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ISOLATED PALATAL PERFORATION DUE TO MUCORMYCOSIS IN A PATIENT WITH ACUTE MYELOID LEUKEMIA

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ABSTRACT
Mucormycosis is an invasive fungal infection, characterized by high mortality and morbidity, which is caused by mukorales class of fungi. It tends to affect people with immune suppression and the palate is a rare site of disease. Treatment strategy should involve the control of underlying disease, application of amphotericin B and extensive surgical debridement. In this paper, we reported a 62 years-old female patient with acute myeloid leukemia and mucomycosis who developed palatin perforation early follow-up. Our patients have developed perforation of the palate despite liposomal amphotericin B therapy and debridement implementation. Although the mortality rate is high, a fungal infectious status of our patients continues to receive intensive chemotherapy regimens under antifungal therapy.

INTRODUCTION

Mucormycosis is an opportunistic fungal infection that occurs mostly among immune compromised patients. It is the third frequent after Candida and Aspergillus [1]. The causative organisms belong to the order of Mucorales from the class of Zygomycetes. Mucormycosis often shows a rapid and invasive clinical course and results in death without early diagnosis and treatment [2]. Fungi from the order of Mucorales are found in dust, soil, decaying plants and starchy food along with the respiratory and gastrointestinal systems of healthy human beings [3]. These microorganisms mainly affect individuals with immunocompromising conditions such as uncontrolled diabetes, uremia, leukemia and use of steroid or cytotoxic agents [4,5]. In this report, we discuss a case of palatal perforation and its clinical course in the early phase of first remission induction therapy in an AML patient, who received the diagnosis in our clinic.

CASE

A 62-year-old female patient presented with fatigue and spontaneous bruising. First-line tests revealed leukocytosis (WBC: 126.500/mm^3, NEU: 8985/mm^3) along with anemia (HGB: 9.8 gr/dL MCV: 107 fL) and thrombocytopenia (PLT: 64000/mm^3). Peripheral blood smear, bone marrow aspiration and biopsy and flow cytometric analysis were performed and the patient was diagnosed with acute myeloid leukemia. She was started on remission induction chemotherapy. On the 8th day of therapy, the patient complained of pain in the mouth, particularly in the upper palate. Inspection findings were not consistent with mucositis. On the 10th day of therapy, pain and soreness increased and a tissue defect of 5-mm width developed. The patient was started on liposomal amphotericin B for mucormycosis. Galactomannan antigen was negative at that time. The tissue defect expanded under amphotericin B treatment and therefore palatal biopsies were obtained. Culture of the biopsy material yielded no growth, yet histopathologic examination revealed mucormycosis (Figure 1).

Liposomal amphotericin B therapy was continued. After the neutropenia resolved, a new bone marrow examination performed revealed that remission was not

achieved. Patient was re-started on remission induction chemotherapy. Liposomal amphotericin B was continued during chemotherapy. After the neutropenic phase was over, the patient was followed in our outpatient clinic and received oral posaconazole treatment. Bone marrow aspiration after the second remission induction therapy revealed <5% blasts and thus the patient was started on consolidation therapy. Antibiotherapy was switched back to intravenous liposomal amphotericin B during consolidation chemotherapy. During this period, the palatine tissue defect expanded and isolated palatal perforation occurred (Figures 2). Palatal debridement was performed in order to prevent more tissue loss after perforation and consolidation therapy was completed under liposomal amphotericin B. The patient has been in remission for one year and continues to be followed-up.

Fig 1. Histopathologic examination revealed mucormycosis

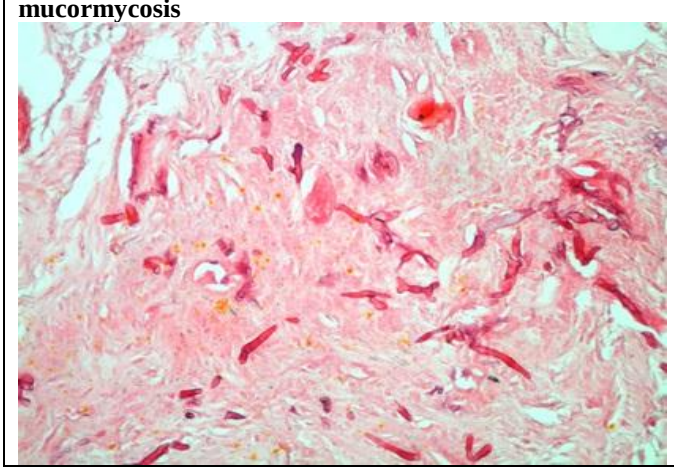

Fig 2. The palatine tissue defect and palatal perforation

DISCUSSION AND CONCLUSION

Mucormycosis is a fungal infection with high mortality rate that progresses rapidly in patients with hematological malignancies. Early diagnosis is a crucial part of treatment. Although rhinocerebral mucormycosis is the most frequent form, pulmonary, cutaneous, gastrointestinal and central nervous system disease are also encountered [6,7]. Mucoraceae can be colonized in healthy individuals, but phagocytosis functions and the presence of oxidative metabolites prevent the microorganisms from causing infections. Patients with hematological malignancies and receiving immunosuppressive treatment, with neutropenia, phagocytic dysfunction, uncontrolled diabetes and patients using deferoxamine are at risk. Elevated serum iron levels as well as acidosis facilitates mucormycosis [8]. The term “rhinocerebral” is used to define the group of mucormycosis cases with paranasal sinus and nasal pathway involvement, which constitutes the majority of patients. The fungi spread via the invasion of hyphae through the elastic lamina of blood vessels and cause thrombosis, tissue necrosis and hemorrhage. This course may progress extremely rapidly [9]. Although clinical presentations may differ, the most common signs and symptoms are fever, nasal congestion, nasal discharge, epistaxis, nasal ulceration, vision loss, proptosis, facial edema, facial paralysis and in later periods cranial nerve involvements or cavernous sinus thrombosis. The presence of lesions with black eschar implicates mucormycosis, yet may not be observed in all cases [10]. Major problems in the treatment of mucormycosis are related to the underlying pathology and its treatment process. Mortality ratios are especially high in patients with hematologic malignancies who received chemotherapy. It has been claimed that prophylaxis and treatment approaches for Aspergillus spp in this particular patient group increases the frequency of mucormycosis [11]. Success in the treatment of mucormycosis lies in early diagnosis and early start of treatment. An analysis performed on patients with hematologic malignancies showed that any delay in treatment increases mortality [12]. Tests for the detection of galactomannan antigen, which found in the cell wall of Aspergillus spp, and 1.3-β-D-glucan, which is a fungal cell wall component, may guide early treatment. However, because fungi from the class of Zygomycetes do not contain galactomannan and the release of β-glucan is low, diagnosis is only possible with culture and histopathologic examination [13, 14]. Galactomannan antigen was also negative in our patient and the diagnosis was achieved with histopathology. First line treatment is amphotericin B. Depending on the localization of infection, surgical debridement either simultaneously with or after medical treatment increases success rates. Most azole antifungals are considered ineffective in mucormycosis. However, Almyroudis et al evaluated in vitro sensitivity of 217 zygomycetes isolate to azoles, echinocandins, flucytosine and amphotericin B and reported that differently than other azoles, posaconazole may be effective against mucormycosis [15].

In conclusion, mucormycosis is a fungal infection with high mortality rates that progresses rapidly in patients with hematologic malignancies and immunosuppression. Early recognition and treatment may decrease mortality.

Surgical debridement when necessary will help keeping the infection limited.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

STATEMENT OF HUMAN AND ANIMAL RIGHTS

All procedures performed in human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

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