Fever and Neutropenia

1. Fever is defined as a temperature > 38.5 C or 101.5 F. Low-grade fever is defined as a temperature > 38.0 or 100.0 F.

2. Mild neutropenia is defined as an actual neutrophil count (ANC)< 1500. (In African Americans, ANC<1000). Moderate neutropenia is defined as ANC 500-1000. Severe neutropenia is ANC < 500. Severe neutropenia creates a risk of overwhelming bacterial infections, as the neutrophils protect against bacteria invading through the skin and mucous membranes. ANC=WBC X (Neutrophil + band %). The actual phagocyte count (APC)=WBC X (neutrophil + band + mono%)

3. Any cancer or aplastic anemia patient with fever, and particularly those who are on high-intensity chemotherapy, should be carefully assessed for the possibility of a serious infection. Patients with true fever (T>101.5; or 2 fevers over 101 more than 1 hour apart during a 24 hour period) and severe neutropenia (ANC<500 or expected to be at this level within 48 hours) are generally hospitalized and observed on antibiotics until their neutrophils begin to recover and they are infection free. Patients with persistent low grade fever or low-grade fever who are ill and have severe neutropenia are also admitted to rule out/treat infection. Patients who have a central line in place and have fever without neutropenia should have a blood culture done. Antibiotic therapy is optional based upon the clinical situation.

4. Ill patients who are afebrile or hypothermic and yet are severely neutropenic can also have serious infections. Therefore, patients who are ill and are at their neutrophil nadir (around 10 days following high dose chemotherapy) should be assessed and possibly admitted. Corticosteroids, particularly decadron, can block febrile responses. Therefore patients receiving steroid therapy for leukemia or lymphoma, particularly those with active marrow involvement, should be evaluated carefully in this setting.

5. Patients in lower intensity phases of chemotherapy (such as maintenance in ALL) and who are neutropenic for short periods of time that have evidence of recovering counts (a rising APC) can be discharged at the judgment of the treating physician.

6. Stay ahead of febrile neutropenic patients because once you get behind the eight ball you and the patient lose.

7. 10-20% of febrile neutropenic cancer patients have bacteremia at presentation.

8. Examination of the mouth, lungs, and perineum/rectal area should be done at admit and every day.

9. No rectal meds to neutropenic patients.

10. For patients who have blood cultures growing gram negative organisms, an aminoglycoside should be added until the organism is identified and sensitivities are complete. When a positive culture is identified, empiric therapy can be modified based upon the organism and sensitivity. Gram negative coverage must be continued until there are signs of count recovery, even if a gram + organism is identified. This is because polymicrobial sepsis is common and you may not have identified all organisms.

12. General criteria for stopping empiric antibiotic therapy for fever and neutropenia. If cultures are negative and there are no clinical signs of infection, antibiotic therapy should be continued until the patient is afebrile for at least 24 hours and there are signs of marrow recovery with an increasing WBC (from 0.1 to 0.2 may be enough in some settings). Patients who have positive blood cultures or an identified clinical infection (e.g. pneumonia) should receive a defined course of antibiotic therapy (7-14 days depending on infection and organism) and continue treatment at least until there are convincing signs of marrow recovery.

13. Patients with acute myelocytic leukemia and ALL patients receiving prolonged corticosteroid therapy such as given during induction or reinduction are at high risk for fungal infections. An appropriate antifungal (amphotericin B or voriconazole) should be added to patients if the patient remains febrile 4-5 days into antibiotics. Consider addition of empiric antifungals on day 5-7 in other patients with fever and neutropenia.

14. Neutropenic patients on broad spectrum antibiotics should be on some type of oral candidiasis prophylaxis, usually Fluconazole or Nystatin. Note that fluconazole alters metabolism of many drugs.

15. Most neutropenic cancer patients who become febrile do not have a source or have positive cultures initially. The use of early empiric antibiotics is justified by reduced morbidity and mortality.

