Case report

Tongue necrosis secondary to mucormycosis in a diabetic patient: A first case report in Malaysia

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Abstract

Mucormycosis is a rare fungal infection and high mortality that commonly affects patients with the weakened immune system. We present an unusual case of tongue necrosis probably due to the healthcare-associated mucormycosis (HCM) in a diabetic patient. Although cannot be proved with certainty, we surmise that intubation as a risk factor in our case. The diagnosis was confirmed by histopathological examination (HPE) of the necrotic tissue specimen. The patient was responded well to lipid complex amphothericin B (250 mg) regime after surgery. Subsequent follow up revealed that no signs of recurrence. Early, recognition, diagnosis, prompt treatment and awareness among clinician are representing the most effective way of managing the disease.

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1. Introduction

Mucormycosis is generally rare, but it is more common among people with the weakened immune system than among people who are otherwise healthy [1–4]. Predisposing conditions include diabetes mellitus, acquired immunodeficiency syndrome (AIDS), neutropenia, corticosteroid administration, immunosuppressive therapy, and hematologic malignancy [1–4]. The primary mode of transmission is through inhalation. The most effective treatment and management often require a combination of antifungal agents, correction of predisposing factors, and surgery [1]. Depending on the immunological status of the patient and anatomic localisation, mucormycosis manifests in six different clinical forms as rhino-cerebral, pulmonary, cutaneous, gastrointestinal, central nervous system or disseminated presentation [1–4]. In the immunocompetent host, these infections generally progress locally via direct adjacent into adjacent tissue and rarely angiinvasive and become disseminated [4]. In contrast, the mucormycosis are vasotrophic, and the spectrum ranges from cutaneous, rhino-cerebral and pulmonary to disseminate among immunocompromised patients [1–4].

Rhino-cerebral mucormycosis is the most commonly reported form, which accounts for up to 50 % of the cases [1]. The rhino-cerebral form is predominantly reported among diabetes patients, especially with the complication of diabetes mellitus such as ketoacidosis where the acid-base balance is altered. The typical presentation includes local manifestation such as facial pain followed by systemic symptoms of fever and headache. Once the fungal enter the bloodstream, they can disseminate to other organs such as cerebrum and lungs making it potentially life-threatening disease [1–4].

We report this case of mucormycosis in the tongue of diabetes mellitus patient, which was treated by both medical and surgical management. Our case is worthy of discussion as lingual mucormycosis, and lingual necrosis is rare. To the best of our knowledge, there were only few cases documented of lingual mucormycosis that currently available in the literature [5–8]. This report aimed to highlight the importance of prompt diagnosis and urgent management of this potentially fatal phenomenon, particularly among high-risk individuals.

2. Case Report

A 56-year-old patient was presented with tongue lesion for five days duration. The patient has a history of poorly controlled diabetes mellitus. Initially, she was admitted to the Intensive Care Unit (ICU) for severe dengue and acute liver failure with hepatic...
encephalopathy, acute kidney injury requiring dialysis and respiratory failure that requires intubation and ventilator support. She was referred to the maxillofacial department on day 9 of admission in ICU due to the sudden tongue lesion which developed 2 days earlier (day 7 in ICU).

Upon initial presentation, she was generally stable, except having the necrotic tongue margin with sloughing wound, which was suspected of traumatic biting as there was no tongue laceration before intubation. Clinical examination revealed no apparent facial asymmetry and no lymph nodes palpable. Intraorally a 3 cm × 2 cm ragged ulcer with greyish black coloured sloughing surrounding the dorsum part was observed on the split anterior part of the tongue (Fig. 1a).

