Headache and Hemiparesis in Immunosuppression

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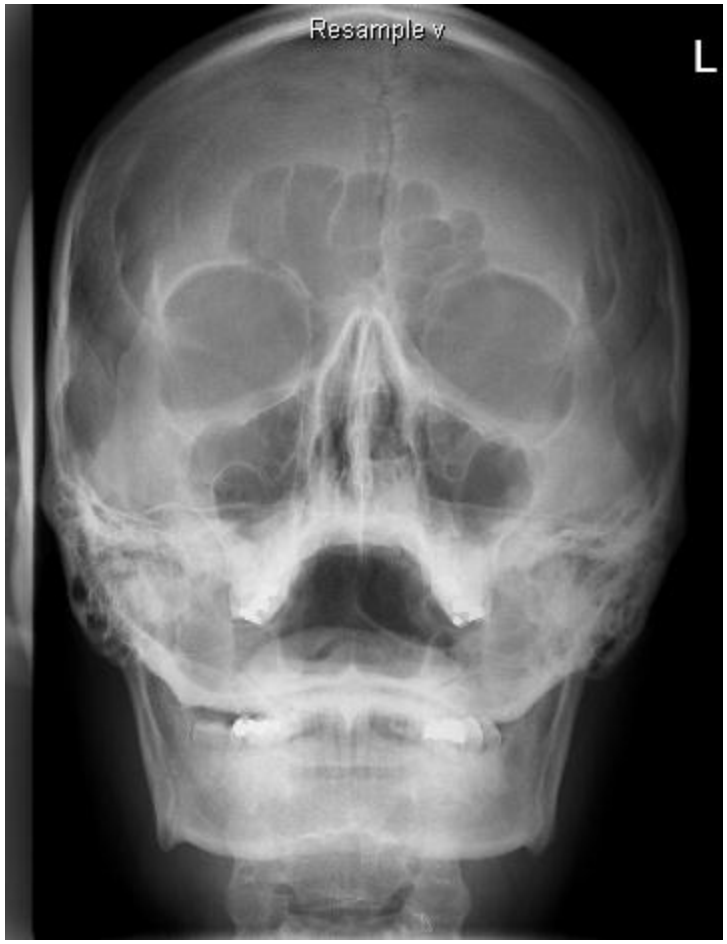
Contents

Case history

- 39-year-old man with Chronic Myeloid Leukaemia
- Underwent allogeneic bone marrow transplantation
- Developed graft-versus-host disease on immunosuppression

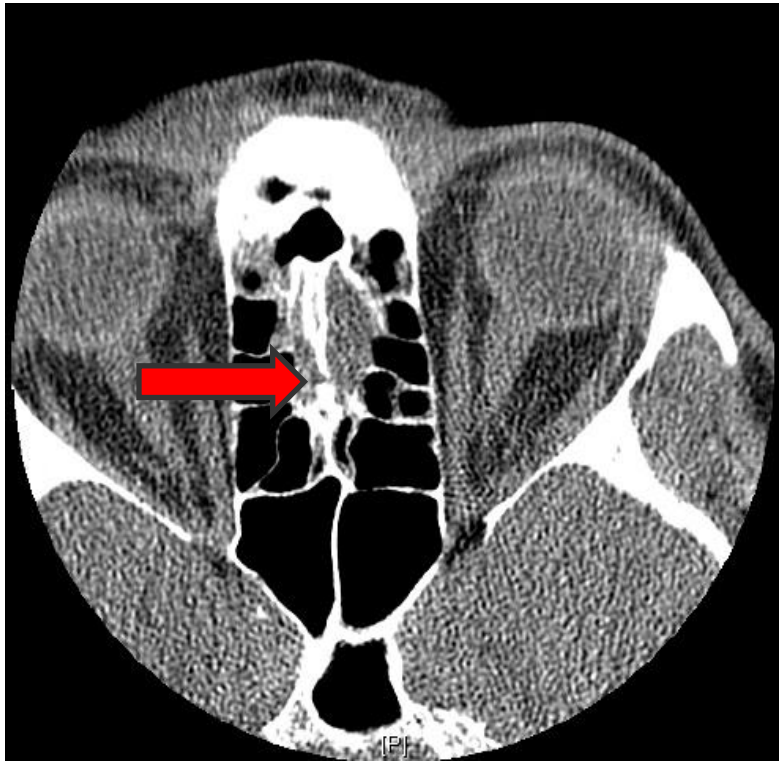
- On Day 89 post-transplant, he complained of fever and sinusitis

