

Imported Mycological Infections



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31-y Thai woman

- Admitted due to fever and weight loss
 - Worked on a farm in Thailand
 - Vacation in DK for 2 months
- 4-months: pulmonary TB
 - by sputum test in Thailand
 - 900 mg rifampicin, 800 mg ethambutol, 200 mg isoniazid & 1 g pyrazinamid daily
- In Denmark
 - ↑ nausea and diarrhoea 6-8 times daily
 - burning sensation top of the epigastrium
 - 11 kg weight loss over the previous 3 -6 months (weight 36.5 kg, height 150 cm).

| Vægt | 30-40 kg |
|-------------|----------|
| Isoniazid | 300 mg |
| Rifampicin | 450 mg |
| Ethambutol | 600 mg |
| Pyrazinamid | 1000 mg |

DK TB recommendations 2010

At admission

■ Clinical examination

- Fever (38.6 °C), dyspnoea, dehydration and raised white lesions in the pharynx.
- There was no lymphadenopathy, hepato- or splenomegaly, or cutaneous manifestations

■ Abnormal Paraclinical findings (normal ranges)

| | | |
|-------------|-------------|--------------------|
| - Potassium | 3.2 mmol/l | (3.5-5.0 mmol/l) |
| - Sodium | 128 mmol/l | (136-146 mmol/l) |
| - LDH | 1133 U/l | (150-450 U/l) |
| - Uric acid | 0.58 mmol/l | (0.15-0.35 mmol/l) |
| - CRP | 31 mg/l | (5-10 mg/l) |

???

■ Tentative diagnoses???

■ Examinations???

1st week on hospital

- X-ray: Normal

- Lab analyses
 - HIV test (Denied HIV positivity)
 - Sputum for microscopy & culture, TB and PCP
 - Blood culture

- On day 8
 - Yeast cells in BC

???

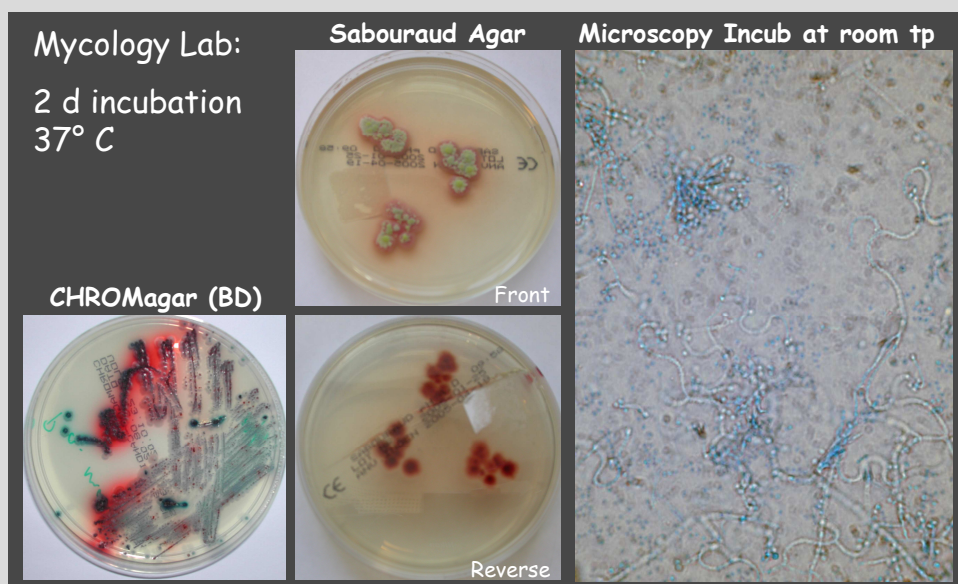
- Diagnosis???

- Treatment suggestions for the yeast?

2nd week on hospital

- Fluconazole 400 mg/day iv
- On day 10
 - HIV pos confirmed → anti-retroviral tx
 - CD4 cell count: $0.02 \times 10^9/l$
 - HIV-RNA: 32,900 copies/ml.

Blood culture isolate



???

- Diagnosis???
- Treatment???

P. marneffei

- Colony characteristics
 - CzA, 30°C flat, sparse, compact, greenish-purplish
 - MEA exuding orange-red pigment into the agar
 - Prim cultures often canary yellow
 - 37 °C restricted, whitish, yeast like
- Microscopy
 - hyphae in part spirally twisted
 - Conidiophores creeping/fasciculate 70-150 x 2.5-3 µm
 - biverticillate / irregularly monoverticillate or complex
 - Metulae 7-11 µm whorls of 3-5; phialides 6-10 µm whorls of 4-7
 - Conidia smooth, ellipsoidal, prominent scars

