Educational *Programme on Transplant Infectious Diseases*

25 - 26 April 2014 - São Paulo, Brazil

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

Clinical Case

Infection in a heart transplantation patient

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European Society of Clinical Microbiology and Infectious Diseases

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Clinical case

- A 53-year-old man
- Heart transplantation
  - February 2007
- Immunosuppression
  - mycophenolate, cyclosporine, and methylprednisolone.
- Prophylaxis
  - acyclovir and trimethoprim/sulfamethoxazole, according to local protocol.

Clinical case:
Heart Tx 1st week

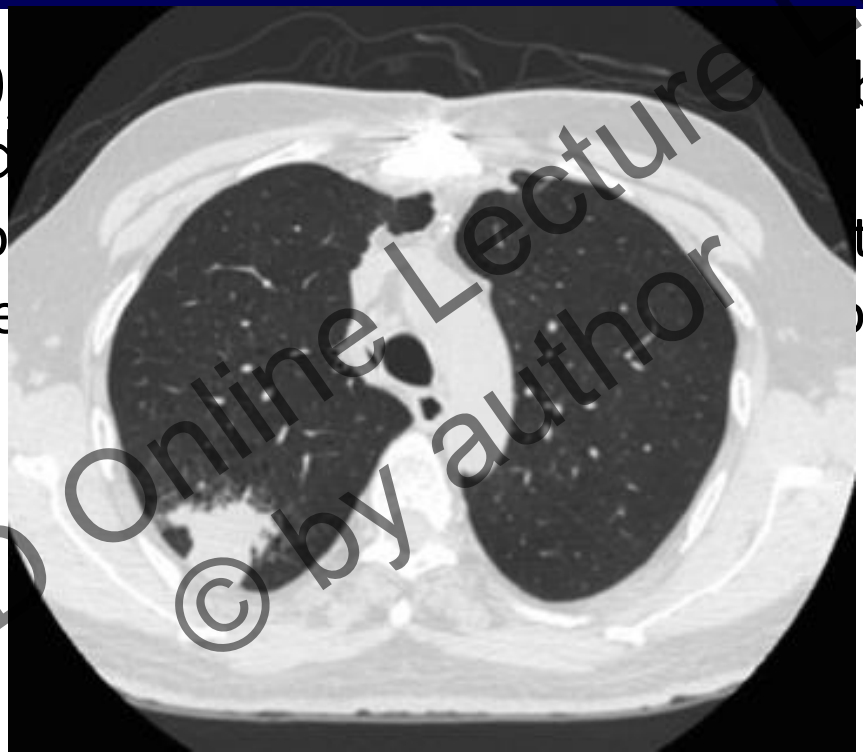
- At day +7, endomyocardial biopsy demonstrated acute rejection type III-R.
  - A total dose of 2.25 g intravenous methylprednisolone was administered with rejection resolution.
- Weekly inhaled liposomal amphotericin B (LAmB) was added for antifungal prophylaxis.
- Patient was discharged without symptoms on day +17.

Clinical case:
Heart Tx 3rd week

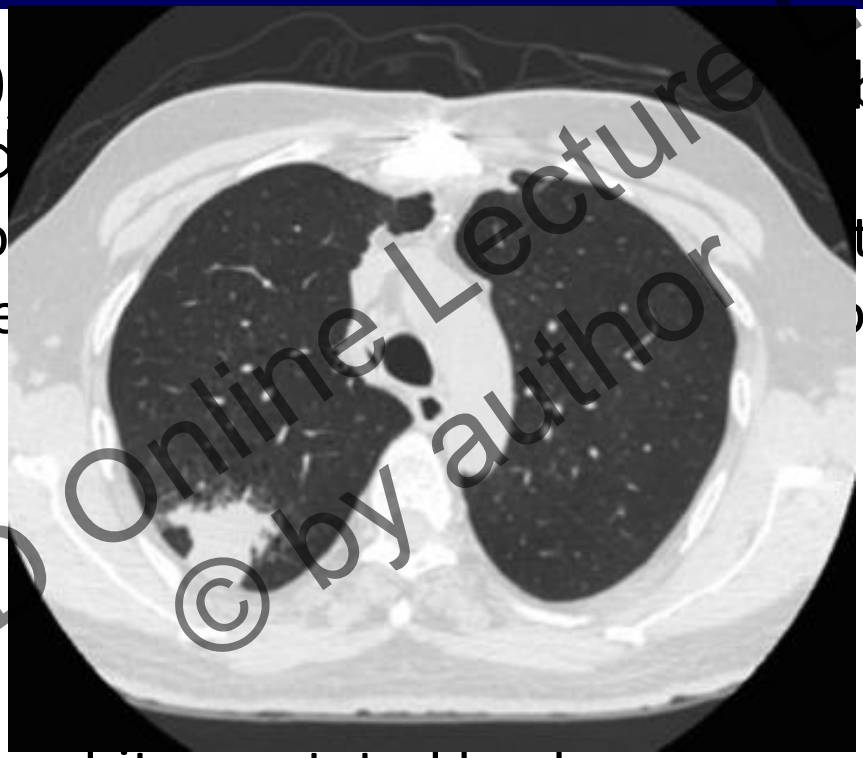
- On day +20, the patient was readmitted because of persistent dry cough.
  - He did not have fever or shortness of breath.
  - C-reactive protein and WBC were normal.

