**Imaging Findings in Neutropenic vs. Non-Neutropenic Patients**

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**Paranasal Sinuses Screening**

- **CT-sinus**
  - n=80, pre-SCT: therapy pre-SCT
  - 15 conservative, 2 OP
  - n=24: no treatment
  - n=39: normal

- **MR-brain**
  - n=116, 1-21J, pre-SCT
  - n=5: surgery / intervention: 1x aspergilloma, 4x cavernoma
  - n=42: sinusitis

**Brain Screening**

- **Aspergillus niger**
  - bone erosion
  - brain invasion
  - T1-Gd

**Need for Early Detection?**

- delay ↑ ⇒ mortality ↑

Morrell et al., Antimicrob Agents Chemother. 2005
**Response after Infection**

- PEG-II, overall response at EOT, n=707

**Affected Organs**
- lungs (30%)
- para nasal sinuses
- gastrointestinal tract
- liver, spleen
- central nervous system (Tx)
- kidneys (BK)

**Chest X-ray Supine**

- BMT & FUO (n=40)
  - sensitivity: 1. Tag: 46%
  - follow-up: 81%
  - neg. prediction: 73%
- Intensive Care (n=20)
  - sensitivity: 25%

**Early Detection**

Prospective Trial (n=230)
- fever (>38.3°C)
- neutropenia (ANG < 0.5/µl) >48h
- empiric antibiotic treatment

- normal CXR → HRCT same day

**Course after HRCT**

- HRCT: infiltrate (60%)
- HRCT: normal (40%)

**Early Detection**

- AIDS, Fever:
  - Day 8
  - Day 3
- AML, Fever:
  - Day 3
  - p < 10⁻⁷, nges = 188

**Febrile Unexplained Fever (FUO)**

- micro.Dx infiltrate other

**Exclusion of pneumonia?**

- normal chest x-ray

- normal

- supine position useful
- useless for pneumonia
Time until defervescence (n=217)

- Neutropenic patients:
  - BM/T PET: 77 days
  - HRCT: 70 days
  - Neutropenia: 21 days
  - HRCT: 29 days

Early Detection

- Neutropenia & FUO: n=230
- Sensitivity: 87%
- Neg. prediction: 88%
- Time gain: ~5-7 days

Exclusion of Pneumonia?
- Normal CXR: no
- Normal HRCT: ~3-5 days

Technique

- Spiral-CT
- HRCT
  - Spiral-CT: volume data
  - HRCT: single slices

False positive

False negative
**Recommendation**

- **A** MSCT
  - slice thickness 1 mm
  - pitch 2
  - increment 1 mm

- **B** HRCT
  - slice thickness 1 mm
  - table feed 10 mm

- **C** Spiral-CT
  - slice thickness 4 mm
  - pitch 2
  - increment 4 mm

- **D** HRCT
  - slice thickness 1 mm
  - table feed 10 mm

**Radiation Exposure**

- **nature p.a.** ~1 mSv
- **CXR** 0.1 – 0.2 mSv
- **MSCT** 2 - 6 mSv
- **low-dose** 0.6 - 2 mSv
- **HRCT** 0.5 - 1 mSv
- **PET** 4 mSv
- **MRI** 0 mSv

**Dose Reduction**

- Immunocomp. pat. n=30, infiltrate n=23, 1mm SD dose simulation => spec low-dose 100% → 86%
MRI
- "hip"
- characterisation
- T1w: signal ↑ = hemorrhage
- T1w: target sign - peripheral rim - central necrosis
- T2w: reverse target sign
- early: CT
- late: CT ~ MRI
- abscess: MRI > CT (pseudo capsule)

CT vs. MRI
FUO, neutropenia, n=30
neg CXR: CT & MRI
- sensitivity 95%
- specificity 88%
- pos. predictive value 95%
- neg. predictive value 88%

Problems with
- small lesions
- cardiac motion

Differential diagnosis:
- typical bacterial pneumonia
  - positive bronchogram
  - consolidation
  - pleural effusion

After Kidney Transplantation (n=19)
- TBC n=11
- CMV n=2
- cryptococci
- streptococci
- aspergillus
- HRCT
  - correct 60%
  - non-specific 15%
  - normal 25%

