INVASIVE MUCORMYCOSIS IN PATIENTS WITH APLASTIC ANEMIA: REPORT OF TWO FATAL CASES.

Abstract

Mucormycosis is a rare, angioinvasive, rapidly progressive invasive fungal infection that occurs preferentially in patients with profound immunosuppression. Hematological disorders, particularly prolonged neutropenia, are major risk factors. Management relies on early diagnosis, antifungal therapy active against Mucorales, surgical debridement when feasible, and correction of predisposing factors. We report two cases of mucormycosis occurring in patients with idiopathic aplastic anemia. The first, a 14-year-old patient, presented with facial and mandibular involvement occurring after dental extraction. Biopsy demonstrated mycelial filaments. Despite liposomal amphotericin B, hematological optimization, and surgical debridement with mandibular curettage, the course was complicated by hemorrhage, delayed healing, progressive necrosis, and fatal septic shock on postoperative day 5. The second patient, aged 40 years, presented with a necrotic palatal lesion associated with maxillary and sinus involvement. Histology confirmed mucormycosis. Fever, cough, and pulmonary foci subsequently developed, raising suspicion of disseminated disease, followed by death in the setting of acute respiratory distress. These cases highlight the particular difficulty of treating mucormycosis in patients with aplastic anemia, in whom the aggressiveness of the infection is compounded by hematological constraints that limit surgery and wound healing. Early clinical suspicion and close coordination among hematologists, infectious disease specialists, surgeons, and intensivists are essential.

Keywords: mucormycosis; Mucorales; aplastic anemia; neutropenia; invasive fungal infection; oral and maxillofacial surgery.

1. Introduction

Mucormycosis is an invasive fungal infection caused by fungi of the order Mucorales. These microorganisms are ubiquitous in the environment, and disease occurs mainly when host defense mechanisms are profoundly impaired. Major risk settings include hematological disorders, transplantation, prolonged neutropenia, diabetes and ketoacidosis, as well as prolonged corticosteroid exposure. In patients with hematological disorders, mucormycosis remains a rare infection associated with high mortality. [1–4]

Pathophysiologically, Mucorales have a marked vascular tropism. Invasion of vascular walls leads to thrombosis, ischemia, and tissue necrosis, explaining both the rapid progression of the infection, its potential for hematogenous dissemination, and the poor penetration of antifungal agents into necrotic tissue. [3,4]

The rhino-orbital-cerebral form is particularly relevant in oral and maxillofacial surgery. It may begin in the nasal cavities or paranasal sinuses and extend to the facial tissues, oral cavity, orbit, and, in advanced forms, intracranial structures. Clinical manifestations may be nonspecific initially, whereas progression can be extremely rapid. [3,5]

International guidelines emphasize the need for early diagnosis, imaging to define disease extent, antifungal treatment with liposomal amphotericin B, and early surgical debridement whenever feasible. Correction of predisposing factors, particularly neutropenia, represents a third essential therapeutic component. [1,2,6]

We report two cases of invasive mucormycosis in patients with idiopathic aplastic anemia to illustrate the diagnostic, surgical, and hematological difficulties encountered in this setting.

2. Case reports

2.1. Summary of the two cases

The clinical and therapeutic data presented below are those available from the original clinical communication. When information was not documented in the presentation, it was not supplemented or inferred.

Characteristic	Case 1	Case 2
Age / sex	14 years	40 years
Underlying condition	Idiopathic aplastic anemia	Idiopathic aplastic anemia
Presentation	Right cheek swelling after extraction of tooth 46	Necrotic palatal ulceration
Main involvement	Facial / mandibular	Rhinosinus / palatal
Imaging	Abscessed collection centered on the mandibular body	Opacification of the left maxillary sinus and ethmoidal cells
Diagnosis	Histology: mycelial filaments; negative parasitological examination	Palatal biopsy: mucormycosis
Documented treatment	Liposomal amphotericin B + debridement/curettage	Therapeutic details not specified in the presentation
Outcome	Bleeding, delayed healing, necrosis, septic shock; death on postoperative day 5	Pulmonary foci; suspected dissemination; death from acute respiratory distress

Table 1. Summary of the two cases.