Clinical case:
Heart Tx 3rd week

- On day +20 … because of persistent d…
  - He did no… th.
  - C-reactive … rmal.



Clinical case:
Heart Tx 3rd week



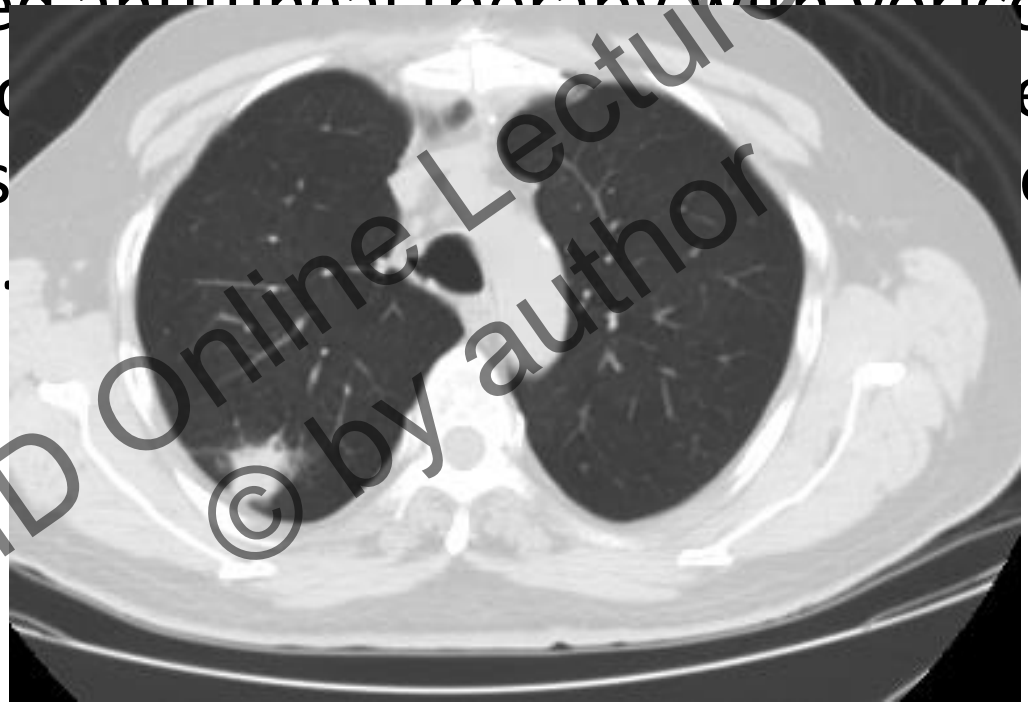
- On day +20 [illegible] because of persistent c[illegible]
  - He did no[illegible]th.
  - C-reactive[illegible]rmal.
- BAL
  - Calcofluor white: septated hyphae.
  - galactomannan antigen was positive. (Also in plasma)
  - Fungal culture: *Aspergillus fumigatus*.

Clinical case:
Heart Tx 3rd week

- Associated antifungal therapy with voriconazole and caspofungin was immediately initiated. His immunosuppressive drug regimen was not modified.

