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Febrile Neutropenia

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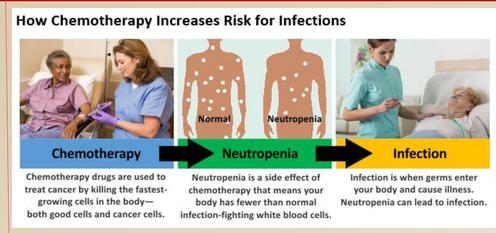
Introduction

- Febrile Neutropenia (FN) is a potentially life-threatening oncologic emergency, which requires immediate and aggressive treatment with broad-spectrum antibiotics. (Bossaer & Cluck, 2013)
- FN occurs when a patient has a temperature of greater than 100.4˚F with an Absolute Neutrophil Count (ANC) of less than 500 cells/mm³, often with fever being the only sign of infection (Bossaer & Cluck, 2013)
- In cancer patients, FN is a common cause of morbidity and mortality, and results in high medical costs. (Flowers et al., 2013)
- Approximately 60,000 patients are admitted for FN annually. (Bennett, Djulbegovic, Norris, & Armitage, 2013)
- As an oncology nurse at The Ohio State University's James Cancer Hospital, I chose the topic of FN as many of our patients receiving chemotherapy experience this complication at some point during their treatment, and nurses play a vital role in both prevention and early recognition of FN.

Presentation of Process

- Neutropenia is a common side effect of chemotherapy, which leads to increased risk for infections.(Weycker, Barron, Kartashov, Legg, & Lyman, 2014)
- Most standard-dose myelosuppressive chemotherapy is associated with 6-8 days of neutropenia, with the lowest point of neutropenia known as the nadir. (Bennett et al., 2013)
- The absolute neutrophil count (ANC) is the lab value monitored to assess the degree of neutropenia, and provides an estimate of a patient's ability to fight off infection. (Weycker et al., 2014)
- For patients receiving myelosuppressive chemotherapy, a complete blood count with differential is monitored twice weekly to assess the ANC. (Weycker et al., 2014)
- While central lines are essential for administration of many chemotherapies, they are a significant risk factor responsible for at least 400,000 blood stream infections in cancer patients per year in the U.S. (Raad & Chaftari, 2014)
- In FN, empirical treatment with broad-spectrum antibiotics is recommended within one hour of a documented fever, even without a confirmed infection to avoid sepsis, and potentially, death. (Bennett et al., 2013)
- Antibiotics are continued while the infectious work up is in progress with blood cultures, chest X-ray, and possibly urine, stool, or sputum cultures. (Bryant, Walton, & Albrecht, 2014).



(Figure 1. Retrieved from: https://www.cdc.gov/cancer/preventinfections/patients.htm

Signs and Symptoms

- Temperature is used to screen patients who are receiving chemotherapy for infection. (Niven et al., 2014)
- Fever is defined as a temperature of 100.4˚F or higher, and may be the earliest and **only** sign in FN. (Niven et al., 2014)
- Due to neutropenia, cardinal signs and symptoms of infection such as redness, warmth, and swelling may not be present. (Lucas, Olin, & Coleman, 2018)
- With severe infection, patients may present with signs of sepsis, such as hypotension and tachycardia. (Bryant et al., 2014)
- In many cases of FN, the infectious etiology will not be determined, with only approximately 30% of cases documented with infections. (Lucas et al., 2018)
- Length and severity of neutropenia are two important factors. An ANC below 500 is considered severely neutropenic, 500-1000 is moderate,1000-1500 is minimal, and greater than 1500 is not clinically significant. (Bryant et al., 2014).
- The ANC is calculated by multiplying the total white blood cell count by the percentage of polymorphonuclear cells and bands. (Bryant et al., 2014)
- The Multinational Association for Supportive Care in Cancer Score (MASSC) is used to calculate whether a patient with FN is high risk (score >21) or low risk (score <21). All high risk patients must be treated in the inpatient setting. (Bergstrom, Magalla, & Gupta, 2018)

Table. The Multinational Association for Supportive Care in Cancer Score

Characteristic	Points
Burden of febrile neutropenia symptoms[a]	
No or mild symptoms	5
Moderate symptoms	3
Severe or morbid symptoms	0
No hypotension (systolic blood pressure >90 mm Hg)	5
No chronic obstructive pulmonary disease	4
Solid or hematologic cancer with no previous fungal infection	4
No dehydration necessitating parenteral fluids	3
Outpatient status at onset of fever	3
Age <60 y	2

[a] The points attributed to this variable are not cumulative. The maximum theoretical score is 26. A score of 21 or greater is considered low risk, and a score of less than 21 high risk.