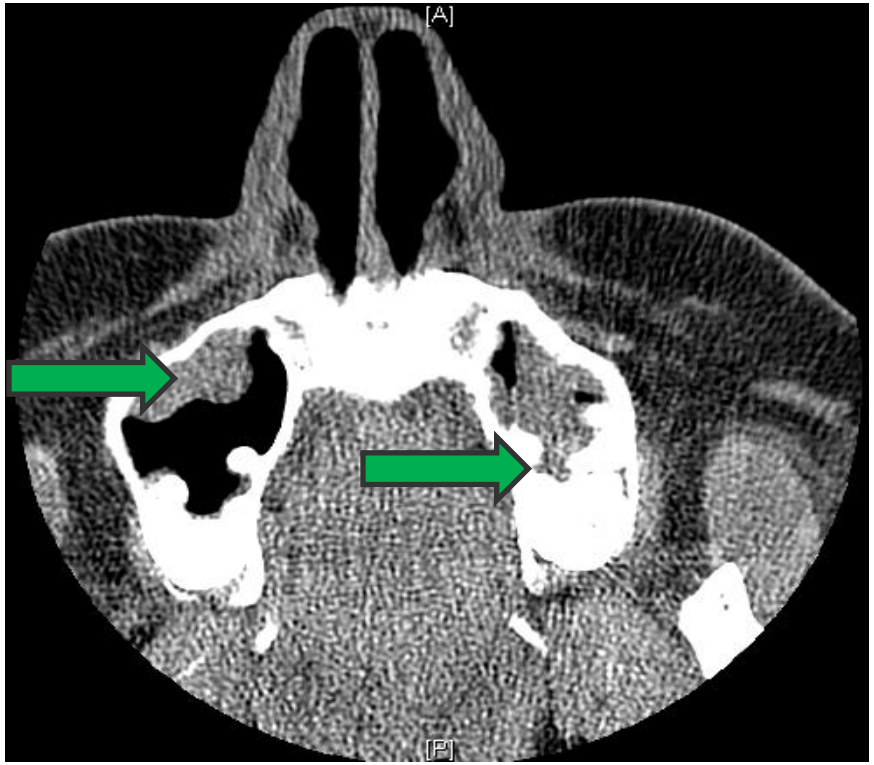
Radiology



- Due to his high risk for infections, imaging studies for his sinuses were performed

Radiology





- **CT Sinuses**: “Minor mucosal thickening in the left frontal and ethmoidal (**red arrow**) air cells. Mild to moderate mucosal thickening in both maxillary sinuses (**green arrows**), particularly inferiorly. No bony destruction.”

Case history

- His sinusitis was managed conservatively
- Four months later he developed acute left eye pain and headaches; he then presented with a dense right hemiparesis and neurological deterioration

- **CT Brain**: “Acute parenchymal bleed in left lentiform nucleus and evidence of sinusitis.”

- **MRI Brain**: “A discrete 22mm left basal ganglia lesion with extensive mass effect and associated surrounding oedema; this may represent a mycotic embolus and have an ischaemic component associated with it.”

Case history

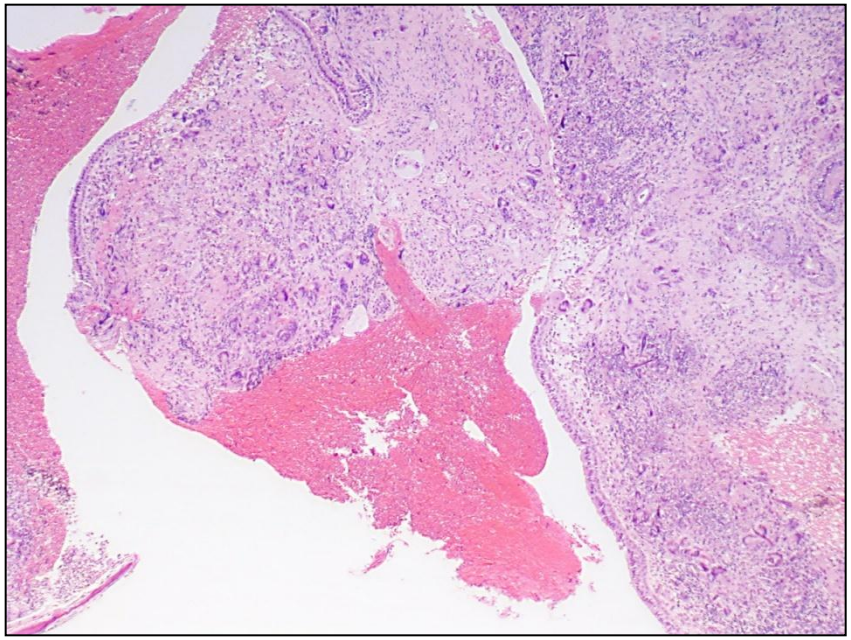
- Appearances suggestive of an invasive process, likely to be infective and related to a process within the sinuses... particularly in the context of immunosuppression

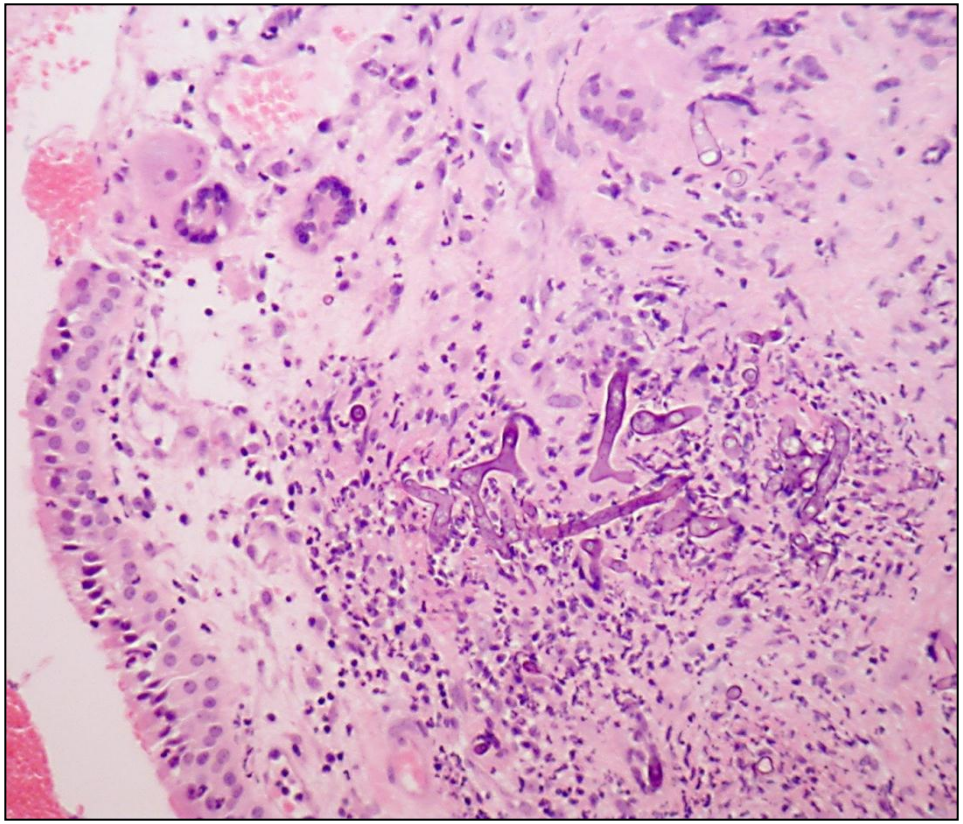
- **CT Sinuses**: “Erosion of the cribriform plate, particularly on the left side, and loss of integrity of the left lamina papyracea. The left ethmoid sinus remains completely opacified. **Appearances support the suspected diagnosis of invasive infection with associated osteomyelitis.** While this could represent lymphoma, it is essential to exclude an invasive infection, in particular fungal. **Examination of material from the sinuses is strongly advised**.”

Macroscopic description

- Two specimen pots received:
  - 11 pieces of mucosal tissue from the right ethmoid, measuring 1.5 x 0.8 x 0.3cm in aggregate
  - 5 pieces of mucosal tissue from the left ethmoid, measuring 1 x 0.8 x 0.3cm in aggregate

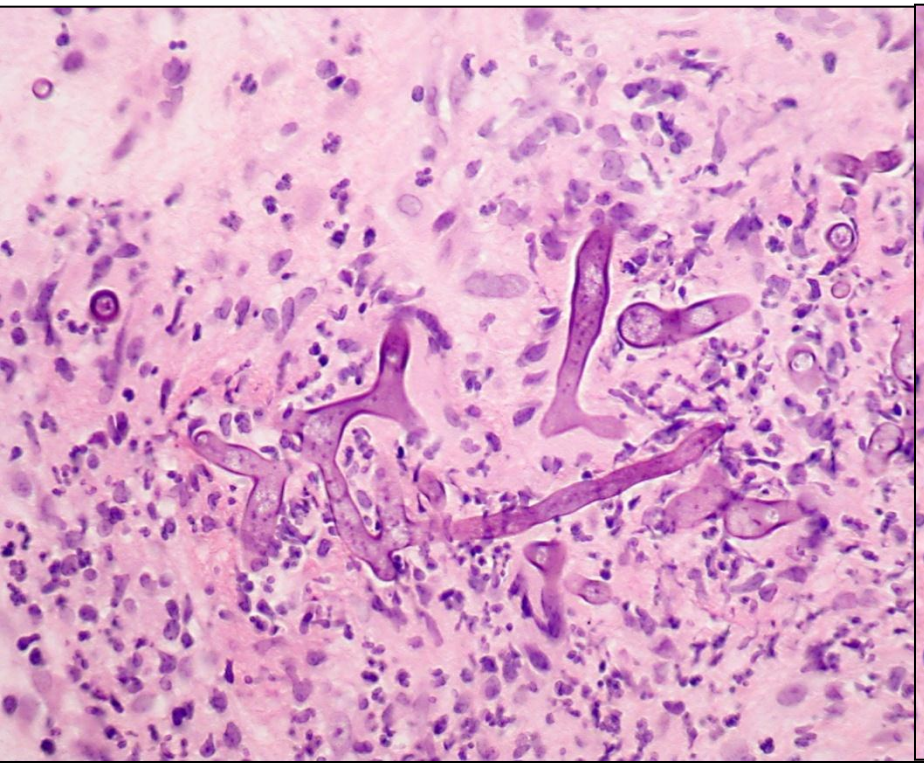
Microscopic images: H&E on low power

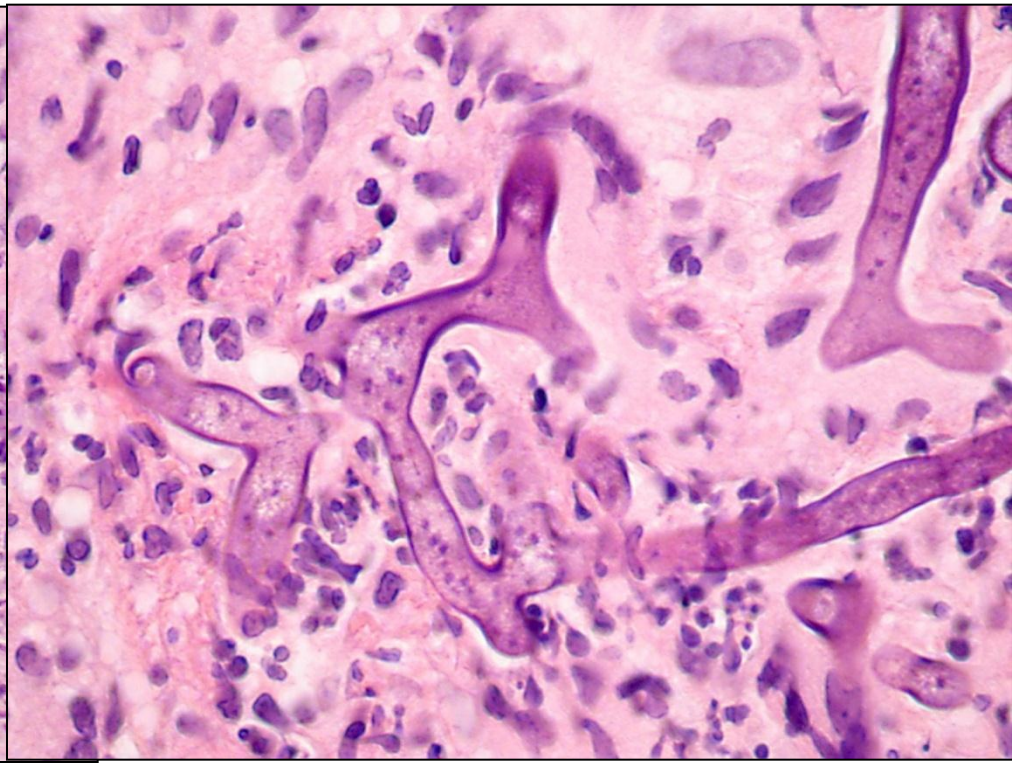




- Both specimens showed inflamed respiratory mucosa. Tissue from the left ethmoid showed a florid granulomatous response to fungal hyphae and spores.