2.2. Case 1

The patient was a 14-year-old patient hospitalized in the pediatric hemato-oncology unit for idiopathic aplastic anemia. An oral and maxillofacial surgery consultation was requested because of a painful, firm right lower cheek swelling that had appeared five days after extraction of tooth 46. The initial diagnosis was odontogenic cellulitis.

Intraoral examination revealed trismus, with mouth opening limited to approximately two finger breadths, gingival hypertrophy in the right mandibular posterior region, vestibular obliteration, and necrotic areas appearing as friable whitish plaques. In the context of profound aplastic anemia, these findings raised early suspicion of an invasive fungal infection.

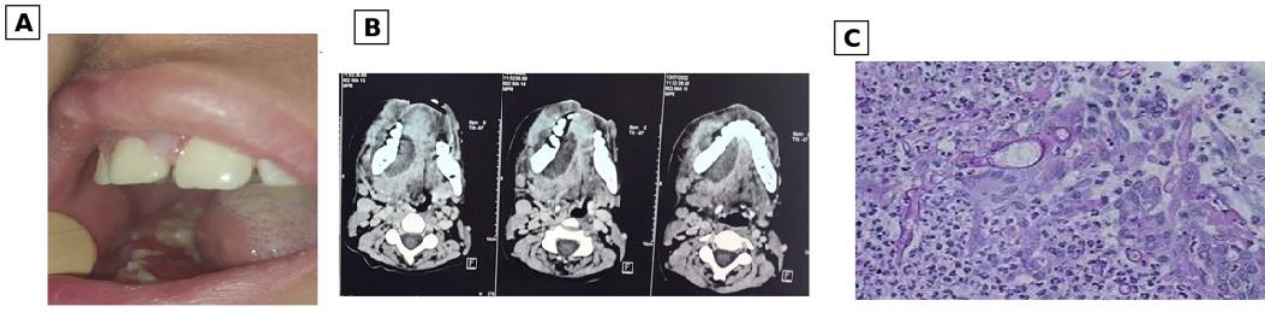

Figure 1. Case 1: clinical, radiological, and histological findings. A: intraoral lesions with areas of necrosis and gingival involvement; B: CT scan showing an abscessed collection centered on the right mandibular body; C: histological appearance reported as showing mycelial filaments.

CT of the facial region showed an abscessed collection containing air bubbles, centered on the mandibular body. Laboratory testing revealed an inflammatory syndrome associated with severe pancytopenia, with hemoglobin 7 g/dL, neutrophils 10/mm³, and platelets 15,000/mm³.

Biopsy specimens were obtained for diagnostic purposes. Parasitological examination was negative, whereas histological examination demonstrated mycelial filaments, establishing the diagnosis of mucormycosis.

Liposomal amphotericin B was initiated at a dose of 3 mg/kg/day, and surgery was considered indicated. Preoperative optimization included transfusion of packed red blood cells and platelets, as well as administration of a granulocyte growth factor. The procedure consisted of debridement of necrotic tissue combined with extensive mandibular curettage.

The postoperative course was complicated by significant bleeding and delayed wound healing. A cutaneous necrotic plaque subsequently developed over the swelling, associated with infiltration of the lower lip. The course rapidly deteriorated with septic shock and death on postoperative day 5.