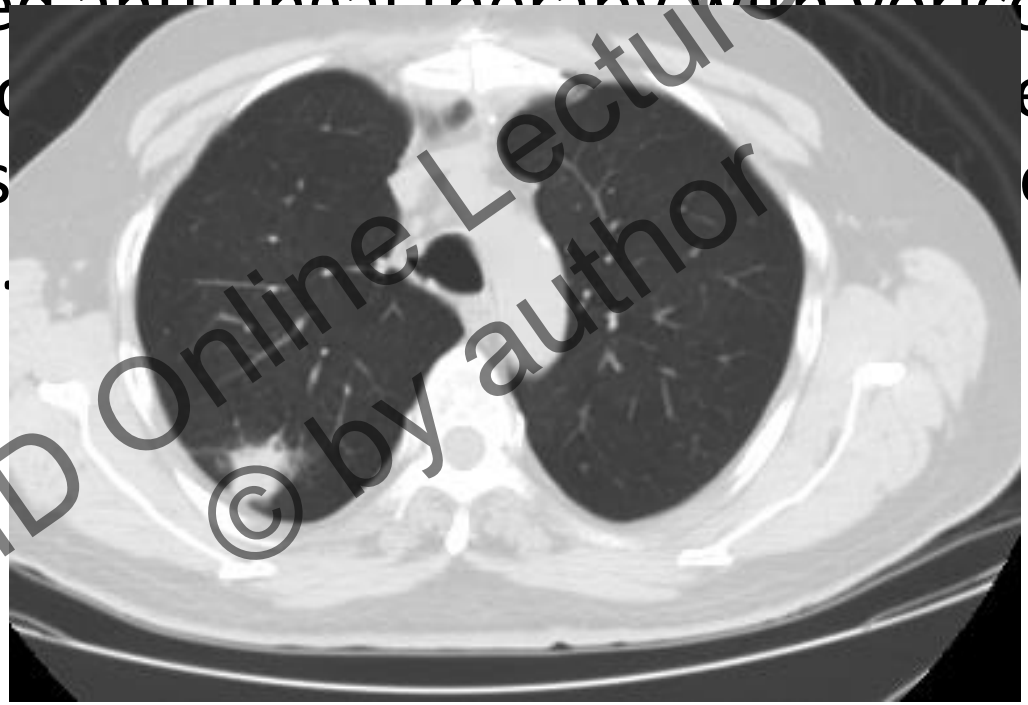
Clinical case:
Heart Tx 5th week

- Associated antifungal therapy with voriconazole and caspo ed. His immunos ot modified.



Clinical case:
Heart Tx 5th to 6th week

- Associated antifungal therapy with voriconazole and caspo ed. His immunos ot modified.



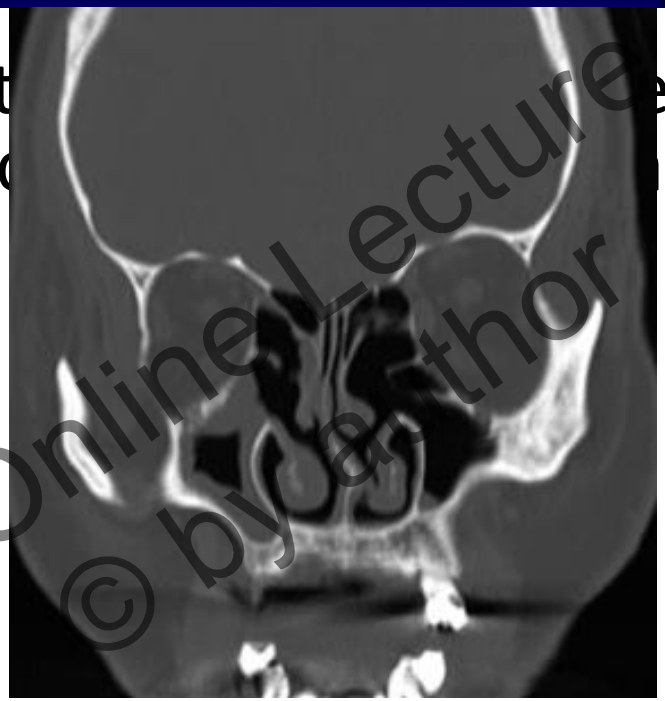
- Patient was switched to oral voriconazole 200 mg/day twice daily and caspofungin was stopped.

Clinical case:
Heart Tx 8th week

- Two weeks later, the patient presented with frontal headache and posterior nasal discharge.