Leutner et al. RöFo 1999; 170: 449-456
Blum et al. RöFo 1994; 161: 292-299
**hints for:**
- pulmonary tuberculosis
  - cavitations
  - consolidation
  - well-defined nodules
  - bronchogenic distribution

Hlawatsch et al. (2000) Radiologe

**Fungal Pneumonia**
- febrile day 8
- day 3
- day 3

1984 described
1985 discussed in 9 patients

1 Gefter et al. Radiology '84
2 Kuhlman et al. Radiology '85

**Halo-sign**
- major
  - Dense, well-circumscribed lesions
  - with or without a halo sign
  - air-crescent sign
- minor

De Pauw et al., Clin Infect Dis 2008

**EORTC Criteria Fungal Pneumonia**
- major
  - Dense, well-circumscribed lesions
  - with or without a halo sign
  - air-crescent sign
- minor

**Fungal Pneumonia halo sign**

(+ hepatolienal C.)

**Fungal Pneumonia**

hepatosplenic candidiasis

**hints for:**
- fungal pneumonia
  - early: ill-defined nodules (“halo”)
  - angiotropic distribution
  - late: cavitations
    - air-crescent sign
  - positive prognosis
  - vessel arosion / aneurysm

Gefter et al. Radiology '84
Kuhlman et al. Radiology '85
De Pauw et al., Clin Infect Dis 2008

**Value of halo-sign**

IPA, n=235

<table>
<thead>
<tr>
<th>Feature</th>
<th>Frequency</th>
<th>Response</th>
<th>3 month survival</th>
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<tbody>
<tr>
<td>makronodules</td>
<td>94%</td>
<td>82% vs. 29%, p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>halo</td>
<td>61%</td>
<td></td>
<td>71% vs. 53%, p&lt;0.01</td>
</tr>
<tr>
<td>consolidation</td>
<td>30%</td>
<td></td>
<td></td>
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<tr>
<td>infarct-shaped</td>
<td>27%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cavitation</td>
<td>20%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>air-crescend</td>
<td>10%</td>
<td></td>
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</tbody>
</table>

**Pro**
- many patients
- ante-mortem trial

**Contra**
- halo = part of inclusion
- 95% hardcopies
- thick section CT
- 270° of halo not defined

**Septic Embolism**

infected port
A. Screening
B. Early detection
C. Characterisation
D. Monitoring
E. Intervention

**Fungal Pneumonia**

- **consolidation**
- **air-crescent sign**
- **cavitation**

**Response Evaluation**

- metastases
- +6 mo.

**Radiological Course**

- day 2, day 7, day 13, day 33, day 108
- halo, air crescent, consolidation, volume, hemoptysis
- day 3, day 43, day 87, day 94, day 125
- ill-defined nodules, hemat. recovery, halo reduction, shrinkage
- antifungal treatment

**Dijon:**

Radiological Course

- day 75
- day 57
- day 50
- day 43
- day 27

Radiation Course

- Neutropenia
- Recovery

Fungal Pneumonia
differential diagnosis

febrile neutropenia
- bacterial pneumonia
- mycobacteria
- pneumocystis jiroveci
- virus or GvHD
- radiation toxicity
- drug toxicity
- congestion

- metastases
- bronchoalveolar cell
- lymphoma
- COP (BOOP)
- amyloidosis
- M. Wegener
- eosinophilic pneumonia

Radiological Course

- ground glass opacity (low °)
- perihilar distribution
  leaving out subpleural space
- late stage:
  - intralobular sept
  - air-space cysts

PcP - Pneumocystis jiroveci pneumonia

- ground glass opacification 66%
- ill-defined nodules 59%
- consolidation 59%
- bronchovascular bundle 22%
- pleural effusion 22%
- tree-in-bud 13%

Fungal Pneumonia
differential diagnosis

- metastases
- bronchoalveolar cell
- lymphoma
- COP (BOOP)
- amyloidosis
- M. Wegener
- eosinophilic pneumonia

Cytophagocytic virus pneumonia (CMV)
(n=32)