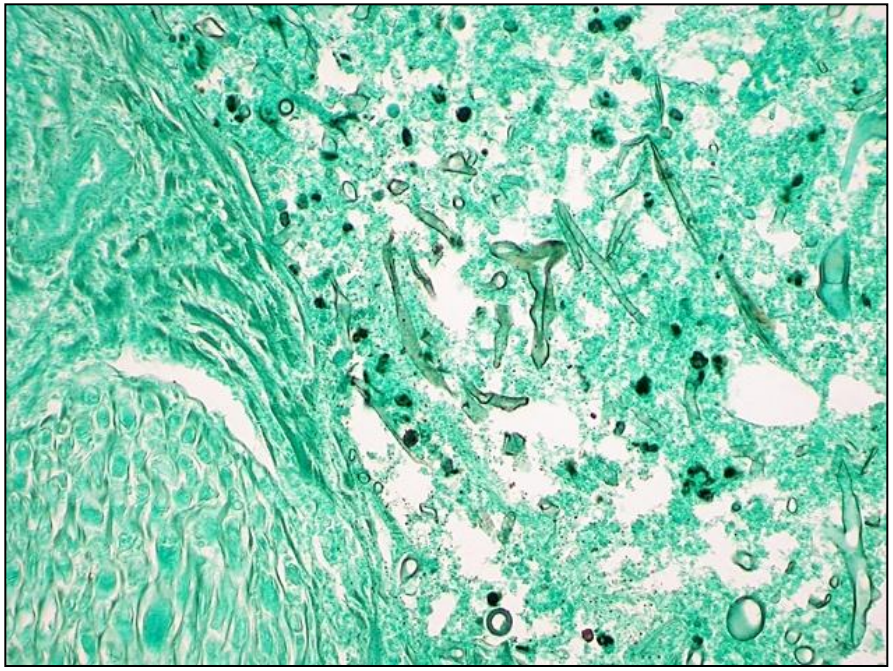
Microscopic images: H&E on high power

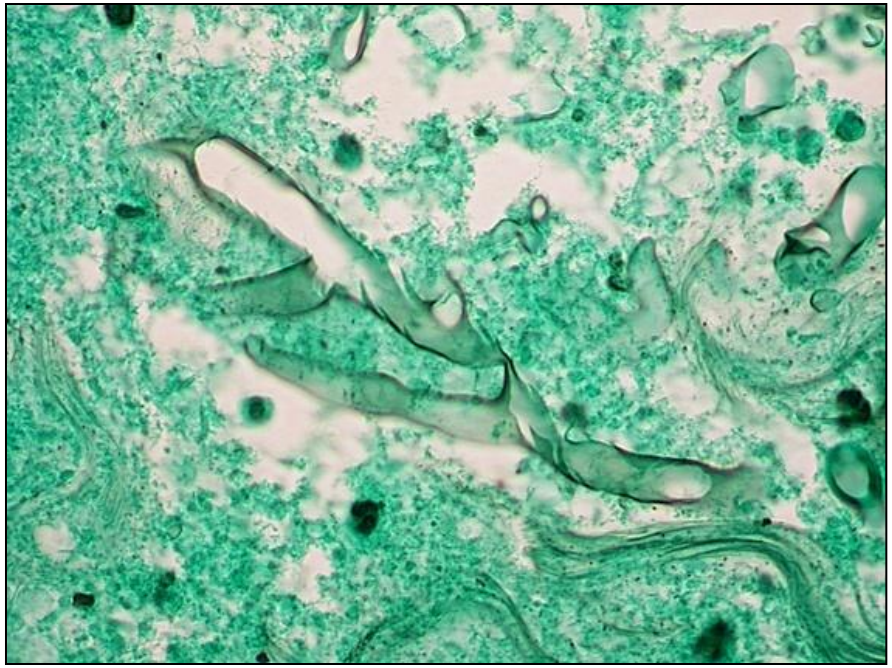




- Morphology: 90-degree angle branching without septation, angulated and elongated hyphae that are wide, irregular and thick-walled, consistent with **MUCORMYCOSIS**

Microscopic images:
Grocott's Methenamine Silver stain





- Microbiology confirmed the infective agent as ***Rhizopus Sp*** from the fungal order Mucorales

