



Rhino-Orbital-Cerebral-Mucormycosis: The Importance of Urgent Assessment

Boynes AC^{1,2*}, Schuringa R^{1,3}, Hickey DG^{1,2}, Reynolds G^{1,3} and Khong JJ^{1,2}

¹Austin Health, Heidelberg, Australia

²The Royal Victorian Eye and Ear Hospital, Australia

³The University of Melbourne, Parkville, Australia

Abstract

A case report highlighting the importance of early assessment and intervention in treating ROCM. This paper is particularly relevant as we are seeing a concerning increase in the incidence of ROCM associated to COVID-19.

A 67-year-old female had a delayed diagnosis of ROCM confirmed with radiological and microbiological findings. Her predisposing risk factors included end-stage renal disease, aplastic anemia with neutropenia, and iron overload requiring deferoxamine infusions. Management included surgical debridement of paranasal sinuses, orbital exenteration and systemic antifungal treatment. The disease progressed despite this management, with the development of multifocal fungal cerebritis and superimposed ischemic infarcts. The patient died five days after the cessation of treatment.

ROCM is a life-threatening emergency. ROCM should be considered in all at risk patients who present with common sinus symptoms and disproportionate facial pain, especially when associated with red flags such as ophthalmoplegia, vision loss and facial numbness.

Introduction

This case report adds to current knowledge by highlighting less well-known risk factors for poor prognosis in Rhino-Orbital-Cerebral-Mucormycosis (ROCM) such as end-stage renal failure and deferoxamine infusions. It describes recent changes in the evidence-based management of ROCM including topical amphotericin B, which is gaining increasing popularity. This report is particularly relevant as we are seeing a concerning increase in the incidence of ROCM associated to COVID-19. Written patient consent was provided and this report adhered to the tenets of the Declaration of Helsinki.

Case Presentation

A 67-year-old female presented to an emergency department with two days of left-sided facial pain and headache. She was diagnosed with acute-on-chronic sinusitis based on Computerized Tomography (CT) and treated with oral Augmentin duo (500/125 mg BD).

Her medical history included end-stage renal disease secondary to polycystic kidney disease, requiring hemodialysis; transfusion-dependent aplastic anemia and associated iron overload, treated with deferoxamine infusions; and left Middle Cerebral Artery (MCA) aneurysm clipping.

She suddenly deteriorated two days later whilst an inpatient, developing left ptosis, proptosis, periorbital discoloration, ophthalmoplegia, and an absent corneal reflex. Her Best Corrected Visual Acuity (BCVA) was 6/9 in both eyes. A CT showed enlargement of the left medial and inferior rectus muscles alongside early orbital fat stranding and left maxillary and ethmoidal sinus opacification. Her medical care was transferred to our hospital with a provisional diagnosis of orbital cellulitis.

On the initial ophthalmology assessment, her BCVA was 6/6 in the right eye and light perception in the left eye. She had a left relative afferent pupillary defect and complete ptosis. Examination revealed 3 mm of proptosis in the left eye and complete ophthalmoplegia (Figure 1). In addition, reduced sensation in the V1 distribution had resulted in an absent corneal reflex. The posterior segment examination in both eyes was grossly normal.

Otorhinolaryngology assessment identified necrotic tissue underlying the sphenoid and

OPEN ACCESS

*Correspondence:

Antony Boynes, Royal Victorian Eye and Ear Hospital, 32 Gisborne Street, East Melbourne, VIC 3002, Australia, Tel: +61 9929 8666;

E-mail: antonyboynes@gmail.com

Received Date: 12 Jan 2023

Accepted Date: 06 Feb 2023

Published Date: 10 Feb 2023

Citation:

Boynes AC, Schuringa R, Hickey DG, Reynolds G, Khong JJ. Rhino-Orbital-Cerebral-Mucormycosis: The Importance of Urgent Assessment. *Ann Clin Case Rep.* 2023; 8: 2393.

ISSN: 2474-1655.

Copyright © 2023 Boynes AC. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Figure 1: Patient photograph on initial ophthalmology assessment with evidence of left ptosis, proptosis and periorbital discoloration.

