

## Post-Covid 19 Rhino-orbito-cerebral Mucormycosis in a Diabetic Patient: A Case Report

Fatma Dhieb<sup>1</sup>, Meriem Jrad<sup>1\*</sup>, Nour Ben Ghorbel<sup>1</sup>, Meriem Boumediene<sup>1</sup>, Rym Lahiani<sup>2</sup> and Ines Riahi<sup>2</sup>

<sup>1</sup>Department of Radiology, Charles Nicolle Hospital, Tunis, Tunisia

<sup>2</sup>Department of Otolaryngology, Charles Nicolle Hospital, Tunis, Tunisia

\*Corresponding Author: Meriem Jrad, Department of Radiology, Charles Nicolle Hospital, Tunis, Tunisia.

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### Abstract

Only a few cases of co-infection of Covid 19 and mucormycosis have been reviewed in literature.

We are presenting a case of a 59 years old diabetic female patient who had a rhino-orbito-cerebral fungal infection one month after being diagnosed positive to Covid-19.

While she was infected by the virus the patient was treated ambulatory with broad spectrum antibiotic therapy and methylprednisolone.

One month after, the patient was admitted to hospital due to nasal obstruction with right purulent rhinorrhea, headache, unilateral right side facial pain, swelling of the right eye, and severe decreased visual acuity with no perception of light. The examination highlighted a right complete ophthalmoplegia with areflective mydriasis, chemosis and periorbital cellulitis. A necrosis of the right side of nasal was seen in nasal endoscopy. Sinusal evacuation and debridement surgery was done, and the patient was put on broad antibiotics in addition to IV liposomal Amphotericin B.

Mucormycosis is a severe infection and often a fatal infection. Our report shows that physicians should consider the potential of secondary invasive fungal infection in patient suffering with Covid-19.

**Keywords:** Mucormycosis; Covid19; Invasive Fungal Infection; CT Scan; MRI

### Case Report

A 59-year-old female patient with a history of an uncontrolled type 2 diabetes, with non-compliance to treatment, who suffered in July 2021 COVID-19, with positive polymerase chain reaction (PCR), complicated of a bacterial pneumonia. The infection was managed with broad spectrum antibiotics, corticosteroid therapy and home oxygen therapy without the need of hospitalization. One month later, the patient presented to the Emergency of Charles Nicolle Hospital Tunis, Tunisia on the 27<sup>th</sup> August 2021 with a ten-day duration of headache, right purulent rhinorrhea, unilateral right side facial pain, swelling of the right eye, and severe decreased visual acuity with no perception of light.

She was referred in emergency to the Department of Otorhinolaryngology.

On physical examination, vital signs were normal with blood pressure at 140/80, and heart rate at 80 bpm.

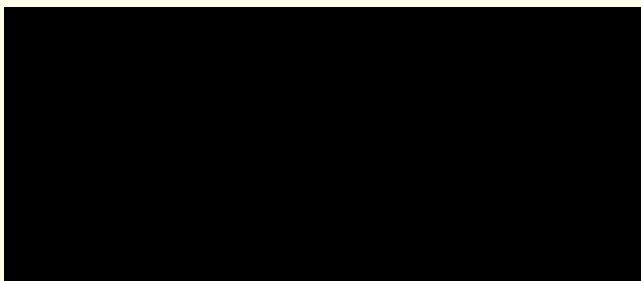
In ophthalmologic examination, a right complete ophthalmoplegia was noted, with unreflective mydriasis, chemosis and periorbital cellulitis.

In nasal endoscopy, a necrosis of the right side of nasal wall and of the middle and inferior right conchae was observed, with visualization of pus in the right middle meatus.