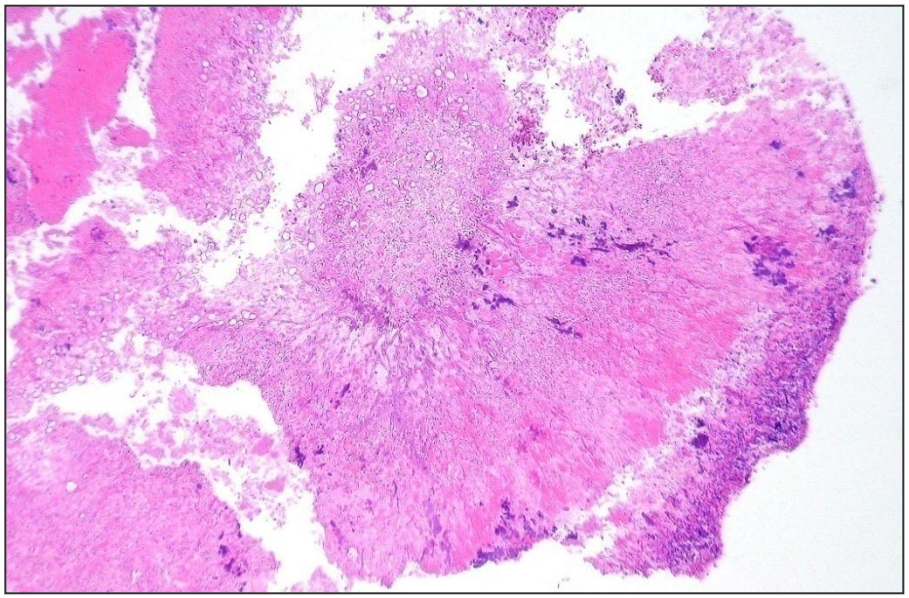
DIAGNOSIS: RHINOCEREBRAL MUCORMYCOSIS

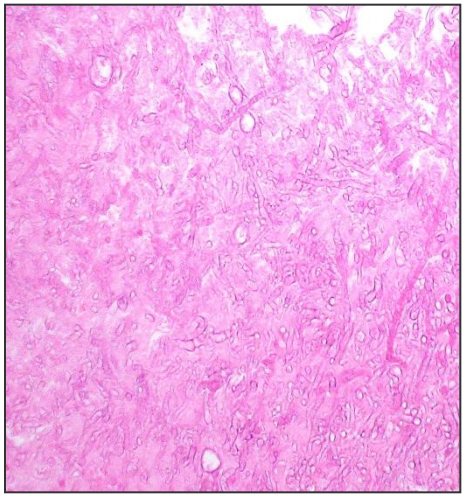
Case history continued

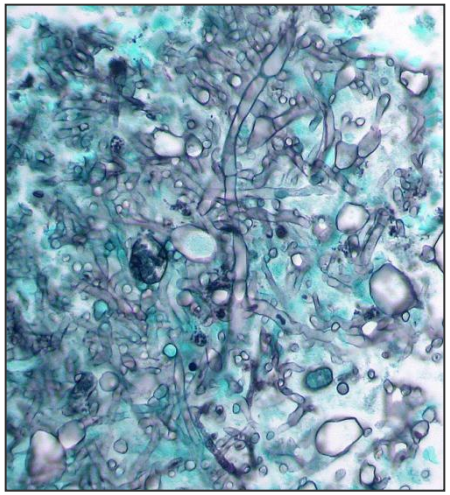
- The patient's GCS continued to deteriorate.
- **MRI Brain**: "Cerebritis in the inferior frontal lobes secondary to direct spread from the paranasal sinuses resulting in a left orbital periosteal abscess. There remains associated mass-effect, midline shift and effacement of the left frontal horn and third ventricle, and extensive sinus disease."
- The patient unfortunately died soon after.

Discussion: Fungal infection in nasal sinuses

- *Aspergillus* species is the most common organism implicated in fungal infection of the sinuses







- Typical Aspergillus ‘fungus ball’ composed of 45-degree branching **septate** hyphae which can be difficult to appreciate on H&E; need Grocott’s Methenamine Silver stain

Discussion: Fungal infection in nasal sinuses

- Fungal infections are broadly classified as ‘non-invasive’ or ‘angioinvasive’

- **Non-invasive disease** is seen in allergic fungal sinusitis or fungus ball (mycetoma)
  - Allergic fungal sinusitis: associated with asthma/atopy; abundant eosinophilic hypocecullar mucin, Charcot-Leyden crystals
  - Mycetoma: features of chronic sinusitis without allergic symptoms

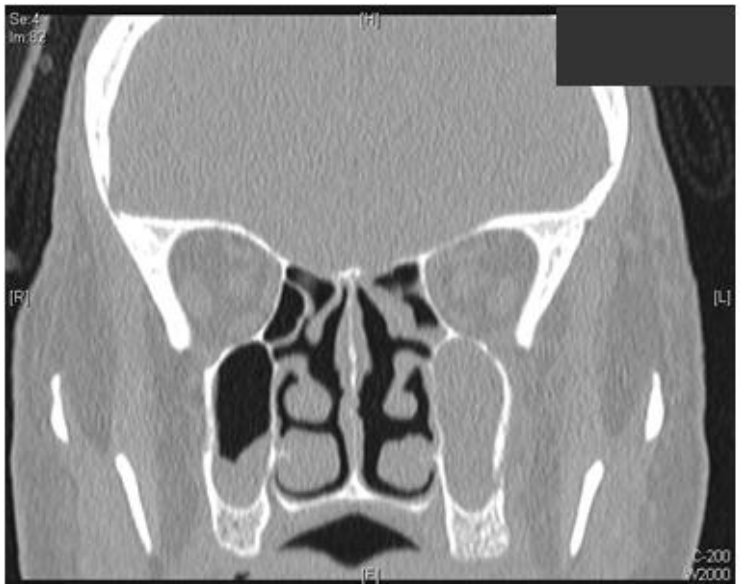
- **Angioinvasive disease, either acute or chronic**
  - In the chronic form, there is slow progression of symptoms and gradual mass effect; becomes fatal when extends into retro-orbital region, cranial vault or parapharyngeal space

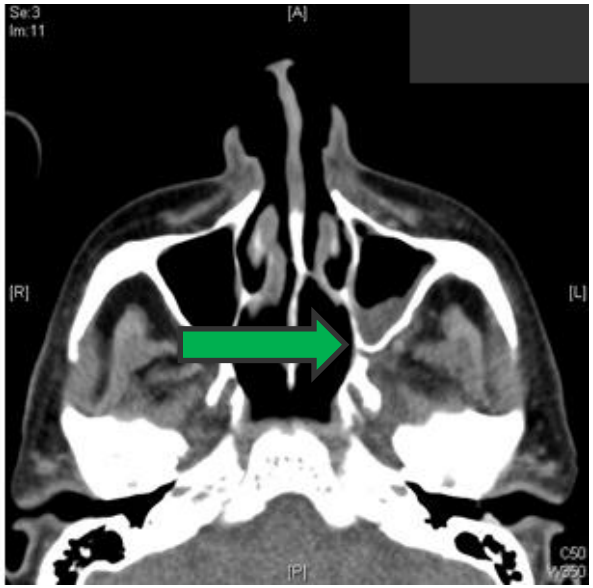
Acute invasive fungal disease: Rhinocerebral Mucormycosis

