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Palatal mucormycosis in a 2-month-old child: A very rare case report and a literature review

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ABSTRACT

A 2-month-old Syrian male child presented with a large blackish ulcerating lesion on his hard palate, along with fever, diarrhea, vomiting, and milk regurgitation from the nose. The child was diagnosed with palatal mucormycosis by histopathology and underwent treatment with liposomal amphotericin B and surgical debridement. However, despite treatment, the child's condition deteriorated, and he died from respiratory failure. An underlying immunodeficiency was not diagnosed, but the family history revealed several deaths of the child's siblings at very early ages due to poorly documented complicated metabolic syndromes. An autopsy was refused by the parents due to cultural reasons.

1. Introduction

Mucormycosis is an emerging global disease with high morbidity and mortality [1]. The transmission of the causal fungi such as *Rhizopus*, *Mucor*, *Rhizomucor*, and *Absidia* species occurs through inhalation of fungal sporangiospores or to the direct inoculation through the disrupted surface of skin or mucosa in vulnerable patients, particularly in immunocompromised patients [2,3]. It is rare for children to be reported with Mucormycosis [4]. In children, as in adults, immunodeficiency remains the most prominent risk factor, although Mucormycosis is not typically associated with any specific primary immunodeficiency [5]. Solid organ transplant, hematopoietic stem cell transplant, hematologic malignancy, chemotherapy, and diabetes are significant risk factors, with 9 %–36 % of cases occurring in diabetics [5]. Iron overload, deferoxamine therapy, and renal failure are less common but acknowledged risk factors in children [4]. Recently, underlying rheumatologic (autoimmune disorders) were identified as a risk for infection and poor outcomes [5]. Prematurity remains a major risk factor for neonatal disease [4]. In around 9.5 % of pediatric cases, no predisposing risk factor has been identified [6]. The most common type of mucormycosis is rhino-orbito-cerebral mucormycosis [1]. Palatal mucormycosis in infants is reported very rarely and a very few cases of palatal mucormycosis have been associated with metabolic defects such as Ornithine Ttranscarbamylase Deficiency (OTC) [7]. Invasion of the vasculature by hyphae that leads to necrosis and infarction of host tissues is characteristic [1]. The diagnosis relies upon the identification of organisms in tissue by histopathology with culture confirmation [8]. In this report, we describe an infant who presented with palatal mucormycosis but was not known with an underlying immunodeficiency or metabolic defect upon presentation.

2. Case report

We present a case of a 2-month-old Syrian male child, who was referred to our department from the pediatric intensive care unit with a large blackish ulcerating lesion on his hard palate since 5 days with a foul smell and lethargy. The child was born at full-term through a vaginal delivery and weighted 3.29 kg at birth. During the first 24 hours of life, the child did not experience any major concerns. The child was feeding well and showed no signs of difficulty swallowing. The medical history of the child began approximately from day 15 of life with persistent fever and recurrent watery foul-smelling diarrhea associated with frequent vomiting. The child was diagnosed with gastrointestinal infection and admitted to the hospital (day 0). Vital signs at admission (day 0) revealed a blood pressure of 95/55 mmHg with a heart rate of 140 beats per minute. His temperature was 38.8 °C. The respiratory rate

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was 40 breaths per minute.

Empirically intravenous treatment with metronidazole (140 mg divided q6hr for 7 days) was started. Milk regurgitation was noticed from the child's nose several times from day +3. A large ulcerating lesion was observed on the hard palate on day +5 and the child then was referred to our ENT department for further evaluation on day +6.

On physical examination, child appeared stressed, toxic, and in respiratory distress with a necrotic black lesion and an extensive ulcer measuring approximately 2 × 3 cm on the hard palate with an associated small perforation (Fig. 1). A black eschar was seen on the nasal turbinates and septum on both sides with vestibulitis. The mucosa of the floor of the mouth, lips, tongue, and buccal mucosa were normal. The lungs were clear to auscultation and abdominal exam was unremarkable. There was no peripheral edema. Chest X-ray revealed a small infiltration in the lower left lobe and the electrocardiogram (ECG) showed sinus tachycardia.

