9.1 Neutropenic Sepsis

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Def: Systemic reaction to an infection during neutropenia (particularly after chemotherapy or radiotherapy).
- **Severe sepsis:** temperature > 38.0°C or < 36°C, heart rate > 90/min, respiratory rate > 20/min or PaCO₂ < 32 mmHg
- **Septic shock:** hypotension with blood pressure (BP) < 90 mmHg (systolic) or BP decrease by 40 mmHg and signs of organ failure: lactate acidosis, oliguria, multiorgan failure (MOF)

ICD-10: A41

Ep: Fever during neutropenia (FN;  ► Chap. 4.2) is a common side effect after myelosuppressive chemotherapy or radiotherapy; the incidence correlates directly with length and severity of the neutropenia. Up to 15% of patients with febrile neutropenia develop severe sepsis or septic shock.

Path: Risk factors → neutropenia → febrile neutropenia → sepsis

Risk of Sepsis in Case of Granulocytopenia
- **Low risk:** granulocytes 0.5–1 × 10⁹/l for 2–7 days → in case of sepsis, mortality 14%
- **High risk:** granulocytes < 0.1 × 10⁹/l for > 7–10 days → in case of sepsis, mortality 47%

Both proinflammatory (TNFα, IL-6, IL-8) and antiinflammatory (IL-1 RA, IL-10) cytokines play an important role.

Sy: • Fever, general symptoms, weakness, reduced performance
  • Local signs of inflammation: catheter infection, skin infections, mucositis, gingivitis, acral focal infections, abscesses
  • Sinusitis, signs of pulmonary infection
  • Gastrointestinal symptoms, pain, diarrhea
  • Meningitis, headache, amentia
  • Sepsis: decrease in blood pressure, tachycardia, hypothermia

Dg: Medical History, Physical Examination
  • Medical history (fever, diarrhea, dysuria, etc.)
  • Physical examination: intravenous access sites, catheter ports, skin, oral mucous membranes, perianal region, pulmonary auscultation and percussion, abdominal pressure pain, pain on tapping / pressure pain of the paranasal air sinuses, lymphadenopathy, monitoring of blood pressure and pulse, meningism

Laboratory Tests
  • Routine laboratory tests, parameters of inflammation, plasmic coagulation, antithrombin III (ATIII), plasminogen activator inhibitor (PAI 1), liver and renal function tests

Microbiology
  • Peripheral blood cultures and cultures from intravenous access and catheters (► Chap. 10.8). Aerobic and anaerobic blood culture, isolator tube bottle. Where applicable, remove catheter, microbiological analysis of the catheter tip.
  • Urine culture, sputum culture, swabs from suspicious lesions, lumbar / pleural / ascites puncture and culture
  • With pulmonary infiltrates: bronchoalveolar lavage (BAL)
  • With diarrhea: stool culture, detection of enterotoxins from Clostridium difficile, Gruber-Widal reaction
Imaging
- Chest x-ray, possibly x-ray of paranasal air sinuses
- Abdominal ultrasound if indicated
- High-resolution CT scan if indicated

Th: Emergency Treatment
With fever during neutropenia, rapid initiation of treatment is essential:
1. Microbiological analysis
2. Immediate initiation of empirical antibiotic treatment: broad-spectrum antibiotic with effectiveness against pseudomonas spp., where applicable in combination with an aminoglycoside and a glycopeptide (particularly in case of catheter sepsis). Rapid escalation with antimycotics has proven benefit (amphotericin B, lipid formulation amphotericin B, azoles, echinocandins) (► Chap. 4.2)
3. Optimization of tissue oxygenation. Administration of oxygen via nasal tube or mask, 2 l/min up to 12 l/min. Where applicable, respiration support (non-invasive: CPAP; invasive: intubation)
4. Volume substitution; where applicable, administration of catecholamines
5. Initiate intensive medical care at an early stage

Further Measures
- Further diagnosis (imaging, ultrasound, bronchoalveolar lavage (BAL), abscess aspiration / biopsy, etc.)
- In case of impaired renal function, initiate dialysis
- If persistence of neutropenia is expected, administer G-CSF to support bone marrow reconstitution. (► Chap. 4.3). Activated protein C demonstrated a positive effect on the overall survival of septic patients, but with marked side effects. Consider granulocyte transfusion (► Chap. 5.4).

Px:
- Basic hospital hygiene; conduct of invasive procedures under aseptic conditions
- Patient hygiene, especially skin care, dental care, mucositis prophylaxis; avoid foods with high germ counts
- If neutropenia persists for more than 7 days: regular monitoring, even if apyrexial → blood cultures, fecal cultures, throat swabs, sputum. Consequent treatment of fever in neutropenia (► Chap. 4.2)
- Administration of hematopoietic growth factors (G-CSF) according to current guidelines (ASCO / ESMO guideline; (► Chap. 4.3)

Ref:
1. Aapro MS, Cameron DA, Pettengell R et al. EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphomas and solid tumours. Eur J Cancer 2006;42:2433–53

Web: