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Case Report

Surgical management of rhinocerebral mucormycosis: A case series

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ABSTRACT

Rhinocerebral mucormycosis (RCM) is a rare and rapidly progressive, destructive, angioinvasive fungal infection, which primarily affects immunocompromised patients. A high suspicion is required to diagnose RCM as initial clinical manifestations are often non-specific. A cornerstone of the management is early diagnosis and radical surgery, which often requires complex reconstructive procedures.

The optimal timing of reconstructive surgery is controversial.

This case series presents the reconstructive perspective on four RCM cases treated with aggressive debridement, targeted antifungal treatment, and hyperbaric oxygen therapy followed by an early local flap or microsurgical reconstruction – to enable adequate local blood perfusion, antifungal treatment, and to decrease the risk of secondary infection. In all four patients, the early reconstructive surgery was successful without relapse of RCM or flap failure.

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We suggest aggressive surgical debridement till clear resection margins are obtained based on histopathology and/or microbiology, at a point which reconstructive surgery can be performed safely.

Introduction

Rhinocerebral mucormycosis (RCM) is an angioinvasive fungal infection, in which infection of the nasal and sinus walls may secondarily invade the orbit, skull base, and brain. RCM usually affects immunocompromised patients.[1,2] The management of RCM is challenging. Diagnosis is often delayed because of unspecific presentation, the rarity of the disease, and difficulties in early microbiological identification. Furthermore, the combination of rapid destructive growth of mucormycosis, the severity of underlying diseases, and sometimes limited effect of antifungal therapy may result in poor outcomes. Aggressive surgical debridement is always required, which may cause complex defects of the midface, skull base, and brain.[3] Rhinocerebral mucormycosis carries high overall mortality with rates up to 46 % in patients with sinus involvement and 62 % in patients with rhinocerebral involvement.[4] The diagnosis of RCM and assessment of the resection margins are based on histopathology, specific cultures, and/or PCR detection of Mucorales species.[5] Aggressive and often repeated surgical debridement ensuring margins clear of disease is adamant. Early microsurgical reconstruction has previously been considered relatively contraindicated owing to the fungal invasion of blood vessels, causing infarction and necrosis. However, early reconstructive surgery is an advantage to cover and preserve vital structures, and to enable adequate antifungal drug penetration through restored blood perfusion. Presently, only a few cases have described the reconstructive management of RCM.

We describe four cases of RCM; which were managed by midface and skull base reconstruction with local and free flap coverage after debridement, targeted antifungal therapy, and hyperbaric oxygen (HBO) treatment.

Case reports

Case 1

A 3-year-old previously healthy girl was admitted with pre-B acute lymphoblastic leukemia (ALL) and treated with intensive chemotherapy. Seven weeks later, during persistent neutropenia, signs of unilateral conjunctivitis were noted. Within a few days, the patient developed fever and severe periorbital edema. An intraoral nonsore brownish ulcer and leukoplakia of the palate were noted (Figure 1). A CT scan demonstrated sinusitis of the right maxillary sinus and bilateral ethmoid sinuses, with preseptal and intraorbital inflammation. Palatal, ethmoidal, and orbital biopsies diagnosed mucormycosis caused by *Lichtheimia corymbifera*. A total of fifteen surgical debridements guided by imaging findings, the gross appearance (necrotic or inflamed tissue), and margins assessed for fungal hyphae on frozen or permanent sectioning and tissue cultures were performed; including skull base resection, leaving the dura intact. Targeted antifungal treatment was delivered locally, intravenously, and intrathecally following placement of an intraventricular catheter system (Ommaya reservoir) and HBO treatment as described elsewhere (Supplemental figure 1).[6] Seven weeks after the debut of RCM, the final debridement was performed and the complex midface and skull base defect was reconstructed. A free fibula flow-through flap was anastomosed to the ipsilateral facial vessels and a free latissimus dorsi (LD) flap was used to obliterate the skull base defect (Supplemental figure 1). The recovery was uneventful and seven years later, the patient is well, with no clinical evidence of RCM recurrence (Supplemental figure 1).

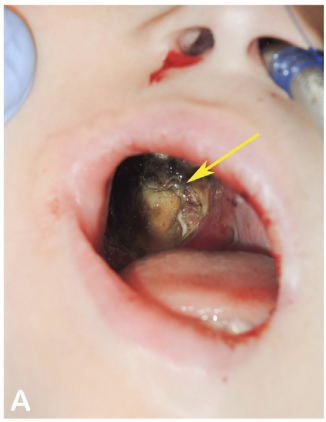

Figure 1. A: Characteristic necrosis of the palate caused by rhinocerebral mucormycosis (arrow).