Baseline blood result in ICU (day 1 of admission) showed arterial blood gas with severe metabolic acidosis, pH (6.9) pCO₂ (24 mmHg) pO₂ (44 mmHg), HCO₃ (5.9 mmHg), HbA1 C (9.7), WBC (15.1 × 10⁹ L), sodium: (134 mmol/L), potassium (5.1 mmol/L), urea (19.5 mmol/L), Creatinine (419 μmol/L). Patient blood glucose and ketone levels were 36 mmol/L and 5.1 mmol/L, respectively. Thus, at the time of admission, she was diagnosed with diabetic ketoacidosis. The patient was already started on intravenous antibiotics (IV Rocephine 2 g OD) in ICU on day 1 of admission. Surgical excision and debridement of the tongue followed by primary closure were done on day 14 of admission (Fig. 1b). Post-operative healing of the tongue was uneventful without any complications. Sutures were removed on day 10 postoperatively (Fig. 1c). The tissue sample was sent for histopathology with haematoxylin and eosin staining. It was revealed partially necrotic fibromuscular connective tissue containing numerous individual and clusters of large, branching, nonseptate hyphae extending deep into the underlying connective tissue, fat and muscle bundles. Several hyphae were also seen surrounding and also invading the nerve bundles and blood vessels, suggestive of Mucorales (Fig. 2). However, species identification by culture or molecular methods was not conducted due to the lack of laboratory resources.

Patient’s diabetic control was managed with the prescription of insulin sliding scale and hydration that was started in ICU (6 units hourly). Glycaemic control was achieved in few days. Antifungal was started on day 14 of admission after the biopsy results were obtained. The patient was administered with lipid complex amphotericin B (250 mg BD) intravenously for 2 weeks which
was slowly infused over 4 to 6 hours. The renal function of the patient was normal. The creatinine level was 114 mmol/L maximally during the antifungal therapy. During the antifungal course, the patient was kept on a soft diet and wound care with normal daily saline, and chlorhexidine mouthwash rinses in the ward.

The patient was discharged after the completion of two weeks course of amphotericin B. The patient was seen in clinic for follow up one week later, and healing was uneventful. Two months after surgery, there was no clinical evidence of mucormycosis, and satisfactory healing was evidenced with no tissue breakdown at the anterior aspect of the tongue. The general condition of the patient was improved, and vital signs were within normal limits.

3. Comments

Mucormycosis refers to several different fungal diseases caused by infection with fungi in the order Mucorales. *Rhizopus* species are the most common causative organisms. Other genera mucormycosis-causing species include *Mucor, Cunninghamamella, Apophysomyces, Lichtheimia, Saksonaea* and *Rhizomucor* [1–3]. Generally, the fungus is characterised by filamentous non-septate hyphae with right-angled branching. These are ubiquitous fungi commonly found in soil, decaying materials and foods [1–3]. Human has usually acquired this infection through inhalation of fungal spores that have been released into the air. Mucormycosis can also develop on the skin after the fungus enters the skin through a cut, scrape, burn, or another type of skin trauma [1–4].

In recent years, the incidence of mucormycosis has been increased [4,9]. Like other invasive fungal infections, impairment of the immune system is the most important predisposing factor to mucormycosis. In our case, the patient had diabetes mellitus, which is a well-known risk factor for mucormycosis. Several reports have shown that diabetic patients represented up to 88% of overall mucormycosis cases [4,9,10]. Diabetes mellitus is a clinical syndrome associated with high levels of the sugar in blood either due to the inadequate production of insulin secretion or function. It is well-known that diabetes mellitus associated with reduced response in T cells, neutrophil function, and responsible for disorders of humoral immunity [11]. As a result, diabetic patients increase the susceptibility to infections by most common pathogens including Mucorales [11]. These infections, in addition to their associated consequences, may prompt diabetes mellitus complications such as ketoacidosis. Despite the increasing number of diabetes worldwide [12], studies reported that mucormycosis cases in diabetic patients as underlying illnesses in a declining trend [4,9]. This finding could be the result of improved glycemic control and decreasing rates of diabetic ketoacidosis and the widespread use of statins in diabetic patients [12].

One of the mechanisms suggested that diabetic mellitus patients are at higher risk of mucormycosis partly due to the impaired phagocytic function which leads to the lack of phagocytes [13]. The dysfunctional phagocytes may impair the chemotaxis and defective intracellular killing by both oxidative and non-oxidative mechanisms which limit Mucorales spores to be eliminated [13]. However, the exact mechanisms by which phagocytes are impaired by diabetes mellitus are yet to be fully understood. Therefore, impaired of phagocytes function alone cannot explain the occurrence of mucormycosis in diabetes mellitus patients, because the incidence of mucormycosis in these patients is increased more than that of infections caused by other pathogens [1,14]. Other mechanisms also suggested that diabetic ketoacidosis patients usually have elevated levels of serum iron, possibly due to the release of iron from binding proteins in the presence of low pH [15]. The serum iron is then utilised by the Mucorales in the presence of copper oxidase and the high-affinity iron permease enzymes which will favour its multiplication [15]. Therefore, the increased vulnerability of patients with diabetic patients to mucormycosis is likely due, at least in part, to elevation in serum iron due to acidosis [15].

