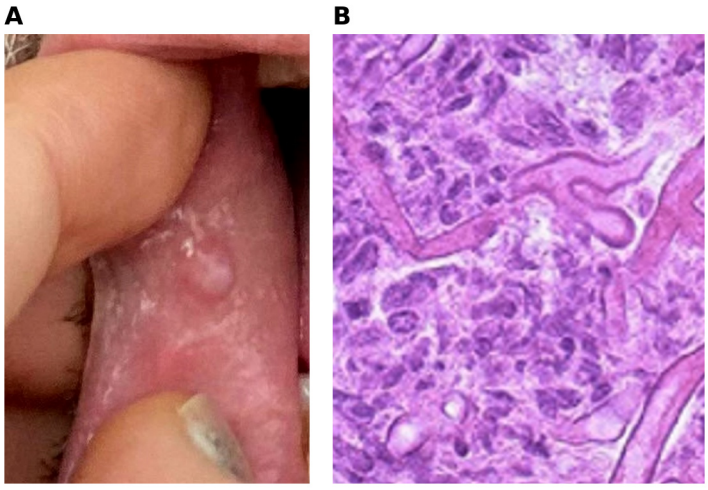


Figure 1. Clinical and histopathological findings. (**A**) Intraoral mucosal lesion observed during the clinical course. (**B**) Representative histopathological image showing fungal elements consistent with mucormycosis.

On 12 April 2025, urgent surgical debridement, including middle turbinate excision, was performed. Liposomal amphotericin B was initiated at 5 mg/kg/day, and immunosuppression was further reduced. Follow-up examinations did not initially reveal an obvious palatal or oral lesion. Management was directed toward the principal components of mucormycosis treatment: rapid initiation of active antifungal therapy, surgical source control, and reduction in immunosuppression when clinically feasible. These interventions had

to be balanced against the risk of allograft dysfunction and rejection in a recently transplanted patient.

Despite antifungal treatment, surgical debridement, and adjustment of immunosuppression, the patient's clinical status progressively deteriorated. Contrast-enhanced cranial and orbital magnetic resonance imaging subsequently demonstrated extensive sinonasal, nasopharyngeal, and orbital involvement. There was no radiological evidence of intracerebral invasion. However, the absence of intracerebral involvement did not indicate a favourable course, as the patient had already developed extensive locoregional disease in the setting of severe systemic illness. He required intensive care support and died during the same hospitalization on 16 May 2025 (Table 1).

Table 1. Timeline.

Date	Clinical Event
24 October 2024	Living-donor kidney transplantation for focal segmental glomerulosclerosis.
10 February 2025	Hospital admission with fever, chills, headache, and febrile neutropenia.
February 2025	Initial otorhinolaryngologic assessment and paranasal sinus CT without findings of invasive fungal sinusitis.
Feb-April 2025	Persistent and recurrent fever with cytopenias and multiple concomitant infectious findings.
April 2025	New middle turbinate lesion; frozen-section biopsy consistent with mucormycosis; surgical debridement performed.
After diagnosis	Liposomal amphotericin B 5 mg/kg/day and reduced immunosuppression; later MRI showed nasopharyngeal, orbital, and sinonasal involvement.
Same admission	Clinical progression and death despite intensive treatment.

3. Discussion

This case highlights a critical diagnostic dilemma in kidney transplant recipients: invasive fungal disease may evolve despite initially unrevealing sinonasal examination and cross-sectional imaging.

Our patient had a profoundly increased net state of immunosuppression, driven by recent kidney transplantation, triple maintenance immunosuppression, corticosteroid exposure, profound neutropenia, prolonged hospitalization, and multiple concurrent infections. These factors created a clinical context in which persistent fever and focal headache should have continued to raise concern for an invasive mould infection, even in the absence of an initial localizing lesion [1–4,6–8].

The diagnostic difficulty was compounded by the detection of *Candida krusei*, *Aspergillus flavus*, *cytomegalovirus*, and *adenovirus* during the same hospitalization. *Candida krusei* and *Aspergillus flavus* were isolated from bronchoscopic respiratory specimens; without tissue evidence, these findings do not establish invasive candidiasis or aspergillosis. *CMV* and *adenovirus* were documented by plasma PCR. Although these microbiological findings were clinically relevant, they may have provided alternative explanations for recurrent fever, cytopenias, and respiratory deterioration. This illustrates an important cognitive and clinical challenge: identification of one or more pathogens should not terminate the diagnostic search when the clinical course remains disproportionate, progressive, or unexplained. In profoundly immunocompromised transplant recipients, more than one opportunistic infection may coexist, and the emergence of new focal symptoms requires renewed diagnostic assessment.