Initial laboratory studies revealed a white blood cell count of 13.5 × 10.3/mm3. LDH was 820 units/L. BUN was 12 mg/dL and creatinine was 0.9 mg/dL. CRP was 78 units/L. Arterial blood gas analysis showed respiratory alkalosis. Laboratory evaluation of the patient's immune function was assessed by the following: IgG and subclasses, IgA, IgM, and IgE were within normal limits, HIV testing was negative complement function (CH50) was normal. Cranial ultrasonography and MRI of the brain were both normal. CT scan of the head and neck in order to rule out other alternative diagnosis was not performed due to poor general condition of the child and his untimely death.

The family history revealed several deaths of the child's siblings at very early ages due to poorly documented complicated metabolic syndromes. Histopathologic examination of the incisional biopsy from the palatal lesion (day +6) showed the presence of broad, hyaline, hyposeptated hyphae, in conjunction with angioinvasion and tissue necrosis (Fig. 2, Fig. 3). Unfortunately, culture was not performed. Promptly, antifungal treatment was initiated on day +9 with 5 mg/kg per day liposomal amphotericin B. In an effort to eradicate all infected and necrotic tissues, an extensive surgical debridement of the hard and soft palate with left maxilla was performed along with drainage of all sinus fluid collections on day +11. Due to financial constrains the child did not undergo any reconstructive surgery. Liposomal amphotericin B was continued with close monitoring of electrolyte values and renal function tests for 3 weeks and then he developed high fevers and a low blood pressure. The child's cardio-respiratory status suddenly deteriorated, and he died from respiratory failure on day +30. The parents of the child refuse to perform autopsy due to cultural reasons.

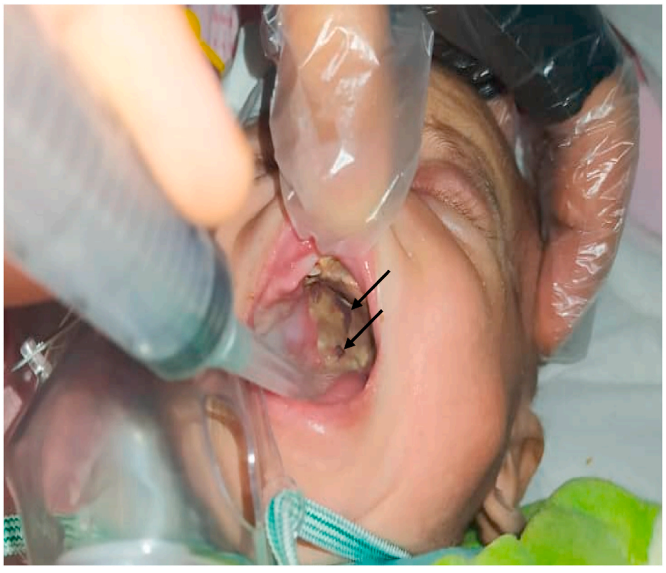


Fig. 1. View of the palatal necrosis on initial presentation. The arrows refer to the perforation of hard palate.

3. Discussion

Invasive mucormycosis has significant morbidity and mortality, especially in low and very low birth weight neonates and immunocompromised hosts and it can affect both adults and children of all age groups [9].

Underlying immunosuppression states that include diabetes mellitus, neutropenia, and prematurity predisposes to the infection with invasive mucormycosis and influences the clinical presentations in the clinical course of the infection [10,11].

Despite higher survival rates associated with limited involvement, in contrast to cases involving brain invasion that result in over an 80 % mortality rate, our patient ultimately succumbed to the illness after aggressive treatment, despite showing no brain involvement on MRI scan [12]. Recurrent aspirations due to the palatal defect resulting in lung infection and decreased lung function might have played a role in our patient, although mucormycosis of the lung could not be ruled out.

Histopathologic examinations form the basis of diagnosis in most cases of mucormycosis, while culture and molecular methods are relied upon in some cases to complement traditional ways [13]. Broad, irregularly branched, and rare septations hyphae with angioinvasion and tissue necrosis can be identified on histopathological examination of the tissue specimens as we found in our case that confirm the diagnosis without doing the culture because of the fragility and the damage of the sample [13,14].

Rhino-Orbito-Cerebral Mucormycosis (ROCM) represents the most prevalent clinical manifestation within the spectrum of mucormycosis. Following its onset, the infection swiftly progresses towards adjacent anatomical regions, implicating the palate, sphenoid sinuses, orbits, cavernous sinuses, and culminating in infiltration of the cerebral region [15]. As the rhinoorbitocerebral mucormycosis infection develops, black tissue necrosis can be noted on the nasal mucosa, palate, overlying facial skin, orbit, and brain [16].