The orofacial presentation is rare. Palatal ulcer, chronic maxillary or mandibular infection, mouth and eye lesions, chronic oral ulceration and diffuse swelling of the face may also be seen in high-risk patients [3,4]. Presentation on the tongue, as seen in our patient, is another rare localisation of the disease. To the best of our knowledge, there were only a few cases on the lingual mucormycosis have been reported in the world literature [5,8]. A report in Turkey demonstrated a case of a tongue mucormycosis involving an old woman with severe aplastic anaemia [8]. In this report, the authors described the use of wooden tongue depressors might have led to the localisation of this infection on the tongue [8]. In addition, another report also describes the lingual necrosis secondary to pulmonary mucormycosis in aplastic anaemia and diabetic patients [5]. The authors summarise that the source of infection may be due to inhalation [5]. Another tongue involvement by mucormycosis was a case of lingual mucormycosis in Down syndrome baby who underwent aggressive treatment for metabolic acidosis [7]. The authors suspected the use of wooden tongue depressor as a source of infection to the baby [7]. Similarly, the use wooden tongue depressor to examine oral cavity have been associated with another case of lingual mucormycosis in an acute lymphoblastic leukaemia patient [6].

In our case, the patient was immunocompromised presenting with severe dengue fever complicated by diabetic ketoacidosis secondary to uncontrolled diabetes mellitus. Nonetheless, the source of infection cannot be found with certainty, but we surmise that it was probably related to the other healthcare-associated mucormycosis such as intubation. In one of the most extensive reviews of healthcare-associated mucormycosis (HCM) cases in the literature, Rammaert and colleagues conclusively summarised that HCM had become a matter of concern, especially in high-risk groups [10]. The authors also concluded that the most common health care procedures for the infection including surgery and presence of medical devices such as catheters or adhesive tape. Most of the outbreaks in the hospital setting were related to adhesive bandages, wooden tongue depressors, ostomy bags, water circuitry damage, and adjacent building construction [10]. Early diagnosis and treatment are essential for patient management. Several reports have indicated that early detection is correlated with less tissue destruction and a better overall outcome [1–4]. Nevertheless, the mortality remains high as a
consequence of delayed diagnosis and lack of optimal treatment [4,9]. The diagnosis of mucormycosis remains challenging. The histopathological examination of Mucorales-like hyphae remains essential for the diagnosis [1–4]. Culture and molecular tools are the preferred methods for identifying different Mucorales genus and species directly from tissue samples [1–4]. In our case, however, the specific species of causative agent was not identified, a subject that is warranted in a future study.

Systematic antifungal treatment includes the amphotericin B, posaconazole, and isavuconazole is commonly used to treat mucormycosis. According to the recommended guideline by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Fungal Infection Study Group (EFISG) and European Confederation of Medical Mycology (ECMM), the first-line treatment against most Mucorales is a lipid formulation of amphotericin B [16]. The treatment regime has been associated with good prognosis [16]. In addition, surgical debridement or resection of infected tissue is often necessary, particularly for rhinocerebral, cutaneous, and gastrointestinal infections [1–4]. In our case, a course of intravenous amphotericin B was initiated for the patient. The patient responded well with the amphotericin B lipid complex regime for two weeks duration. A subsequent follow up revealed no signs of recurrence.

The prognosis of mucormycosis is dependent on several factors. Early recognition, diagnosis, and prompt administration of appropriate antifungal treatment are important for improving outcomes for patients with mucormycosis. Successful mucormycosis treatment with antifungal therapy also requires correction of the clinician awareness, underlying risk factors, and surgery. This represents the most effective way of managing patient with mucormycosis.

Ethical approval

The patient has been informed regarding the case report that there is no risk against her well-being, integrity or right to anonymity.

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Disclosure of interest

The authors declare that they have no competing interest.

References