Clinical case:
Heart Tx 8th week

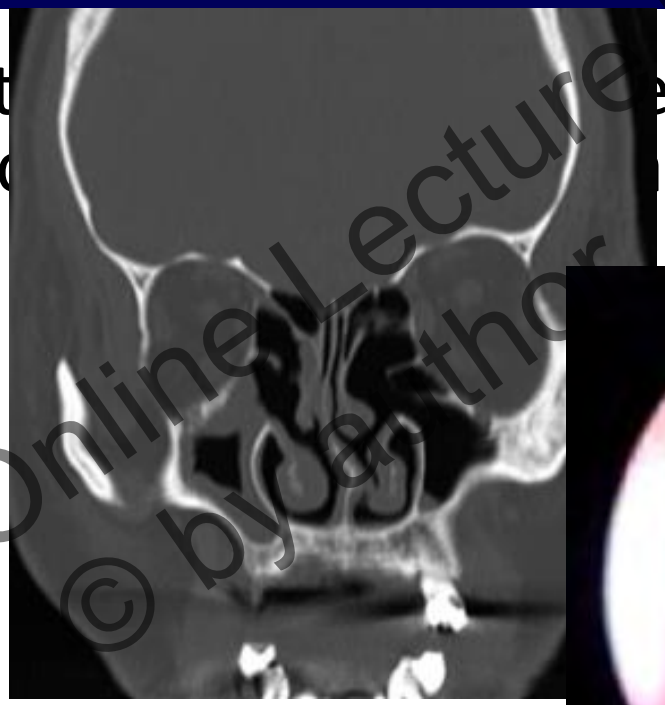
- Two weeks lat ented with frontal headac sal discharge.

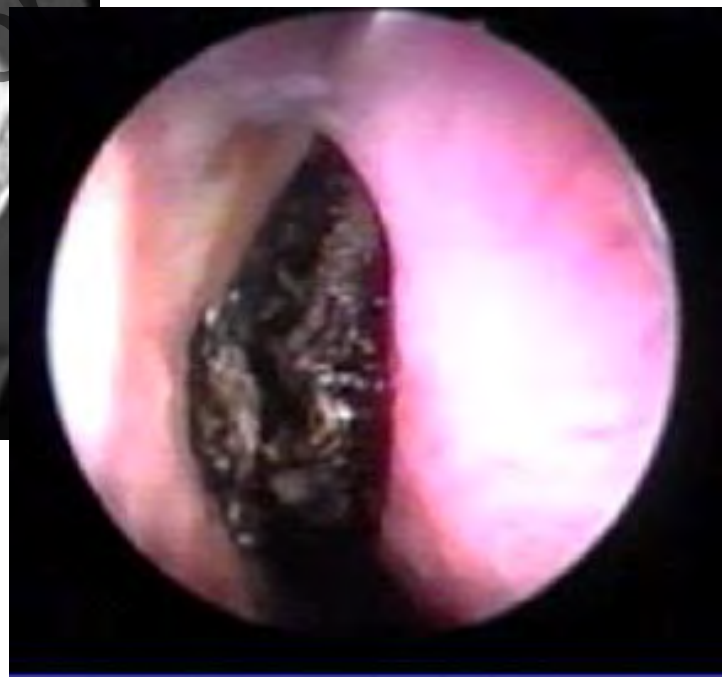


Clinical case:
Heart Tx 8th week

- Two weeks lat ented with frontal headac sal discharge.