Laboratory investigations showed : normal white cells count  $5.51 \times 10^3/\text{mm}^3$ , no lymphopenia 27% (range 18-44), anemia with Hemoglobin at 7.7 g/dL (range 11.5 - 17.5 g/dL), high C- reactive Protein CRP at 81.5 mg/L (range < 0.8 g/dL), Fasting blood sugar 112 mg/dL (range 70 - 110 mg/dL), Post-prandial blood sugar 156 mg/dL (range 110 - 140 mg/dL).

A computed tomography scan of brain and sinuses with intravenous contrast performed prior admission showed total filling of the ethmoidal cells, more marked on the right, associated with mucosal thickening in the maxillary sinuses, frontal and sphenoidal sinus, in line with pan sinusitis.

It also objectivated a significant enhancement in the right palpebral and intraconical fat, suggestive of pre and retroseptal orbital cellulitis with eye proptosis. Peripheral enhancement of the right optic nerve was also noted (Figure 1).



**Figure 1**

**A:** Coronal CT-scan image with contrast showing orbital fat edema (white arrow), and peripheral enhancement of optic nerve (red arrow).  
**B:** Axial CT-scan image with contrast revealing eye proptosis (white arrow), filling and enhancement of right ethmoidal cells (red arrow).

The bone study showed lysis of the right middle and inferior turbinates, and of the cartilaginous septum.

It also showed a minimal erosion of the cribriform lamina (Figure 2).

**Figure 2:** Coronal CT-scan image in bone window, showing erosion of the cribriform lamina (white arrow), and lysis of right conchae (red arrows).

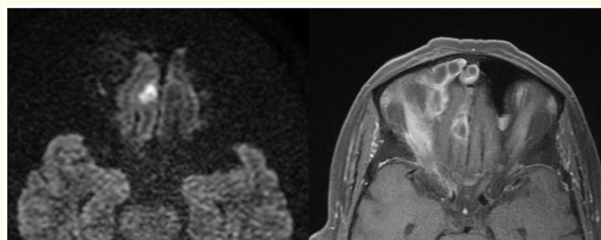
However, no abnormal extension of the inflammatory process towards brains or cavernous sinus regions was detected.

A cerebro-orbital MRI realized one day later on 1.5 Tesla field revealed diffuse enhancement of ethmoidal cells, especially on the right, with true diffusion restriction denoting acute sinusitis. Right orbital cellulitis was confirmed with evidence of diffuse edema and enhancement of the intra and extra conical fat, associated to the presence of an intra orbital collection (Figure 3).

Abnormal fatty stranding surrounding the right optic nerve, extending beyond the optic canal was also demonstrated, confirming the optic neuritis.

MRI also showed an intracranial extension through a breach of the cribriform lamina, with demonstration of an extended collection from the ethmoidal sinus to the right frontal lobe, in low T1 weighted signal, diffusion hypersignal, peripherally enhanced after contrast (Figure 3 and 4).

**Figure 3:** Axial and coronal T1-Fat-Suppressed sequence images after contrast showing mucosal enhancement ethmoidal and maxillary sinuses, marked on the right.



**Figure 4:** Axial Diffusion (A) and T1-Fat-Suppressed Gadolinium (B) images showing a cerebral collection in diffusion hypersignal with annular inhancement after contrast.

Cavernous sinus study in T1 weighted sequence after injection of Gadolinium revealed peripheral enhancement and filling defect, confirming thrombosis and cavernous extension (Figure 5).

**Figure 5:** Coronal T1 Fat-Suppressed-Gadolinium image demonstrating filling defect with peripheral enhancement (red arrow).

Internal carotid artery was reduced in caliber, while remaining permeable.

Since clinical and imaging results suspected the possibility of rhino-orbito-cerebral mucormycosis, treatment with IV liposomal Amphotericin B was initiated according to guidelines.

Biopsies of the right middle conchae and of the right maxillary sinus mucosa were realized and specimens were sent to both mycology and pathology laboratories.

Direct examination noted the presence of Mycellium filaments. Special stains for fungal hyphae were positive.