- Mucorales order (*Mucor, Rhizopus, Absidia*) is a common cause of **acute invasive fungal disease**
- Usually opportunistic infection in immunocompromised (diabetes mellitus, **following transplantation**, rarely HIV)
- In the immunocompetent (~20%), risk factors include penetrating trauma, surgery or burns
- Complications: cavernous sinus thrombosis, necrosis, occlusion and pseudo-aneurysm of internal carotid artery
- Address the underlying cause, initiate antifungal therapy and prompt surgical debridement of affected tissues
- In advanced cases, complete clearance may only be achieved by extensive surgery (e.g. orbital exenteration)

Example Case: Surgical Management of Rhinocerebral Mucormycosis

- 63-year-old gentleman with recent resection of a parasagittal meningioma developed left cranial nerve palsies of nerves V, VI and VII; and became blind in the right eye





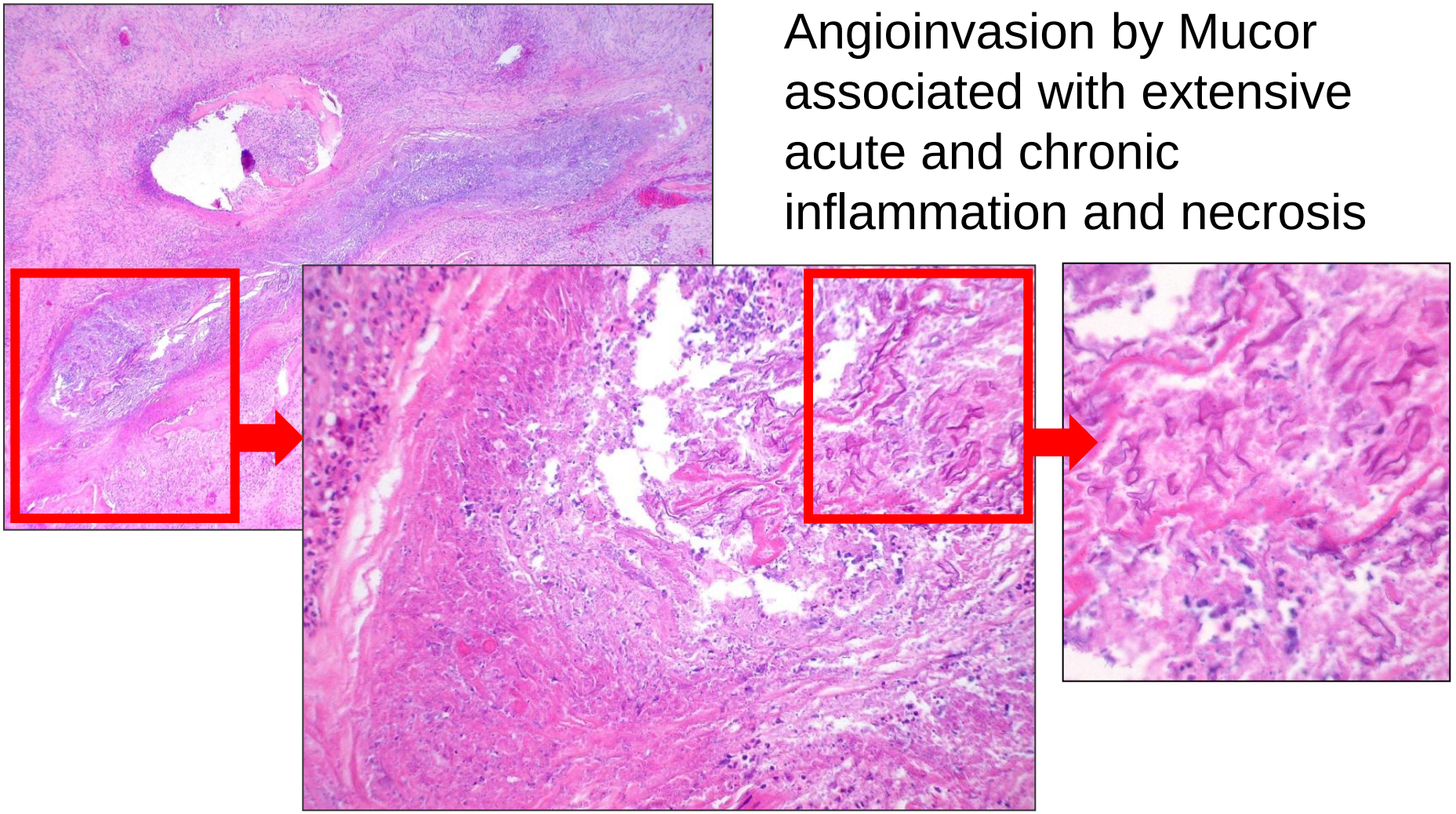
- **CT Sinuses**: Subtotal opacification of the ethmoid air cells and moderate to severe polypoid mucosal thickening in the floor of maxillary sinuses (**green arrow**)

