



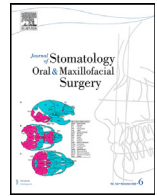
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Available online at
ScienceDirect
 www.sciencedirect.com

Elsevier Masson France
EM|consulte
 www.em-consulte.com



Case Report

A case series of mucormycosis after covid infection in two hospitals



Hélder D.D. Martins^{a,*}, Arturo Rangel Pares^b, Armando Torres Martínez^c, Rogelio Alberto Ponce Guevara^d, Sirius D. Inaoka^e, Davi F.N. Costa^e, Carlson B. Leal^e, Ciro D. Soares^f, Alexandre R. da Paz^g, Danyel E. da C. Perez^h, Ricardo Martínez Pedraza^b, Paulo R.F. Bonan^a

^a Post Graduation Program in Dentistry, Universidade Federal da Paraíba (UFPB), Campus I - Cidade Universitária, João Pessoa, Paraíba 58033-455, Brazil

^b Universidad Autónoma de Nuevo León, Mexico

^c Oral and Maxillofacial Surgeon, Benemérita Universidad Autónoma de Puebla, Mexico

^d Oral and Maxillofacial Surgeon, School of Dentistry, Torreon Unit, Universidad Autónoma de Coahuila, Mexico

^e Oral and Maxillofacial Surgeon, Hospital Universitário Lauro Wanderley, Universidade Federal da Paraíba, João Pessoa, Paraíba, Brazil

^f Immunohistochemistry and Histopathology Group / International Research Group, Natal, Brazil

^g Pathological Anatomy Service, Hospital Universitário Lauro Wanderley, Universidade Federal da Paraíba, João Pessoa, Paraíba, Brazil

^h Department of Clinical and Preventive Dentistry, Universidade Federal de Pernambuco, Recife, Pernambuco, Brazil

ARTICLE INFO

Article History:

Received 25 April 2022

Accepted 8 June 2022

Available online 11 June 2022

Keywords:

Coronavirus
 Mucormycosis
 Infections
 Oral diagnosis

ABSTRACT

This paper aims to discuss clinical aspects of mucormycosis. This case series was conducted in two services, comprising six mucormycosis cases during COVID-19 pandemic. About gender, there are 4 (66.7%) males and 2 (33.3%) females with mean age (48.7 ± 9.4) years. All cases presented complaints of pain and swelling in oral cavity and had an aggressive clinical presentation. Five patients had diabetes and one had a nasal non-Hodgkin lymphoma. Histologically, large, branched, hyphae associated with necrotic areas were observed, confirming microscopically such as mucormycosis through PAS and GMS stains. In four cases, treatment consisted in surgical debridement associated with antifungal therapy. All patients were submitted to debridement and received antifungal treatment (amphotericin B). Five patients were followed up without clinical recurrence, but unfortunately one patient died. Diagnosis of mucormycosis should be early because it is related to high mortality. The treatment consists of surgical debridement associated with antifungal therapy.

© 2022 Elsevier Masson SAS. All rights reserved.

1. Introduction

COVID-19, caused by SARS-CoV-2 virus, was firstly reported in December 2019. Since then, a pandemic situation has increased and up to now (March 2022), with 452 million of cases confirmed worldwide [1]. COVID-19 can present oral manifestations, because SARS-CoV2 has the property of disrupting the immune system and triggering a cytokine storm [2,3]. Moreover, atypical clinical presentations have been reported during pandemic and they are more probably caused by co-infections, adverse reactions, and immunity impairment instead of direct COVID-19 infection [4,5].

Recently, some cases of an uncommon fungal infection in post-COVID-19 patients were described as known as mucormycosis [5]. Rhino-orbital-cerebral presentation is the most common type caused by inhalation of spores into paranasal sinus of immunocompromised patients. Fatality rate of this fungal infection is up to 46% occurring due to vascular thrombosis, angioinvasion, and tissue necrosis [6,7].

Thus, this paper aims to describe and discuss clinical aspects of rhinomaxillary mucormycosis diagnosed in two referral services.

2. Case series

Among six cases, there are 4 (66.7%) males and 2 (33.3%) females with mean age (48.7 ± 9.4) years. Clinical data, treatment, and follow-up in 6 cases of OM were listed on Table 1.