Histologic examination revealed large areas of necrosis along the nasosinusal tissue, rich of inflammatory polynuclear neutrophil infiltrate, with aseptate branching broad based fungal hyphae.

Some bone spans were also colonized by Mycellium filaments.

Sinusal evacuation and debridement surgery was planned, and the patient was put on broad antibiotics in addition to IV liposomal Amphotericin B.

### Discussion

- The acute invasive fungal rhinosinusitis (AIFRS) is a rare and severe opportunistic fungal infection. It is characterized by direct invasion that causes infarction and necrosis

of tissues [1], followed by rapid progression and angio-invasion from the nasal and sinus mucosa into orbit and brain.

- The incident rate of mucormycosis varies from 0.005 to 1.7 per million population [2].
- Fungal co-infections in patient with COVID-19 have been reported in a limited number of studies. The few studies published show that the median age of patients was 53 years (range 20-86 years).
- Predisposing situation for AIFRS are hematological malignancy, diabetes mellitus, pharmacological immunosuppression, neutropenia, previous pulmonary pathology and HIV.
- The immune dysregulation caused by COVID-19 with the diffuses alveolar damage and the severe inflammatory exudation that decrease in CDA and CD8 T cells may lead to secondary fungal infections [3].
- Patients who were admitted to the intensive care unit and that required mechanical ventilation and longer duration hospital stays are more likely to develop fungal co infections.
- In our patient, the fungal infection was noticed 1 month after COVID-19 during which time the patient had ambulatory treatment, with broad spectrum antibiotics, corticosteroid therapy and home oxygen therapy.
- Rhino-orbital-cerebral infection is the most common clinical presentation, such in our case believed to be secondary to a direct inhalation of spores into para nasal sinuses of susceptible host.
- The rate of fatality is high between 50 and 80% [4]. An early diagnosis and prompt antifungal therapy and surgical debridement can help to control the severe infection.
- The patients co infected with COVID 19 and mucormycosis have higher mortality (53% versus 31% without) [3].
- The infection usually presents acute sinusitis, fever, nasal congestion, purulent nasal discharge and headache.
- Some clinical presentations are highly suggestive of mucormycosis like unilateral facial pain, orbital swelling or proptosis, ophthalmoplegia and rapid visual loss. In our case, the patient lost her sight after ten days.
- To confirm the diagnosis, an endoscopic evaluation of the sinuses should be performed to look for tissue necrosis

and a nasal biopsy to obtain specimens. Non-pigmented hyphae are showed in the invaded tissue stained with hematoxylin eosin.

- Special stains such as Gomori methenamine silver or periodic acid Schiff are used to better observe the fungus species.
  - The infection can rapidly extend to adjacent tissues, to the pallet, sphenoid sinuses, orbits, the cavernous sinuses and to the brain.
  - CT and MRI findings include severe soft tissue edema of the nasal cavity mucosa, maxillary and ethmoidal sinus mucosal thickening, bone erosion, orbital invasion, facial soft tissue swelling, retroantral fat pad thickening, cavernous sinus thrombosis and even occlusion of the internal carotid artery [5].
  - MRI is more sensitive for detecting AIFRS and to show cavernous sinus thrombosis and brain invasion. It also provides better distinction between brain abscess and infarcts, and a more precise study of posterior fossa. In our case, MRI revealed the frontal abscess that was not visible in the CT-scan.
  - The treatment is an antifungal therapy with intravenous Amphotericin B (or Posaonazole or isavuconazole if patients don't respond to Amphotericin B). It also requires an aggressive surgical debridement of all involved tissues. A glycemic control and electrolyte repletion should be aggressively addressed.
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## Conclusion

- In summary, we reported a case of an acute rhino-orbital-cerebral mucormycosis infection post covid-19 infection in a 59 years old woman with an unbalanced diabetes mellitus.
- These two infections require difficult care management not only because they share independent high-risk mortality but also have conflicting treatment needs.

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