These concurrent infections complicated interpretation of fever and clinical deterioration but did not exclude a coexisting invasive mould infection.

Rhino-orbital-cerebral mucormycosis is particularly challenging because early sinonasal symptoms may be nonspecific, while classical findings such as black eschar, palatal necrosis,

orbital signs, or cranial neuropathies can occur late in the disease course [1,3,4,7]. In the present case, the initial otorhinolaryngologic examination and paranasal sinus CT did not suggest invasive fungal sinusitis. However, the subsequent appearance of a pale, crusted middle turbinate lesion during recurrent fever provided a crucial diagnostic clue.

Frozen-section examination of the middle-turbinate biopsy showed hyphal structures compatible with mucormycosis in necrotic tissue. The available report did not specify special stains, detailed hyphal morphology, or explicit tissue or vascular invasion; fungal culture and molecular identification were not documented.

Molecular methods, including Mucorales-specific PCR, may help identify the causative fungi in tissue specimens and, when available, selected body fluids or blood. Although fresh tissue is generally preferred for molecular testing, testing may also be possible on formalin-fixed, paraffin-embedded tissue. These tests can complement histopathology and culture; however, because they are not available at all centers, their results should be interpreted alongside the clinical and pathological findings [5,11].

The progression to nasopharyngeal, orbital, and sinonasal involvement despite antifungal treatment reflects the characteristic angioinvasive biology of *Mucorales*. Vascular invasion can result in thrombosis, tissue ischemia, and impaired antifungal penetration, thereby limiting the effectiveness of medical therapy alone [1,3]. Consequently, successful management requires a combined strategy of early tissue diagnosis, repeated surgical debridement when feasible, liposomal amphotericin B, and reduction in reversible predisposing factors, especially immunosuppression and neutropenia [1,9].

In this case, liposomal amphotericin B and debridement were initiated on the day of tissue diagnosis, and immunosuppression was reduced. Despite treatment, disease progressed in the setting of persistent neutropenia and worsening allograft function. Liposomal amphotericin B is strongly recommended as first-line therapy; intravenous isavuconazole is also supported as an option for first-line and salvage treatment [1].

Evidence for isavuconazole prophylaxis is more limited and comes mainly from lung transplant recipients. In a single-center retrospective cohort, breakthrough invasive fungal infection rates were similar with isavuconazole and voriconazole prophylaxis, while discontinuation due to adverse events was less frequent with isavuconazole (11% vs. 36%) [12]. These findings do not establish routine isavuconazole prophylaxis in kidney transplant recipients or its efficacy in preventing mucormycosis.

The principal message of this case is that diagnostic vigilance must outlast an initially negative evaluation. In kidney transplant recipients with profound neutropenia and persistent or recurrent fever, unilateral headache, sinonasal symptoms, or any newly emerging nasal mucosal abnormality, serial otorhinolaryngologic assessment and early repeat tissue sampling should be considered. A dynamic reassessment strategy may be more valuable than reliance on a single early imaging study, because the clinical window for preventing orbital or cerebral extension can be narrow.

Despite timely and appropriate treatment, mucormycosis may still lead to poor outcomes. Future studies should evaluate strategies that could shorten the time to diagnosis and support earlier initiation of targeted therapy. Metagenomic next-generation sequencing (mNGS) may help identify the causative pathogen in selected cases, particularly when routine tests are nondiagnostic or obtaining tissue from the site of infection is difficult [13]. At present, mNGS should be regarded as a promising adjunctive approach rather than a replacement for histopathology, culture, or established molecular tests. Further studies are needed to clarify its clinical role in mucormycosis.

4. Conclusions

In kidney transplant recipients with profound neutropenia and persistent fever or evolving sinonasal symptoms, mucormycosis should remain under consideration despite an initially unrevealing examination or imaging, prompting repeat focused assessment and timely biopsy of new lesions.