- ground glass opacification 66%
- ill-defined nodules 59%
- consolidation 59%
- bronchovascular bundle 22%
- pleural effusion 22%
- tree-in-bud 13%

CMV

- ground glass opacification ( high / low °)
- mosaic distribution (secondary lobe)
- high-risk:
  - allo-Tx, AIDS
  - T-cell depleted Tx
  - anti-CD20

Hints for:
- Pneumocystis jiroveci pneumonia

Hints for:
- CMV pneumonia
- graft versus host disease (GvHD)
hints for:
- **drug toxicity:**
  - ground glass opacification (high / low °)
  - mosaic distribution (secondary lobe)
  - Bleomycin, MTX, Ara-C etc.

hints for:
- **radiation toxicity:**
  - paramediastinal distribution
  - even after total body irradiation (TBI)
  - ground glass opacification
  - intralobular sept
  - weeks to month later

hints for:
- **congestion:**
  - thickening of lymphatic sept
  - demarcation of secondary lobe
  - pleural effusion

hints for:
- **lymphangiosis carcinomatosa:**
  - conic thickening of lymphatic sept
  - mikronodules
  - breast / gastric cancer

hints for:
- **pulmonary hemorrhage:**
  - thrombocytes / platelets ↓
  - plasmatic coagulation ↓
  - hemoptysis
  - sedimentation phenomenon
  - perifocal
CT guided Biopsy

CT guided Ampho B instillation
- total: n = 15
  - 3 repetition
  - CR / PR / SD: 0 / 12 / 3
- total: n = 13
  - 1-5 repetition
  - CR / PR / SD: 8 / 4 / 1

CT guided Ampho B instillation
- post

Aspergillus Pneumonia + Pseudo-Aneurysm
- pre
- post embolisation

Vessel Arrosion
- hemoptysis in 10-40% of IPA
- ~1 week after reconstitution
- acute pulmonary hemorrhage
- mortality ~10%
- contrast enhanced CT
- bronchial- / pulmonary arteries
- resection ± embolisation

A. Screening
B. Early detection
C. Characterisation
D. Monitoring
E. Intervention
A. Early Detection  
B. Characterisation  
C. Intervention  
D. Extra-pulmonary

**EORTC Criteria Fungal Sinusitis**

Sinusitis plus:
- Acute localized pain
- Nasal ulcer with black eschar
- Extension from the paranasal sinus across bony barriers, including into the orbit

**EORTC Criteria Fungal CNS Infection**

- Focal lesions on imaging
- Meningeal enhancement on MRI or CT

**Sinusitis**

- Level bone arrosion

**Rhino-Cerebral Infection**

- Aspergillus niger
- Bone arrosion
- Brain invasion

**Cerebral Lesion**

- CT
- T2

**Meningoencephalitis**

- CT
- T2w
- T1w + Gd

**Toxoplasmosis in HIV**

- FLAIR
- T1w
- T2w + Gd
EORTC Criteria
Disseminated Candidiasis

After an episode of candidemia within the previous 2 weeks:
- Small, target-like abscesses (bull’s-eye lesions) in liver or spleen
- Progressive retinal exudates on ophthalmologic examination

De Pauw et al., Clin Infect Dis 2008

EORTC Criteria
Disseminated Candidiasis

T1wT1w
T2w
T1w Gd

NHL, PSCT, hepatic Candidiasis

Summary

| Chest:      | thin section CT          | no supine chest x-ray |
| Para Nasal: | CT                        | no plain radiograph   |
| Brain:      | MRI                       | CT in emergency (hemorrhage) |
| Abdomen:    | liver → MR > CT          | vessels / peritoneum → CT |
|             | VOD → duplex              |                          |

Limits

US
- adipositas, investigator, training

CT
- i.v. contrast: allergy, renal impairment, Metformin, thyroid autonomy
- oral contrast
- breath-hold

MRI
- claustrophobia
- pace maker, defibrillator, pump
- foreign body containing iron
- confusion, convulsion, agitation
- limited monitoring
- breath-hold

Literature

Halo: Greene et al. CID (2007) 44
Fungal Pneumonia: Heussel et al. Radiologe (2000) 40