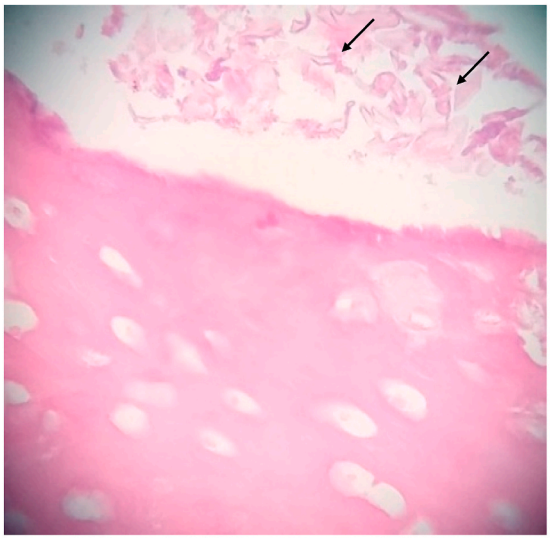
Palatal mucormycosis that appears in isolation is an uncommon occurrence, characterized by ulceration and/or necrosis of the mucosa that specifically affects palatal tissues in the absence of any accompanying sinonasal presentation. Our case denotes localization in the hard palate, with a confined extension to a small area of the septum, along with limited necrotic lesions observed in both lower turbinates [15].

Preceding the prompt onset of necrosis and ulceration, there is observable mild discoloration or swelling of the palatal mucosa. Such preceding clinical signs have also been documented in occurrences of rhino-orbital mucormycosis involving the palate. Regular surveillance of the mucous membranes of the oral cavity, either through the oversight of healthcare professionals, self-examination, or parental observation in the case of vulnerable infants, may facilitate the prompt identification of mucormycosis affecting the palate. In our patient, the palatal mucormycosis was diagnosed most likely as a presenting sign of an underlying disorder such as a primary immunodeficiency or metabolic disorder. Unfortunately, the work-up to detect such an underlying disorder could be not be completed due to the untimely death of the infant.

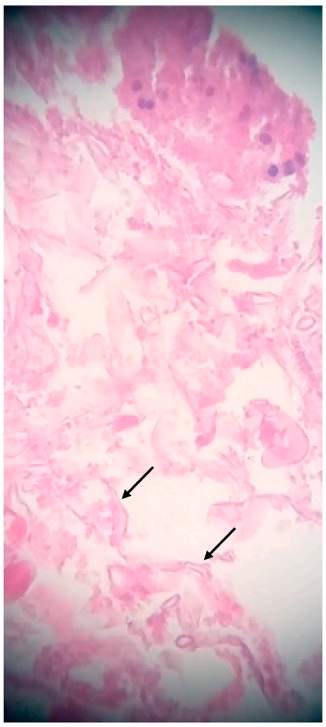
Liposomal amphotericin B is the drug of choice for primary therapy of mucormycosis in children with surgical debridement if possible.

Surgical assessment can be conducted urgently for both diagnostic purposes and for debridement. Surgical intervention can be difficult in some cases because of the extent of the infection and/or the severity of the underlying disease. Radical surgical debridement is required in most cases to achieve cure, and sometimes requires multiple surgeries [17]. Despite initiating early combination treatment for our patient, the child's overall deteriorating condition tragically resulted in the child's death.

Our case represents a rare instance of a two-month-old infant



A



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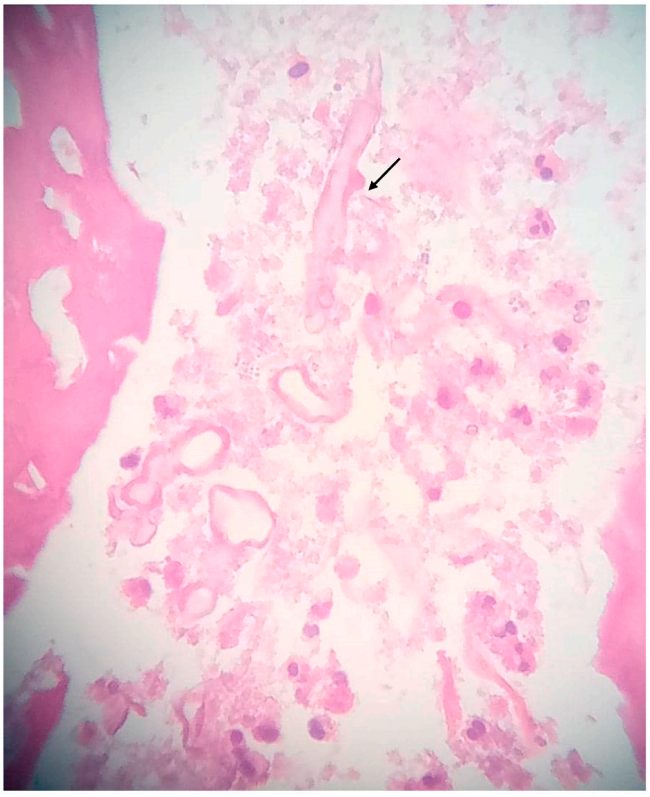