All cases presented complaints of pain and swelling in oral cavity and had an aggressive clinical presentation manifested as bone loss and irregular destruction, ulcers, necrosis, and tooth mobility. In addition, all cases had a recent history of COVID-19 or positivity for spike protein in the tissue. Histologically, large, branched, hyphae associated with necrotic areas were observed, confirming microscopically such as mucormycosis through PAS and GMS stains (Figs. 1 and 2).

Five patients presented decompensated diabetes and one had a history of non-Hodgkin lymphoma.

In four cases, treatment consisted in surgical debridement associated with antifungal therapy (Amphotericin B). In addition, case 2

* Corresponding author.

E-mail address: helderdomiciano@hotmail.com (H.D.D. Martins).

Table 1
Clinical data, treatment, and follow-up in 6 cases of OM.

Case	Sex	Age (yo)	Location	Clinical presentation	Comorbidities	Pain	Mucormycosis	Treatment	Follow up (in months)
1	M	58	Maxilla	Bone irregular destruction	Decompensated diabetes	Yes	+	Surgical excision + Amphotericin B	9
2	M	45	Maxilla	Multiple ulcers on maxilla	A nasal non-Hodgkin lymphoma a decade ago	Yes	+	Meropenem, Vancomycin + oncological treatment ^a	6
3	F	35	Hard palate (right maxilla)	Necrosis	Diabetes Hypertension	Yes	+	Surgical debridement Amphotericin B	Died (after 19 days)
4	F	50	Hard palate	Nodule	Decompensated diabetes	Yes	+	Surgical debridement + Amphotericin B	4
5	M	44	Maxilla	Bone loss and tooth mobility	Diabetes Hypertension	Yes	+	Surgical debridement + Amphotericin B	Treatment recently initiated
6	M	60	Maxilla	Ulcers and necrosis	Decompensated diabetes	Yes	+	Surgical debridement + Amphotericin B	Treatment recently initiated

^a The recurrence of Non-Hodgkin Lymphoma was diagnosed through nose specimen histopathology, and the patient was referred to oncologic treatment (radiotherapy and chemotherapy).