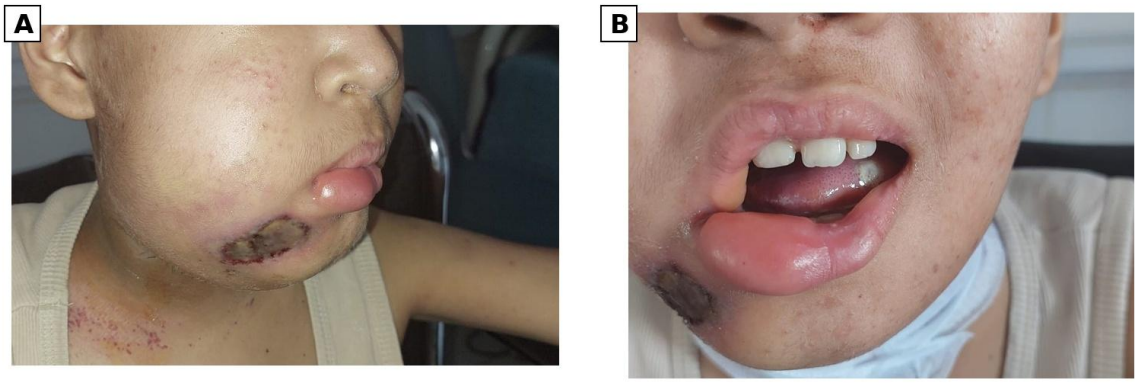

Figure 2. Case 1: unfavorable postoperative course with extension of the cutaneous and labial lesions.

2.3. Case 2

The second patient was 40 years old and was also hospitalized for management of idiopathic aplastic anemia. The patient presented with a pearly-white necrotic palatal lesion extending to the buccal gingiva.

Figure 3. Case 2: clinical and radiological findings. A–B: necrotic palatal ulceration with gingival extension; C: CT scan (coronal sections) showing opacification of the left maxillary sinus and left ethmoidal cells.

CT of the facial region showed opacification of the left maxillary sinus and left ethmoidal cells. Palatal biopsies were performed, and histological examination was consistent with mucormycosis.

The subsequent course was marked by the development of fever, cough, and pulmonary consolidation foci on chest CT. Secondary pulmonary involvement and disseminated disease were suspected in the original presentation but were not confirmed by pulmonary mycological or pathological testing. The patient died during the same week in the setting of acute respiratory distress.

3. Discussion

Mucormycosis is an invasive infection caused by Mucorales, of which Rhizopus, Mucor, and Lichtheimia account for a large proportion of cases. Marked angioinvasion leads to thrombosis and tissue infarction, accounting for the characteristic necrotic lesions and the occasionally fulminant progression of the infection. Malignant hematological disorders and prolonged neutropenia are major risk factors, and published series report high mortality in invasive forms. [1,3,7,8]

In patients with aplastic anemia, the depth of neutropenia is a particularly critical factor. In our first patient, the neutrophil count was 10/mm³, with concomitant thrombocytopenia at 15,000/mm³ — a setting that not only favors progression of the infection but also limits the possibilities for surgical control and compromises wound healing.

The first case also illustrates the diagnostic difficulty at presentation: a clinical picture following dental extraction could initially suggest odontogenic infection, but the combination of mucosal necrosis, rapid progression, and profound immunosuppression should prompt early consideration of invasive fungal infection. Histological examination plays a decisive role in this setting: identification of mycelial filaments compatible with mucormycosis allowed the diagnosis to be established despite a negative parasitological examination. Guidelines emphasize that a negative culture or microbiological specimen does not exclude the disease when compatible histological findings are available. [2,6]

Imaging helps define local extension and assess for sinus, orbital, cerebral, or pulmonary involvement. In rhino-orbital-cerebral disease, CT is particularly useful for evaluating the sinuses and osseous structures, whereas MRI can complement the assessment of soft tissues and intracranial extension depending on the clinical presentation. [1,6] In the first case, imaging demonstrated a collection centered on the mandibular body. In the second, it showed involvement of the left maxillary sinus and ethmoidal cells, followed by the appearance of pulmonary foci raising suspicion of systemic extension. This course illustrates the importance of clinical and radiological surveillance adapted to the patient's condition and the initial site of infection.

