

# Febrile neutropenia

**Febrile neutropenia** is a **life-threatening condition** that occurs as a **complication of hematopoietic attenuation**.

Neutropenia occurs as a result of marrow suppression most often during chemotherapy in cancer patients, exceptionally as a side effect of some other drugs. Febrile occurs in response to infection. Due to neutropenia, it is one of the **urgent conditions** in hematology. Mortality increases exponentially after each hour without adequate treatment (especially suitable ATB).

## Definition

Febrile neutropenia is defined as a **decrease in the number of neutrophilic granulocytes** below **1000 /  $\mu$ l**. In addition, a **body temperature above 38.3 °C** must be measured once or a body temperature above **38.0 °C** (at least 1 hour between the two measurements) at least twice during one day.

## Etiology and pathophysiology

In granulocytopenia, the body's ability to form an inflammatory infiltrate is limited and antibacterial and antifungal immunity is impaired. Infections are atypical. For example, skin infections, rather than abscesses, produce unbounded phlegmon. Also typical is pneumonia **without pneumonia** with an auditory finding corresponding to pneumonia, high CRP but with a negative radiological finding. Febrile neutropenia can progress to neutropenic sepsis, which can progress to multiorgan failure. For up to 50% of patients, these complications can be fatal and end in death.

## Examination

It is necessary to specifically search for the site of infection (periodontium, nasopharynx, lungs, perineum, surgical wounds, injection sites, catheters ...).

If febrile neutropenia is suspected, it is necessary to take **samples for cultivation** from all suspicious places (blood culture, urine, urinary sediment, sputum, catheter surroundings, periodontium, oral cavity - Candida, ...), or to perform a more invasive examination to obtain them (BAL). According to the results of cultivation we can divide into:

- 1. febrile neutropenia simple** - we do not cultivate any agent,
- 2. febrile neutropenia complicated** - we find the cause of the infection.

Other examinations: Skiagram of the chest - always (a finding in the lungs is a sign of a worse prognosis, more intensive treatment is necessary), sono, bronchoscopy, ...

## Therapy

The main therapy is the rapid administration of **empirical antibiotics** immediately after the collection of **blood culture**. In certain cases, the administration of so-called *empirical antifungal therapy* is indicated. Part of the comprehensive care is the stimulation of granulocyte cells in the bone marrow.

Hospitalization is appropriate for patients with severe conditions or risk factors. **Patients in good condition and without risk factors** can be left in home care, where there is no risk of infection with nosocomial strains. However, it is necessary to ensure that the patient has the opportunity to travel to the hospital within 1 hour at any time and to consult their condition by telephone at any time. Scoring systems (eg MASCC) exist to select patients with a low risk of complications, and it is possible to estimate how long neutropenia will be and how deep the neutrophil count will decrease.

## Antibiotic therapy

The antibiotics administered must be **broad-spectrum** and administered empirically immediately after taking the blood culture. It must cover the basic G- and G + strains of bacteria, it is chosen according to the situation at the workplace, the intensity of treatment, the expected length of neutropenia, it is not waiting for the results of culture examinations, then it is adjusted according to the culture results. If febrile neutropenia develops within or early after hospital stay, antibiotics must also be effective against nosocomial strains (antipseudomonas ATB).

**The basic antibiotic is piperacillin / tazobactam** 4.5 g after 8 hours, or cefepime 2 g after 8 hours. (Cefepime is used less, there is no such experience with it.)

If the patient is in **shock**, **gentamicin** 5 mg / kg after 24 hours or amikacin 15 mg / kg after 24 hours (suitable combination for G-strains) is added. (In some workplaces, the combination of carbapenem, colimycin, echinocandin, nimesulide is used in shock.)

The combination of **vancomycin** with **ceftazidime** is given to patients with a central venous catheter. If the patient is febrile even after 48 hours of treatment, the combination of **vancomycin** with **carbapenems** is given.

(If suitable antibiotics are not available in the workplace at the patient's arrival, it is better to give the patient any antibiotics with the widest possible spectrum than none.)

## Antifungal therapy

If a fungal etiology is suspected, **azoles** (itraconazole or voriconazole) or **amphotericin B** on a lipid carrier or **echinocandins** are added to the antibiotics.

Mycosis should be treated before it can be proven, otherwise the effect of treatment may be insufficient. Therefore, antifungals are always used in patients who have febrile neutropenia after adequate antibiotic treatment for more than 4 days, even though they have only about 10% mycosis. Echinocandin **caspofungin** is most often used for **empirical antifungal therapy** (despite its high cost), mainly due to its virtually zero side effects. It is also possible to use **amphotericin B** in a lipid suspension.

Posaconazole is most commonly used for **antifungal prophylaxis**.

## Complementary treatment

The proliferation and maturation of granulocyte cells in the bone marrow is stimulated by cytokines, only the G-CSF analogue **filgrastim** is registered in the Czech Republic.

## Prevention

Prevention is especially important, it consists in:

1. reduction of exposure to infectious agents,
2. adjustment of granulocytopenia (eg by administration of hematopoietic growth factors - G-CSF),
3. strengthening the patient's immunity (i.v. immunoglobulins),
4. last but not least, educating the patient about the possible risk of his condition.

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