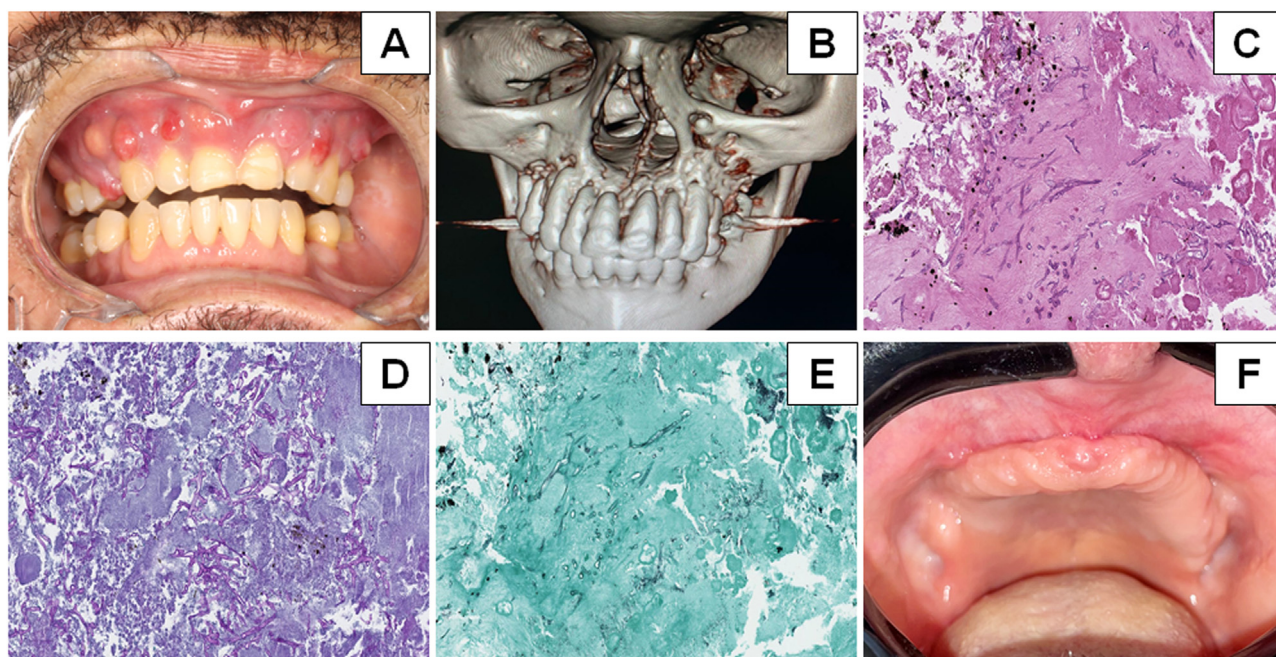


Fig. 1. (a) Clinical features of multiple periodontal abscesses affecting maxilla. (b) Tomographic reconstruction revealed severe bone loss. (c–e) Microscopically, necrotic area was associated with hyphae structures, confirmed such as mucormycosis (HE, PAS, Grocott stainings). (e) Clinically, it is possible to observe good healing after two months of surgical and antifungal intervention.

was referred to oncological treatment due to a concomitant non-Hodgkin lymphoma and mucormycosis. Unfortunately, one patient died, and the others are being followed up without recurrence.

3. Discussion

These reports are particularly important because mucormycosis could be a serious late complication in patients' recovery from COVID-19 infection [8]. In addition, there is a need for more reports to spread the possibility of mucormycosis in the oral cavity to reach faster diagnoses, since delay in diagnosis can be fatal [6].

Oral manifestations of mucormycosis in COVID-19 patients occurs more frequently in the palate and may include mucosal discoloration, swelling, ulcerations, bone exposure and superficial necrosis or necrosis with dark eschar formation [5]. Generally, ulcerations on the palate could be the first symptom. Furthermore, draining abscesses,

oro-antral communication are other clinical characteristics associated with them [8]. These clinical characteristics were observed in all cases reported.

Oral manifestations could be explained to the immune suppression caused by reduction in CD4+ T cells and CD8+ T cells [5]. Uncontrolled diabetes, the excessive use of corticosteroids, prolonged neutropenia, hemopoietic malignancies are the most common causes attributed to the rise of mucormycosis in COVID-19 [5,9]. Herein, six cases were reported (five cases associated with uncontrolled diabetes and one case associated with non-Hodgkin lymphoma) which may explain the onset of mucormycosis in these patients.

Early diagnosis and correct management are required to improve the prognosis and decrease the morbidity and computed tomography is the gold standard tool to evaluate mucormycosis involvement. The European Confederation of Medical Mycology and the Mycoses Study