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References

1. Cornely, O.A.; Alastruey-Izquierdo, A.; Arenz, D.; Chen, S.C.A.; Dannaoui, E.; Hochhegger, B.; Hoenigl, M.; Jensen, H.E.; Lagrou, K.; Lewis, R.E.; et al. Global guideline for the diagnosis and management of mucormycosis: An initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect. Dis.* **2019**, *19*, e405–e421. [CrossRef] [PubMed]
2. Palomba, E.; Lombardi, A.; Colaneri, M.; Azzarà, C.; Fava, M.; Maccaro, A.; Renisi, G.; Viero, G.; Kaur, H.; Chakrabarti, A.; et al. Epidemiology, clinical manifestations, and outcome of mucormycosis in solid organ transplant recipients: A systematic review of reported cases. *Open Forum Infect. Dis.* **2024**, *11*, ofae043. [CrossRef] [PubMed]
3. Lanternier, F.; Sun, H.Y.; Ribaud, P.; Singh, N.; Kontoyiannis, D.P.; Lortholary, O. Mucormycosis in organ transplant recipients: Report of 11 cases and review of the literature. *Clin. Infect. Dis.* **2012**, *54*, 1629–1636. [CrossRef] [PubMed]
4. Ponnaiyan, D.; Anitha, C.M.; Prakash, P.; Subramanian, S.; Rughwani, R.R.; Kumar, G.; Nandipati, S.R. Mucormycosis diagnosis revisited: Current and emerging diagnostic methodologies for the invasive fungal infection. *Exp. Ther. Med.* **2023**, *25*, 47. [CrossRef] [PubMed]
5. Roden, M.M.; Zaoutis, T.E.; Buchanan, W.L.; Knudsen, T.A.; Sarkisova, T.A.; Schaufele, R.L.; Sein, M.; Sein, T.; Chiou, C.C.; Chu, J.H.; et al. Epidemiology and outcome of zygomycosis: A review of 929 reported cases. *Clin. Infect. Dis.* **2005**, *41*, 634–653. [CrossRef] [PubMed]
6. Jeong, W.; Keighley, C.; Wolfe, R.; Lee, W.L.; Slavin, M.A.; Kong, D.C.M.; Chen, S.C.-A. The epidemiology and clinical manifestations of mucormycosis: A systematic review and meta-analysis of case reports. *Clin. Microbiol. Infect.* **2019**, *25*, 26–34. [CrossRef] [PubMed]
7. Petrikkos, G.; Skiada, A.; Lortholary, O.; Roilides, E.; Walsh, T.J.; Kontoyiannis, D.P. Epidemiology and clinical manifestations of mucormycosis. *Clin. Infect. Dis.* **2012**, *54*, S23–S34. [CrossRef] [PubMed]
8. Skiada, A.; Lanternier, F.; Groll, A.H.; Pagano, L.; Zimmerli, S.; Herbrecht, R.; Lortholary, O.; Petrikkos, G.L. Diagnosis and treatment of mucormycosis in patients with hematological malignancies: Guidelines from the 3rd European Conference on Infections in Leukemia. *Haematologica* **2013**, *98*, 492–504. [CrossRef] [PubMed]
9. Spellberg, B.; Edwards, J., Jr.; Ibrahim, A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. *Clin. Microbiol. Rev.* **2005**, *18*, 556–569. [CrossRef] [PubMed]

10. Lynch, J.P., 3rd; Fishbein, M.C.; Abtin, F.; Zhanel, G.G. Part 1: Mucormycosis: Prevalence, risk factors, clinical features, and diagnosis. *Expert Rev. Anti Infect. Ther.* **2023**, *21*, 723–736. [CrossRef] [PubMed]
11. Brown, L.; Tschiderer, L.; Alanio, A.; Barnes, R.A.; Chen, S.C.-A.; Cogliati, M.; Cruciani, M.; Donnelly, J.P.; Hagen, F.; Halliday, C.; et al. The diagnosis of mucormycosis by PCR in patients at risk: A systematic review and meta-analysis. *EClinicalMedicine* **2025**, *81*, 103115. [CrossRef] [PubMed]
12. Samanta, P.; Clancy, C.J.; Marini, R.V.; Rivosecchi, R.M.; McCreary, E.K.; Shields, R.K.; A Falcione, B.; Viehman, A.; Sacha, L.; Kwak, E.J.; et al. Isavuconazole is as effective as and better tolerated than voriconazole for antifungal prophylaxis in lung transplant recipients. *Clin. Infect. Dis.* **2021**, *73*, 416–426. [CrossRef] [PubMed]
13. Zhang, M.; Lu, W.; Xie, D.; Wang, J.; Xiao, X.; Pu, Y.; Meng, J.; Lyu, H.; Zhao, M. Metagenomic next-generation sequencing for diagnostically challenging mucormycosis in patients with hematological malignancies. *Infect. Drug Resist.* **2022**, *15*, 7509–7517. [CrossRef] [PubMed]

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