Clinical challenges when handling immunodeficient patients at Rigshospitalet.

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Patients receiving treatment for malignancies

- **Oncology**
  - Solid tumors
    - Chemotherapy
    - Radiation
    - Chemotherapy/radiation
    - Biologic modifiers

- **Hematology**
  - Lymphoma, myeloma
    - Chemotherapy
    - Radiation
    - Chemotherapy/radiation
    - Biologic modifiers
  - Leukemias
    - Chemotherapy ++
  - Bone marrow transplantation
    - Chemotherapy +++
    - Chemotherapy +++/radiation
    - Immune suppression post transplant
Chemotherapy and neutropenia

![Graph showing log ANC (x 10^9/L) over days, with chemotherapy administered and grade 4 neutropenia marked.](image-url)
Neutrophil host defence
Chemotherapy side effects

- Neutropenia
- Thrombocytopenia
- (Lymphopenia)
- Stomatitis
- Diarrea
- Nausea
Neutropenic fever*

Neutrophil count <0.5 mia/L and Temp. ≥ 38 gr. C for min. 1 hour

Low-risk: ≤ 7 days of neutropenia
High-risk: > 7 days of neutropenia

Severe neutropenia: <0.1 mia/L

Febrile neutropenia, a clinical challenge


174 patients with solid tumors/lymphoma
  – 108/174 (62%) developed neutropenic fever

165 patients with leukemia
  – 113/165 (68%) developed neutropenic fever
Febrile neutropenia, a clinical challenge


174 patients with solid tumors/lymphoma
  – 108/174 (62%) developed neutropenic fever
  – 73/108 (68%) were culture negative

165 patients with leukemia
  – 113 (68%) developed neutropenic fever
  – 74/113 (65%) were culture negative
97 Patient with neutropenic fever (heme/onc), not treated with prophylactic antibiotics:

Culture-positive: 10/97 (10%)

PCR-positive for 16s and 18s RNA gene: 20/97 (20%)

Risk score in neutropenic fever

<table>
<thead>
<tr>
<th>Clinical parameters</th>
<th>Score*</th>
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</thead>
<tbody>
<tr>
<td>Burden of illness: no or mild symptoms†</td>
<td>5</td>
</tr>
<tr>
<td>No hypotension</td>
<td>5</td>
</tr>
<tr>
<td>No chronic obstructive pulmonary disease‡</td>
<td>4</td>
</tr>
<tr>
<td>Solid tumour or no previous fungal infection§</td>
<td>4</td>
</tr>
<tr>
<td>No dehydration</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient status</td>
<td>3</td>
</tr>
<tr>
<td>Burden of illness: moderate symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Patient’s age &lt; 60 years</td>
<td>2</td>
</tr>
</tbody>
</table>

MASCC: Multinational Association for Supportive Care in Cancer.
Scores > 21 indicate a low risk for medical complications.
*The maximum theoretical score is 26.

MASCC-score is for patients who HAVE neutropenic fever....
Questions:

- Risk factors for developing neutropenic fever?
- Risk factors for fatal course of neutropenic fever?
Bone marrow transplant patients

- 90% are transplanted because of malignant disease (relapse).
- Are severely immunosuppressed (T-cell function).
- Some of these patients are T-cell mixed chimeras.
- Graft versus Host Disease.
- Long period with low cell numbers
• **CMV**
  - Pneumonia
  - Enteritis
  - Retinitis

• **EBV**
  - "EBV-disease"
  - Post Transplant Lymphoproliferative Disease (PTLD)

• **Polyoma BK virus**
  - Nefritis (renal transplant patients)
  - Hemorragic cystitis (bone marrow transplant patients)

• **HHV-6**
  - Encephalitis (?)
Case:
28-year old male received a bone marrow transplant with brother as donor for acute myeloid leukemia.

Myeloablative conditioning including 12 Gy total body irradiation. Transplant course included 18 days with neutrophils = 0.0 mia/l. Neutropenic fever, treated with empric antibiotics, no complications. Discharged 25 days after transplant, neutrophils = 1.7 mia/l. Routinely immunosuppressed with Cyclosporine. No Graft versus host disease.

Day 90 after transplant, he was admitted with high fever, malaise, neutrophils = 3.5 mia/l.
Other patient categories?

- Patients in dialysis?
- Rheumatologic patients receiving biologic modifiers?
- Long-term low-grade fever?
- Other?