Treatment of mucormycosis relies on three complementary principles: active antifungal therapy against Mucorales, control or correction of predisposing factors, and surgery when feasible. [1,2,6] Liposomal amphotericin B is the recommended first-line antifungal treatment. ECMM/MSG guidelines recommend a dose of at least 5 mg/kg/day, with higher doses in certain situations, particularly in cases of cerebral involvement. Isavuconazole and posaconazole are options for step-down or salvage therapy depending on the clinical context. [1,6] In our first patient, the dose actually administered was 3 mg/kg/day; this reflects the treatment practice reported in the original 2023 clinical communication and should not be interpreted as the currently recommended dose.

Surgery aims to remove necrotic and infected tissue, an area of poor antifungal penetration, and international guidelines recommend prompt surgical intervention whenever possible. Observational data and multicenter series associate surgery with better outcomes, although the available evidence is predominantly retrospective because of the rarity of the disease. [1,7,9]

In patients with aplastic anemia, however, this recommendation must be weighed against major constraints. Thrombocytopenia increases the risk of bleeding, whereas neutropenia compromises infection control and wound healing. In our first case, despite transfusion preparation and administration of a granulocyte growth factor, significant hemorrhagic complications and delayed wound healing occurred. Prognosis depends on several factors: site, extent, immune status, the possibility of restoring neutrophil function, treatment timing, and the ability to achieve surgical control of the infection. In an international multicenter study of rhino-orbital-cerebral mucormycosis, hospital survival was 56.8%, and absence of surgical debridement was independently associated with an increased risk of death. [9]

The two cases reported here illustrate two different but convergent mechanisms of death: in the first case, rapidly progressive local extension complicated by septic shock; in the second, progression to pulmonary

involvement with respiratory distress and suspected dissemination. In both situations, the profound immunosuppression was a major prognostic factor.

For the oral and maxillofacial surgeon, several findings should raise suspicion in a profoundly immunocompromised patient: unusual facial pain or swelling, necrotic palatal or gingival lesions, rapidly progressive ulceration, poor evolution of a presumed dental infection, or the development of necrosis after a dental procedure. Such a presentation should prompt rapid assessment, including imaging, deep tissue sampling, and multidisciplinary discussion. The objective is not only to establish the diagnosis but also to avoid any delay in treatment, whose effectiveness depends largely on how early it is initiated.

4. Limitations

This series includes only two cases and does not allow any conclusion regarding the comparative efficacy of different therapeutic strategies. The data originate from a clinical communication presented in 2023, and some information, particularly the detailed treatment modalities for the second patient and microbiological confirmation of possible pulmonary involvement, is not available in the presented record. Disseminated disease in the second case should therefore be considered a clinical hypothesis rather than a formally documented diagnosis.

5. Conclusion

Invasive mucormycosis in a patient with aplastic anemia constitutes a diagnostic and therapeutic emergency with a very high risk of mortality. These two cases demonstrate the particular difficulty of reconciling the need for antifungal treatment and aggressive surgical debridement with the constraints imposed by neutropenia, thrombocytopenia, and impaired wound healing.

In any severely immunocompromised patient presenting with facial swelling, a necrotic oral or palatal lesion, or an atypical maxillofacial infection, mucormycosis should be considered promptly. Histological diagnosis, imaging to assess disease extent, liposomal amphotericin B, surgery when possible, and correction of the underlying condition should be considered in a coordinated manner. Multidisciplinary management and early diagnosis remain the main factors that may improve prognosis.

6. Statement regarding illustrations and publication

The figures in this manuscript are extracted from the clinical presentation provided by the author. The CT images were cropped to prevent nominal identifying information visible in the source images from appearing. The most identifiable facial photographs were also cropped. Before submission to a journal, it remains essential to verify that appropriate consent for publication of the clinical photographs has been obtained and to comply with the journal's requirements regarding image anonymization.

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