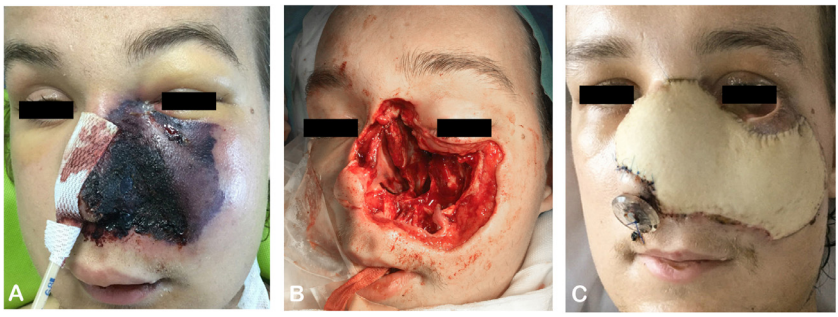

Figure 2. A: Rhinocerebral mucormycosis at the time of diagnosis. B: Intraoperative view of the midface defect before free myocutaneous latissimus dorsi flap. C: Eleven days postoperatively.

Case 2

A 22-year-old previously fit and healthy man was admitted to the hospital with acute liver failure of an unknown cause. Nine days later, he received an orthotopic liver transplant. Two days postoperatively, he developed necrosis on his left nasal ala, which was initially misinterpreted as a pressure ulcer because of his nasal oxygen catheter. A skin biopsy revealed hyphae and *Rhizopus arrhizus* was confirmed based on PCR (Figure 2). Involvement of maxilla, paranasal sinuses, orbital floor, and extensive involvement of the nose was found by MRI. Targeted systemic and local antifungal treatment was initiated. Over the following seven days, three debridements were guided by microscopy of fungal hyphae on frozen and permanent sectioning, cultures, and fungal DNA detected by PCR. Supportive HBO therapy was given. Four days after the last debridement, a free LD flap was performed to reconstruct the midface defect (Figure 2). The recovery after microsurgery was uneventful. Ten months after the reconstructive procedure, the patient showed no signs of recurrent RCM.

Case 3

A 13-year-old previously healthy boy was admitted with sudden onset of acute myeloid leukemia (AML) and started on chemotherapy. Four months later, a toothache and a sore discoloration of the gingiva around the left second premolar was noted (Supplemental Figure 3). As the lesion increased in size and the black eschar developed, fungal infection was suspected. A buccal mucosal and mandibular bone biopsy confirmed *R. arrhizus,* based on cultures, microscopy, and PCR. Combined systemic anti-

fungal treatment and aggressive surgical debridement were performed for the following three days, guided by CT and MRI scans, microscopy, cultures, and PCR. HBO therapy was also started. Immediately thereafter, the defect following mandibular bloc resection an ipsilateral pedicled facial artery musculomucosal flap (FAMM flap) was performed (Supplemental Figure 3). Two months after the reconstruction, the patient is without signs of RCM recurrence and still undergoing hematological treatment.

Case 4

A 19-year-old man was admitted with a sudden onset of T-lymphoblastic lymphoma and started on high-dose intensive chemotherapy. Two weeks later, he complained of a toothache, and gingivitis secondary to antibiotic treatment was suspected. Five days later, edema over his right maxillary sinus and necrosis of the right side of the hard palate were noted. Computer tomography scan (CT) supported the suspicion of RCM. Palatal, maxillary, and dental biopsies revealed *R. arrhizus*. Combined local and systemic antifungal treatment, forty-four surgical procedures with sterile dressing changes and debridement, and HBO therapy were administered. To facilitate adequate antifungal drug perfusion and to prevent further progression and secondary infections, a free myocutaneous LD-flap was performed to reconstruct the intraoral defect – 3.5 months after the diagnosis of RCM. The patient made an uneventful recovery of the reconstruction with no signs of RCM recurrence. However, the patient relapsed and succumbed to his T-lymphoblastic lymphoma seven months post reconstruction.

Discussion

The initial onset of RCM is often subtle with unspecific signs, as shown in our case series, which may delay diagnosis. Few case reports have illustrated an initial presentation and the detailed reconstructive management of the secondary complex defects after primary debridement. The Mucorales species are difficult to identify with the sensitivity of microscopy, Mucorales-PCR, and cultures of 76%, 70%, and 53%, respectively.[2] It is, therefore, advisable to use all three types of laboratory investigations. Our case series showed that the number of procedures is to be decreased to achieve radical resection with time. This may be attributed to earlier recognition of the extent of the disease and improvements of laboratory investigations providing rapid intraoperative results with microscopy and PCR. The early aggressive debridement and early reconstruction are of utmost importance in a population of severely immunocompromised patients, in whom, possible treatment delay of the underlying condition may be fatal. Our experience has led us to believe that reconstruction should be performed as soon as the local infection is under control.

Conclusion

The surgical treatment of RCM requires early diagnosis, aggressive surgical debridement, and early reconstructive surgery. The debridement should be continued until clear resection margins are obtained –based on the assessment of microscopical findings of hyphae, fungal cultures, and/or fungal DNA detected by PCR. At this point, a local flap or free microvascular reconstruction can be performed safely, addressing aesthetic and functional demands, which more importantly might serve as a delivery method for systemic antifungal treatment and treatment of the underlying condition.

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Patient Consent

Confirmed consent obtained.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpra.2021.04.013.

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