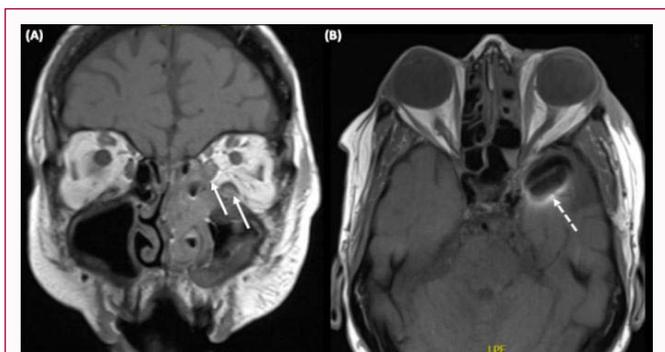


Figure 2: Preoperative MRI brain/orbits (A) T1 coronal view showing opacification of the left maxillary and ethmoid sinuses as well as thickening of the inferior and medial rectus muscles (white arrows). (B) MRI brain/orbits T1 axial view showing inflammatory changes involving the intraconal optic nerve and thickening of the left medial rectus muscles. Image quality at the cavernous sinus and orbital apex is degraded by artefact related to middle cerebral artery metallic clip (dashed arrow).

ethmoid sinuses, and throughout the left turbinates. Magnetic Resonance Imaging (MRI) showed inflammatory changes compatible with acute invasive fungal sinusitis involving the left optic nerve. There was significant artefact over the cavernous sinus due to previous MCA aneurysm clipping (Figure 2). A provisional diagnosis of mucormycosis was made, and she was commenced on intravenous amphotericin, ceftazidime and flucloxacillin. That same day, paranasal sinus debridement and orbital exploration were performed, during which extensive tissue necrosis including the left turbinate's, maxillary/ethmoid sinuses, internal maxillary artery, extraconal fat and medial rectus were noted. Intraoperative tissue samples were consistent with mucor species showing angioinvasive fungal hyphae with extensive necrosis extending to the orbital apex (Figure 3). A diagnosis of ROCM was made, as was a decision to proceed to left orbital exenteration with amphotericin only at the orbital apex and orbital fissures, alongside further debridement of left paranasal sinuses. Postoperatively she experienced ongoing fever and became increasingly confused. A postoperative MRI showed features consistent with multifocal fungal cerebritis with superimposed ischemic infarcts. As this represented a terminal event, active treatment was withdrawn, and the patient died five days later.

Discussion

This case highlights the importance of understanding risk factors for ROCM and the need for urgent assessment and management. Rhino-orbital-cerebral-mucormycosis is a rapidly progressive disease with a mortality rate between 15% to 85% [1]. Clinicians need to be

Table 1: Clinical Features of rhino-orbital-cerebral mucormycosis and associated mortality rate by degree of infiltration.

Anatomical structure involved	Clinical feature	Assoc. mortality rate (%)
Sinus/Non-specific	Epistaxis	50
	Headache	47
	Fever	44
	Nasal or oral necrosis	41
	Nasal congestion	38
	Facial pain	33
	Nasal discharge	29
Orbit	Periorbital/orbital pain	53
	Periorbital oedema	47
	Ptosis	47
	Periorbital discoloration	47
	Afferent pupillary defect	45
	Ophthalmoplegia	44
	Facial nerve palsy	43
	Proptosis	38
	Trigeminal anesthesia	37
	Decreased vision	35
	Diplopia	31
Cerebral	Seizures	67
	Internal carotid occlusion	67
	Mental status change	66
	Hemiplegia or Stroke	61
	Cavernous sinus thrombosis	57

† Mortality rate reported by Vaughan et al. [1]; Mortality data extracted from Honavar et al. [2]

aware of the warning symptoms and signs of ROCM as highlighted in Table 1 [2,3].

In the setting of the COVID-19 pandemic there has been a concerning increase in the global incidence of ROCM [2,4]. Globally, diabetes is the single most important risk factor for ROCM [5]. In our case, predisposing risk factors that warrant early suspicion of ROCM included a history of renal failure, hematological disorder-associated pancytopenia, and iron overload requiring deferoxamine therapy [1].