- Nasal endoscopy:
  - extensive necrosis of mucosa

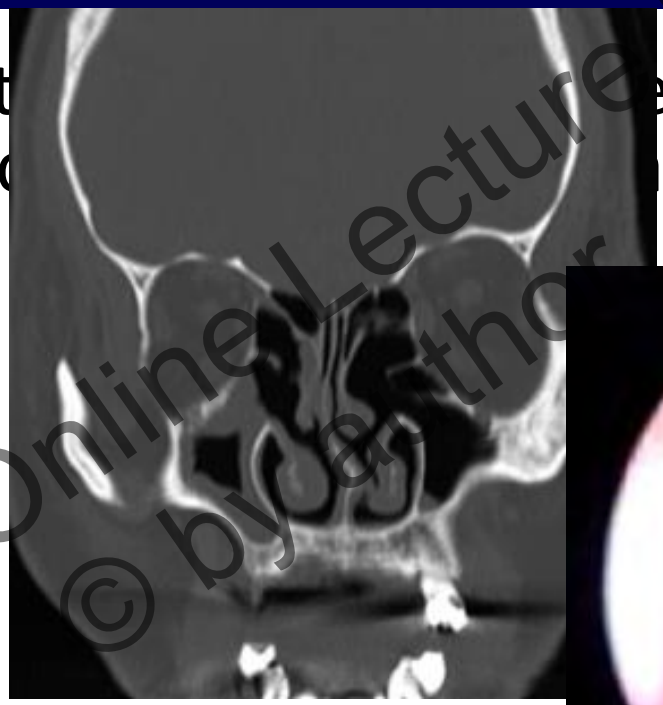


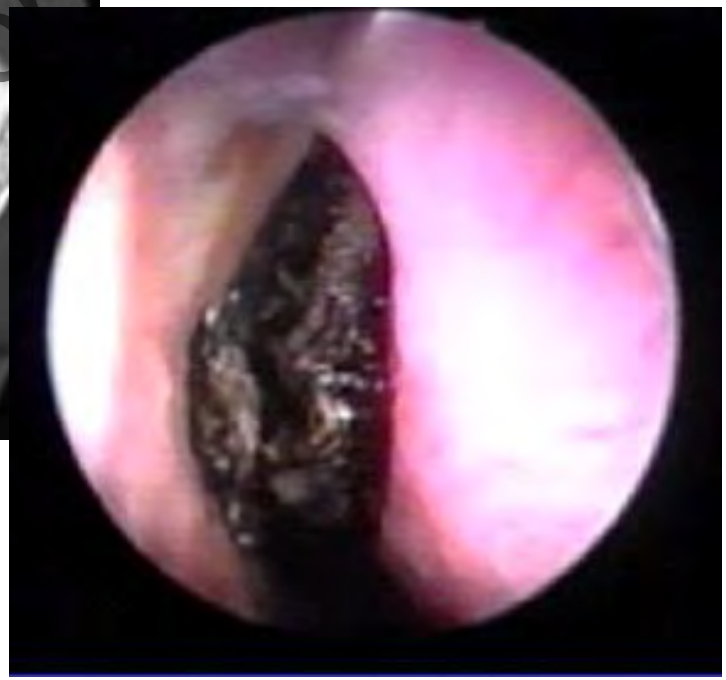


- What is your diagnosis?

Clinical case:
Heart Tx 8th week

- Two weeks lat ented with frontal headac sal discharge.





- Nasal endoscopy:
  - extensive necrosis of mucosa
    - Calcofluor stain: nonseptated hyphae
    - Nasal mucosa biopsy:
    - mucosal and vascular hyphae invasion
    - fungal culture: *Rhizopus spp*.

Clinical case:
Heart Tx 9th to 11th week

- L-AmB 5 mg/k/day was started
  - voriconazole was suspended.
  - Surgical debridement
- Two weeks later:
  - In the 3rd surgical debridement procedures:
    - nasal mucosa remained positive for nonseptated hyphae.
- L-AmB was increased to 7.5 mg/k/day for 2 more weeks.
  - Progressive renal impairment (creatinine 2.66 mg/dL)
- Again new samples demonstrated persistence of fungi infection.

- Therapy options?

Clinical case:
Heart Tx 9th to 11th week

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  - Progressive renal impairment (creatinine 2.66 mg/dL)
- Again new samples demonstrated persistence of fungi infection.
  - Posaconazole 200 mg 4 times a day was added.
  - Cyclosporine was replaced with everolimus.

Clinical case:
Heart Tx 12 to 23 week

- After 2 weeks, the patient showed significant improvement.
  - No new necrotic zones were seen by nasal endoscopy
  - Calcofluor stain and fungal culture of sinus samples were negative.
- At this time, LAmB was suspended and posaconazole was continued for 80 total days.
- The patient was discharged 23 weeks after transplantation in good condition.
- He has continued routine post-transplant care in our clinic without evidence of recurrent fungal disease for 7 years.

Final Diagnosis

- Probable Invasive Pulmonary Aspergilllosis
- Proven ethmoidal and maxilary sinus Zygomycosis
- Heart transplantation

Conclusions

- The management of opportunistic fungal infections in heart transplantation patients remains challenging.
  - Aspergillosis is the most frequent.
  - Zygomycosis is a relatively rare disease
  - Prophylaxis? Who, What & When?
- In general, the prognosis of both fungal diseases is poor.
  - The role of early diagnostic and therapy including several surgical debridement
- The evidence of benefit of antifungal association in solid organ tx is limited to cases series
  - ❑ Voriconazole plus caspo/anidula
  - ❑ Liposomal amphotericine-B plus posaconazole

Many Thanks!