(Table 1. Bergstrom et al., 2018)

Underlying Pathophysiology

- Hematologic cancers comprise several different cancers, such as leukemia, lymphoma, and multiple myeloma, and affect the blood, bone marrow, and lymphatic systems, which increases susceptibility to infection. (Bryant et al., 2014)
- Neutrophils are the most common type of white blood cell in the bloodstream. A key part of the immune system, they are early responders to pathogen invasion and ingest bacteria through phagocytosis. (Bennett et al., 2013)
- Treatment of these cancers with myelosuppressive chemotherapy affects all rapid cycling cells. While chemotherapy targets rapid cycling cancer cells, normal rapid cycling cells within the gastrointestinal (GI) tract and bone marrow are negatively affected. (Bennett et al., 2013)
- Rapid cycling hematopoietic cells of the bone marrow undergo immediate and cumulative damage, resulting in neutropenia. (Bennett et al., 2013)
- Neutropenia may result from bone marrow injury due to the cancer directly, chemotherapy and radiation, other underlying diseases, or a combination of all events, further increasing susceptibility to infection. (Lucas et al., 2018)
- Rapid cycling cells within the mucosal linings of the gastrointestinal (GI) tract provide natural defenses against pathogens. Mucosal barrier injury from chemotherapy or radiation leads to mucositis, allowing bacteria from the GI tract to seed in the bloodstream, causing a sustained inflammatory response with fever. Bacteria from the altered GI tract are often responsible for infections in FN. (Lucas et al. 2018)
- When chemotherapy-induced neutropenia develops, endogenous cytokines are released by epithelial cells and may result in fever even in the absence of infection. (Bennett et al., 2013)
- Microorganism access through central lines, may lead to microbial invasion in the immunocompromised cancer patient (Lucas et al., 2018)

Significance of Pathophysiology

- Neutropenia in cancer patients results in a high risk of infections, many of which are bacterial, but may also be fungal or viral. (Bryant et al., 2014)
- Patients with cancer are at high risk for gram negative-infections, such as *Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Stenotrophomonas maltophiliadue,* due to neutropenia, lymphocyte dysfunction, mucositis, and use of central lines. (Perez, Adachi, & Bononmo, 2014)
- Coagulase-negative staphylococci are currently the most common pathogen identified in blood cultures. (Flowers et al., 2013)
- Gram-positive organisms are also leading causes of serious infection in cancer patients with neutropenia, including *Staphylococcus aureas, Streptococcus pneumoniae, and Enterococcus faecalis.* (Raad & Chaftari, 2014)
- Viral and fungal infections are less common, but patients are treated empirically with acyclovir and fluconazole to prevent viral and fungal illnesses when severe neutropenia is expected. (Bryant et al., 2014)
- Granulocyte colony-stimulating factors (GCSF), typically filgrastim or pegfilgrastim, are subcutaneous injections used prophylactically to minimize the risk of FN by shortening the duration and severity of neutropenia. Injections are initiated 24-72 hours after completion of chemotherapy. (Bennett et al, 2013)

Implications for Nursing Care

- Nurses play an important role in educating patients, families, and caregivers of infection prevention strategies, as well as the signs and symptoms of infection, with clear instructions of when and how to contact healthcare providers. (Flowers et al., 2013)
- The Oncology Nursing Society recommends protective precautions such as hand hygiene, avoiding visitors with respiratory illnesses, drinking filtered water and ice, avoiding live plants, and avoiding animal feces to decrease exposure to infectious organisms while neutropenic. (Bryant et al., 2014)
- Neutropenia following myelosuppressive chemotherapy typically lasts 6-8 days, which is the most critical timeframe to avoid potentially infectious exposure. (Bennett et al., 2013)
- Patients receiving chemotherapy should be instructed to monitor temperatures twice daily, and report any value over 100.4˚F immediately. (Bryant et al., 2014)
- Use of rectal thermometers is contraindicated in the neutropenic patient due to infection risk from the altered GI tract. (Niven et al., 2014)
- In the ED setting, nurses should be aware that FN is a potentially life-threatening, oncologic emergency, thus these patients should receive "fast tracking" to avoid delays in treatment. (Keng et al., 2015)
- Broad spectrum antibiotics should be initiated within one hour of documented fever, if possible. (Flowers et al., 2013)
- FN is mainly treated in the inpatient setting, but low risk patients may receive more outpatient management in the future to contain costs. (Flowers et al., 2013)
- GCSF is an effective, yet very costly medication used to decrease the duration and intensity of neutropenia.(Bennett et al., 2013)

Conclusions

- FN is a potentially life-threatening, oncologic emergency which requires immediate attention and aggressive management. Bossaer & Cluck, 2013)
- Broad spectrum antibiotics should be initiated within one hour of documented fever, if possible, even if infection cannot be confirmed. (Bennett, et al., 2013)
- Hand hygiene is the single most effective measure in preventing infection. (Flowers et al., 2013)
- Nurses play a vital role in patient and family education regarding the risks associated with FN. (Flowers et al., 2013)
- A better understanding of the etiology and prevention of FN have led to a reduction in morbidity over the past twenty years, with recognition of the importance of early administration of broad-spectrum antibiotics. (Flowers et al., 2013)

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