Headache and Hemiparesis in Immunosuppression

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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
Due to his high risk for infections, imaging studies for his sinuses were performed.
**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
Both specimens showed inflamed respiratory mucosa. Tissue from the left ethmoid showed a florid granulomatous response to fungal hyphae and spores.
Mucormycosis

- 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


Feedback and microscopic images courtesy of

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