C

Fig. 2. Histological examination shows broad nonseptate hyphae irregular branching at 90° (the arrows in the pictures), accompanied by numerous neutrophils and necrotic material, adjacent to bone tissue. The specimen is stained with Hematoxylin and Eosin (H&E). Magnification is 40x.

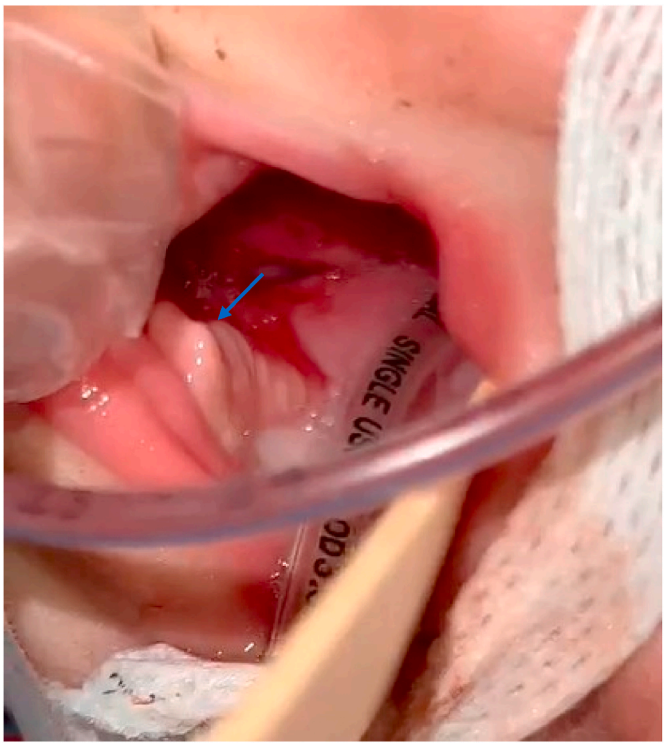

Fig. 3. Intra-operative view of the surgical resection. The arrow refer to the hard palate after debridement.

presenting with mucormycosis of the hard palate, initially noticed due to milk regurgitation. Upon examination, a perforation in the palate was identified, exacerbating the condition and increasing the likelihood of regurgitation and aspiration frequency. As highlighted in Kalaskar's article, a similar palatal lesion was observed in an 18-month-old patient exhibiting identical symptoms to our case. In that instance, the management of the recurrent aspiration was done by a palatal prosthesis, notably improving the child's condition [18]. However, in our case, this procedure was not feasible, leading to increased aspiration, potentially contributing to the respiratory distress observed and considered one of the factors implicated in the infant's demise.

We have summarized similar cases previously published in Table 1.

In conclusion, palatal mucormycosis in infants is very rare condition and can be a presenting symptom of an underlying disorder (see Table 2). A rapid evaluation and high suspicion are needed, especially in children, to identify this potentially fatal condition and for timely management.

FUNDING

The authors received no financial support.

Ethical approval

Our institution does not require ethical approval for reporting individual cases. Written informed consent was obtained from the patient for publication of this article.

Data availability statements

The data that support the findings of this study are available from Author or Corresponding Author upon reasonable request.

Contributorship statement

Al-Ghabra and Shamso conceived the presented idea. Al-Ghabra supervised the finding of this work and wrote the manuscript. Alkheder revised the introduction. Shamso collected the pictures and organized them. Hamdi rewrote the discussion. Kammasha is the corresponding author and supervised the review process. Mohsen supervised the case report and performed the surgery mentioned in the case. All authors discussed the results and contributed to the final manuscript.

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There are none.