P. marneffei Susceptibility

Table 1. MIC range of *in vitro* drug susceptibility tests against *Penicillium marneffei* isolates

| Authors | Number of patients | MIC range ($\mu\text{g/ml}$) | | | |
|----------------------|--------------------|--------------------------------|------------------|---------------------|---------------------|
| | | AMB* | Fluconazole | Itraconazole | Ketoconazole |
| Jayanetra (1984) | 3 | 0.78–3.12 | N/A | N/A | N/A |
| So (1985) | 1 | N/A | N/A | N/A | 1.0 |
| Sekhon (1992) | 10 | <0.195–1.56 | 0.195–100 | <0.195 | 0.195–0.39 |
| Sekhon (1993) | N/A** | 3.125–25.0 | 6.25–25.0 | 25.0–100 | N/A |
| Supparatpinyo (1993) | 30 | 0.25–4.0 | ≤ 0.313 –20 | ≤ 0.002 –0.078 | ≤ 0.002 –0.078 |
| This study (1998) | 30 | 0.125–0.5 | 4.0–8.0 | <0.032 | <0.125 |

P. marneffei Treatment and outcome

■ Treatment

- → Ambisome 2 mg/kg/d for 2 weeks
- developed anaemia (hbg 4 mmol/l) → blood transfusions
- → Itraconazole 200 mg x2 daily for 10 weeks

■ Outcome

- apyretic on d 28 → discharged
- gained weight and was in a better general condition.

■ Abnormal Paraclinical findings at discharge

- Amylase 175 U/l (28 -100 U/l),
- Alkaline phosphatase 338 U/l (80-275 U/l),
- ASAT 75 U/l (<35 U/l)

P. marneffei: epidemiologi

- Southern China
- Burma (Myanmar)
- Laos
- Thailand
- Cambodia
- Vietnam
- Malaysia
- Indonesia



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Penicilium marneffei infections

- Typically in immunodeficient people
 - 29 cases reported 1958-1988
 - 1995: 1300 cases/year in Thailand
- Chronic progressive course
 - ✓ Fever (95%)
 - ✓ Weight loss (81%)
 - ✓ Anaemia (86%)
 - ✓ Cough (52%)
 - Lymphadenopathy (50%)
 - Skin manifestations (76%)



Supparatpinyo Lancet 1994

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Invasive fungal infections & skin

■ Endemic fungi

■ Yeast and moulds:

- *Trichosporon* (>50%)
- *Fusarium* (60-80%)
- *Candida*
- *Cryptococcus*
- *S. prolificans*
- ...

Trichosporon



Cryptococcus



Candida



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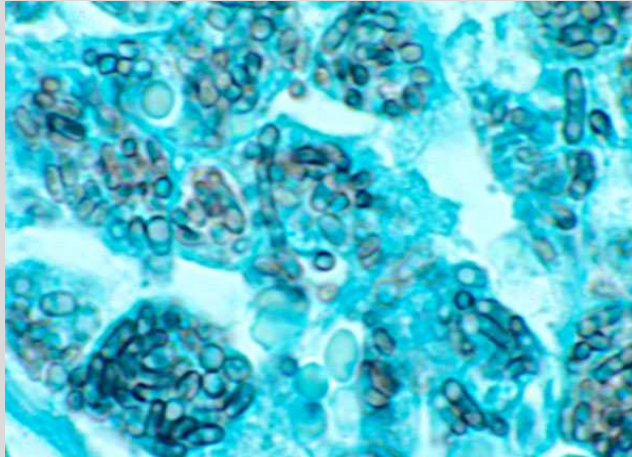
Diagnostics *P. marneffe*

■ Culture

- *P. marneffe* >50% pos BD
- BAL / biopsy / CSF
- Temp dependent growth:
 - room tp mould × yeast at 37 °C

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Microscopy



P. marneffeii
Spleen, Silver stain.

P. marneffeii
at 35°



Malt

P. brevicompactum
at room tp



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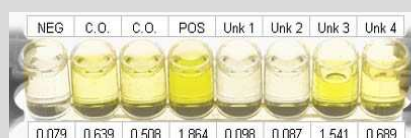
Diagnostics *P. marneffeii*

■ Culture

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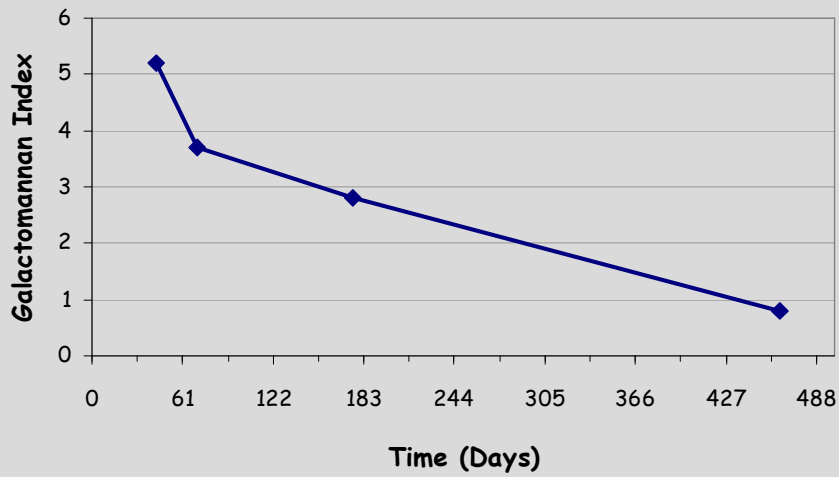
■ Serology

- Antigen: *P. marneffeii* (*Aspergillus galactomannan*)



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Galactomannan Ag for *P. marneffei*



Mens SJID 2004

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Thank you for your attention