Example Case: Surgical Management of Rhinocerebral Mucormycosis

- Biopsies from the left maxilla: “Oedematous respiratory mucosa with focal areas of necrosis particularly around and within the vessels. Admixed with the necrosis were Grocott positive fungal hyphae which resemble Mucor.”

- The patient underwent left orbital extenteration, lateral rhinotomy and clearance of infra-temporal fossa:
  - Invasive fungal sinusitis was present in the surrounding soft tissues, skull base and left ethmoid bone
  - The left optic nerve was not involved

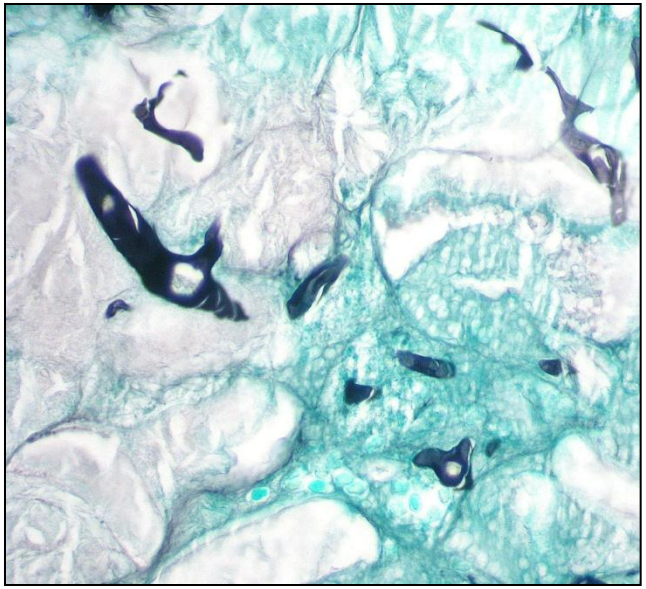
Example Case: Surgical Management of Rhinocerebral Mucormycosis

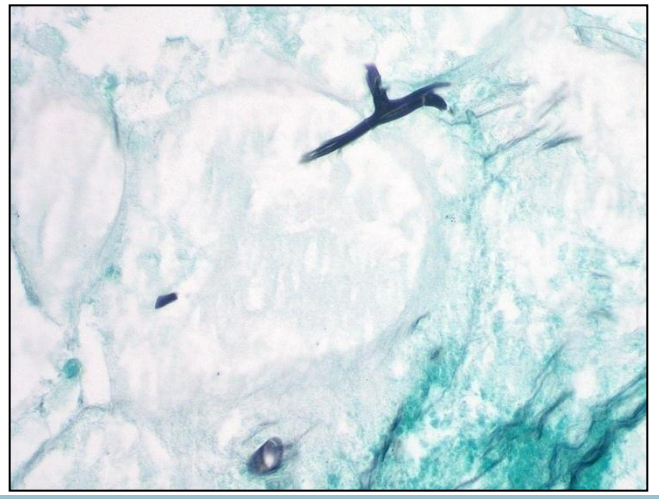


Angioinvasion by Mucor associated with extensive acute and chronic inflammation and necrosis

Example: Surgical Management of Rhinocerebral Mucormycosis

Skull base: Necrotic bone with Mucor present in the marrow spaces (as seen on H&E and Grocott)





Take home messages

- Angioinvasive fungal disease is an **acute emergency**
- Clinically suspected cases must be prioritised
- Clinicians should be informed without delay
- Microbiology confirmation is necessary for accurate subtyping of the organism
- In advanced cases, complete clearance may only be achieved by extensive surgery

Further reading

- Wright HN, JS Lewis Jr. Chapter 3: Nasal cavity, paranasal sinuses and nasopharynx. In: *The Washington Manual of Surgical Pathology, Second Edition*. Washington: Lippincott, Williams and Wilkins; 2012.

- Mills SE. Chapter 21: The nose, paranasal sinuses and nasopharynx. In: *Sternberg's Diagnostic Surgical Pathology, Fifth Edition*. Philadelphia: Lippincott, Williams and Wilkins; 2010.

- Kumar P, Malhotra S, Sharma S, et al. Rhinocerebral mucormycosis: a rare fungal infection linked to diabetes. *OA Case Reports*. 2013: Oct 21;2(12): 119. Available at <http://www.oapublishinglondon.com/article/930> [Accessed: 10 June 2014]

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