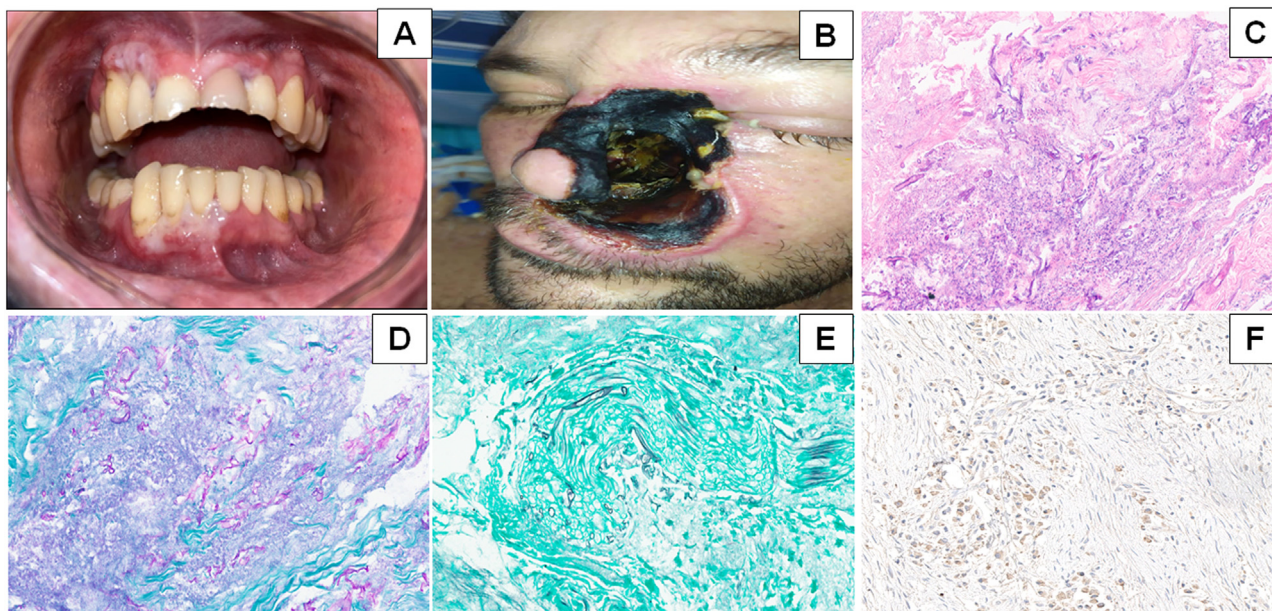


Fig. 2. (a,b) Multiple ulcerative lesions affecting maxilla with necrosis. (c) A necrotic area was associated with hyphae structures, confirmed microscopically such as mucormycosis (d–f) PAS, Grocott and Spike protein stainings, respectively.

Group Education and Research Consortium recently published guidelines and a diagnostic algorithm for mucormycosis that requires species identification by hematoxylin and eosin (H & E), periodic acid Schiff (PAS) or Grocott methenamine-silver (GMS) staining or specimen culture [10]. In this paper, the cases were positive for PAS and GMS and, associated with the clinicopathological features, were characterized as mucormycosis.

Mucormycosis treatment can be an association of medicinal (systemic antifungals) and surgical approaches. The first line of anti-fungal therapy involves liposomal amphotericin B which should be carried out initially for 4–6 weeks [11]. Surgical debridement includes resecting infected and necrotic tissues to reduce the fungal load. All cases were treated as recommended and we had a good response, despite the death of one patient.

4. Conclusion

Diabetes was the most common predisposing factor followed by arterial hypertension. Thus, dentists play an important role on management of this condition because mucormycosis primarily involves orofacial tissues and is necessary an early diagnosis to reduce mortality and morbidity in these patients.

Funding

None.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jormas.2022.06.003.

References

- [1] Organization W.H.. WHO Coronavirus (COVID-19) Dashboard 2022. <https://covid19.who.int/> (accessed Apr 22, 2022).
- [2] Santos JA, Normando AGC, Silva RLC, Acevedo AC, Canto GDL, Sugaya N, et al. Oral manifestations in patients with COVID-19: a living systematic review. *J Dent Res* 2021;100:141–54. doi: 10.1177/0022034520957289.
- [3] Santos JA, Normando AGC, Silva RLC, De Paula RM, Cembranel AC, Santos-Silva AR, et al. Oral mucosal lesions in a COVID-19 patient: new signs or secondary manifestations? *Int J Infect Dis* 2020;97:326–8. doi: 10.1016/j.ijid.2020.06.012.
- [4] La Rosa GRM, Libra M, De Pasquale R, Ferlito S, Pedullà E. Association of viral infections with oral cavity lesions: role of SARS-CoV-2 infection. *Front Med* 2021;7:571214. doi: 10.3389/fmed.2020.571214.
- [5] Ahmed E, Abou-Bakr A, Hussein RR, El-Gawish AA, Ras A bakr E, Ghalwash DM. Oral mucormycosis in post-COVID-19 patients: a case series. *Oral Dis* 2021. doi: 10.1111/ODL.13973.
- [6] Jain A, Taneja S. Post-COVID fungal infections of maxillofacial region: a systematic review. *Oral Maxillofac Surg* 2021. doi: 10.1007/S10006-021-01010-5.
- [7] Verma DK, Bali RK. COVID-19 and mucormycosis of the craniofacial skeleton: causal, contributory or coincidental? *J Maxillofac Oral Surg* 2021;20:165–6. doi: 10.1007/S12663-021-01547-8.
- [8] Sood A, Nayyar V, Mishra D, Kakkar A, Priya H. Post-COVID mucormycosis: ascertainment of the pathological diagnostic approach. *J Oral Maxillofac Pathol* 2021;25:219–22. doi: 10.4103/0973-029X.325117.
- [9] Raut A, Huy NT. Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave? *Lancet Respir Med* 2021;9:e77. doi: 10.1016/S2213-2600(21)00265-4.
- [10] Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European confederation of medical mycology in cooperation with the mycoses study group education and research consortium. *Lancet Infect Dis* 2019;19:e405–21. doi: 10.1016/S1473-3099(19)30312-3.
- [11] Nambiar M, Varma SR, Jaber M, Sreelatha SV, Thomas B, Nair AS. Mycotic infections - mucormycosis and oral candidiasis associated with COVID-19: a significant and challenging association. *J Oral Microbiol* 2021;13. doi: 10.1080/20002297.2021.1967699.