Antifungal medications and controlling the underlying disease are the mainstay of initial treatment in ROCM. Amphotericin B, 5 mg/kg/day to 10 mg/kg/day has been shown to effectively treat mucormycosis [5]. In cases with predominant sinonasal manifestation with no or limited involvement of the orbit and preserved vision, early and aggressive debridement of paranasal sinuses is indicated, and retrobulbar amphotericin B injections (3.5 mg/ml) and sinus irrigation with amphotericin has been advocated [2]. Adjuvant orbital amphotericin B injections have been increasingly used in early-stage ROCM, especially during COVID-19 pandemic where 22% received injections in an Indian series [4]. Orbital exenteration is considered when early management fails with progressive orbital involvement, and in late stages with extensive orbital involvement with visual loss and intracranial extension [2]. While it was shown previously that orbital exenteration did not significantly change survival in ROCM [1], recent analysis of large series of over 2,000 COVID-19 related ROCM cases suggested orbital exenteration was associated with

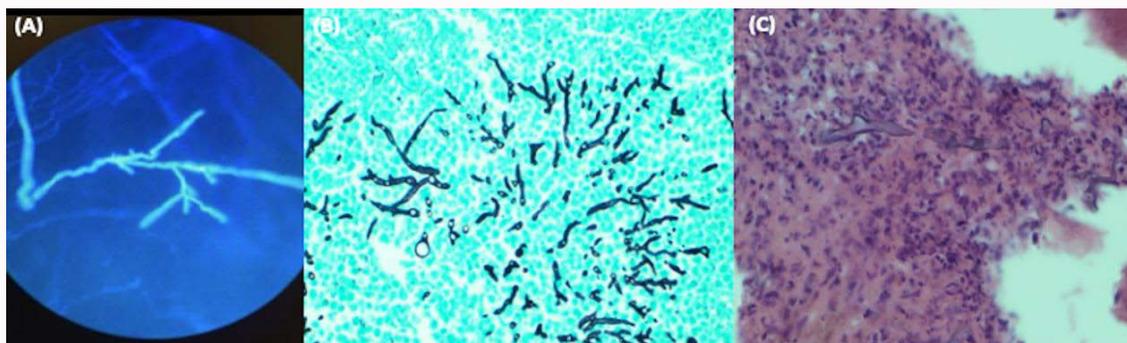


Figure 3: (A) Calcofluor stain demonstrating broad non-septate hyphae with right-angle branching. (B) Grocott's methenamine silver stain highlighting fungal elements. (C) Hematoxylin and eosin stain demonstrating broad non-septate fungal ribbons.

mortality reduction from 52% to 39% in ROCM stage 4 disease with intracranial extension [4]. Decision on globe survival is based on aggressiveness of presentation, type of underlying disease process and response to initial therapy [1].

Conclusion

Rhino-orbital-cerebral-mucormycosis is a life-threatening emergency and should be considered in all at risk patients with diabetes, renal failure, and those on deferoxamine therapy who present with sinus symptoms and pain. Red flags such as ophthalmoplegia, vision loss or facial numbness are late-stage features that warrant immediate attention.

References

1. Kashkouli MB, Abdolalizadeh P, Oghazian M, Hadi Y, Karimi N, Ghazizadeh M. Outcomes and factors affecting them in patients with rhino-orbital-cerebral mucormycosis. *Br J Ophthalmol*. 2019;103(10):1460-65.
2. Honavar SG. Code Mucor: Guidelines for the diagnosis, staging and Management of rhino-orbital-cerebral mucormycosis in the setting of COVID-19. *Indian J Ophthalmol*. 2021;69(6):1361-5.
3. Vaughan C, Bartolo A, Vallabh N, Leong SC. A meta-analysis of survival factors in rhino-orbital-cerebral mucormycosis-has anything changed in the past 20 years? *Clin Otolaryngol*. 2018;43(6):1454-64.
4. Sen M, Honavar SG, Bansal R, Sabyasachi S, Raksha R, Usha K, et al. Epidemiology, clinical profile, management, and outcome of COVID-19 associated rhino orbital cerebral mucormycosis in 2826 patients in India – Collaborative OPAI IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. *Indian J Ophthalmol*. 2021;69(7):1670-92.
5. 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-e421.