Consent

Written informed consent was obtained from legal guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Table 1
Previously published cases of palatal mucormycosis in children & neonates.

Authors and year of publication	Age	Gender	Associated condition/s	Management protocol (Medical and/or surgical)	Outcomes
Samanta et al., 2009 [19]	8 years	M	ALL with febrile neutropenia	Surgical debridement then liposomal Amphotericin-B (dose of 1 mg/kg of bodyweight)	Recovered
Abdulai et al., 2009 [20]	14 years	F	AML with bone marrow transplant and refractory neutropenia	Oral posaconazole and caspofungin (adjunct therapy) then liposomal amphotericin and caspofungin.	Expired[A]
Srivastava et al., 2015 [21]	2 months	M	Nil	Surgical debridement and Voriconazole	Recovered
Kalaskar et al., 2016 [22]	18 months	M	Nil[B]	Amphotericin B for 31 days	Recovered[C]
Devaraja et al., 2021 [23]	9 years	M	ALL	Surgical debridement, amphotericin B, and posaconazole	Recovered
Devaraja et al., 2021 [24]	12 years	M	ALL	Surgical debridement, amphotericin B, and posaconazole	Recovered
Patil et al., 2023 [25]	4 months	M	Ornithine transcarbamylase deficiency[E,F]	Antifungal agent[D]	Expired

Abbreviations: **AML**: acute myeloblastic leukemia. **ALL**: acute lymphoblastic leukemia. **Recovered** means recovery from the episode of mucormycosis without any evidence of relapse even after discontinuing antifungal therapy. **D**: Lost to follow-up during ongoing treatment but had shown significant clinical improvement to therapy. **E**: Recovered from fungal disease but died due to novel Coronavirus-19 infection.
A: Death was most likely secondary to coexisting another disseminated fungal infection (Hormographiella aspergillata infection). **B**: History of pneumonia one-month prior to initial presentation. **C**: Palatal prosthesis was applied. **D**: The type of antifungal agent was not mentioned. **E**: A form of urea cycle disorders. **F**: with coexisting enterococcus sepsis.

Table 2
Showing previously published cases of palatal mucormycosis in children & neonates.

Authors and year of publication	Age	Gender	Associated condition/s	Management protocol (Medical and/or surgical)	Outcomes
Samanta et al., 2009 [25]	8 years	M	ALL with febrile neutropenia	Surgical debridement then liposomal Amphotericin-B (dose of 1 mg/kg of bodyweight)	Recovered
Abdulai et al., 2009 [26]	14 years	F	AML with bone marrow transplant and refractory neutropenia	Oral posaconazole and caspofungin (adjunct therapy) then liposomal amphotericin and caspofungin.	Expired[A]
Srivastava et al., 2015 [27]	2 months	M	Nil	Surgical debridement and Voriconazole	Recovered
Kalaskar et al., 2016 [28]	18 months	M	Nil[B]	Amphotericin B (5.5 mg) for 31 days	Recovered[C]
Devaraja et al., 2021 [29]	9 years	M	ALL	Surgical debridement, amphotericin B, and posaconazole	Recovered
Devaraja et al., 2021 [30]	12 years	M	ALL	Surgical debridement, amphotericin B, and posaconazole	Recovered
Patil et al., 2023 [31]	4 months	M	Ornithine transcarbamylase deficiency[E,F]	Antifungal agent[D]	Expired
Our case	2 months	M	Nil[G]	Surgical debridement and amphotericin B	Expired[H]

Abbreviations: **AML**: acute myeloblastic leukemia. **ALL**: acute lymphoblastic leukemia. **Recovered** means recovery from the episode of mucormycosis without any evidence of relapse even after discontinuing antifungal therapy. **D**: Lost to follow-up during ongoing treatment but had shown significant clinical improvement to therapy. **E**: Recovered from fungal disease but died due to novel Coronavirus-19 infection.
A: Death was most likely secondary to coexisting another disseminated fungal infection (Hormographiella aspergillata infection). **B**: History of pneumonia one-month prior to initial presentation. **C**: Palatal prosthesis was applied. **D**: The type of antifungal agent was not mentioned. **E**: A form of urea cycle disorders. **F**: with coexisting enterococcus sepsis. **G**: History of gastrointestinal illness 15-day prior to initial presentation. **H**: Died in hospital due to persistent disease.

Declaration of competing interest

The authors have declared no potential conflicts of interest.

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