16. Risk of infectious complications form neutropenia increase with the length of time the patient is neutropenic. A low risk patient is one whose neutropenia is anticipated to resolve within 1 week of starting antibiotics.

17. Antibiotics must be started STAT within 1 hour of admit. Mono-therapy with Cefepime (or comparable antibiotic) is used for a majority of patients. This is the most important therapeutic intervention, and is chosen because of its broad spectrum & coverage of pseudomonas.

18. Patients who received high dose ARA-C (Cytarabine) with their most recent chemotherapy or have a source suggestive for gram positive infections should be started on Vancomycin and Cefepime. Patients who receive high dose ARA-C have a high incidence of gram positive infections/sepsis, and toxic death from Strep viridians. The presence of an indwelling catheter is <u>not</u> an indication for routine empiric use of vancomycin.

19. Fever that recurs after defervescing can be result of fungal infection. Fungal blood cultures should be sent and consideration of imaging of sinuses and chest to pelvis by CT to look for fungus. Consider also echocardiogram.

20. If patient has a line tunnel infection, persistently positive blood cultures, recurrent cultures with same pathogen, candida, VRE or polymicrobial sepsis, central line should be removed.

21. Bronchoscopy should be considered in patient with pulmonary infiltrates not responding to broad spectrum antibiotics. A serum galactomannin level is a non-invasive way to assay for Aspergillus, although its predictive value has not yet been validated in children. Transbronchial or open lung biopsy may be necessary to diagnose aspergillus or other forms of invasive fungus.

22. Aztreonam is useful in patients needing gram negative coverage who are allergic to cephalosporins.

23. Viral respiratory cultures can be useful in patients with respiratory symptoms. Empiric anti-influenza therapy should be considered during “flu season”.

24. Typhlitis (neutropenic colitis) is an infection of the colon that involves invasion of colonic flora the colonic bowel wall, presenting with abdominal pain, vomiting, diarrhea and styptic shock. Typhlitis is treated with bowel rest and antibiotics typically double coverage (third generation cephalosporin plus aminoglycoside plus metronidazole for anaerobes).

Case #1

16 year boy being treated with AML presents with fever and WBC 200. His most recent chemotherapy was ARA-C 1 week ago, but he isn't sure of dose. The best choice for antibiotic coverage would be:
1. Cefepime
2. Vancomycin
3. Vancomycin and Cefepime

Answer # 3. Better to cover for gram + in patient with history of ARA-C since incidence of Strep viridans sepsis is significant with high dose ARA-C. If it turns out not to be high dose ARA-C you could stop the Vancomycin.

Case #2

An 18 year-old girl has neutropenia secondary to AML. She has been on treatment with Vancomycin & Cefepime and on day #4 she develops recurrent fever. On PE she says the nurse examined her rectal area; the nurse is not around for you to check with but she well be back in AM. You should:
1. Wait till tomorrow to talk to nurse
2. Examine the perirectal area.

Answer #2. Examine the perirectal area yourself. If there are signs of a perirectal infection, you should add a second gram negative drug such as an aminoglycoside and add an anaerobic coverage such as metronidazole.

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Case #3

A 5 year old boy is on maintenance treatment for ALL. He is on 6 M.P. daily and MTX weekly. He is admitted for F& N. After two days, he is afebrile. His counts are increasing with an AGC of 750, and his cultures are negative. You would:
1. Keep him to complete at least 3 days of antibiotics.
2. Wait till the AGC is 1000
3. D/C home on no antibiotics.

Answer #3. This is a "low risk patient" and his counts are recovering.

Case #4

An 8 year old boy being treated for lymphoma has chemo was 1 week ago. He presents with fever and ANC 500, you order blood and urine cultures. The patient can't urinate at this time. You tell the nurse to:
1. Give antibiotics after the blood culture drawn and get the urine culture later
2. Wait until patient urinates to give the antibiotics
3. I & O catheter patient

Answer #1. Start antibiotic STAT in fever & neutropenia patient. We avoid I & O catheters unless absolutely necessary. [1-6]

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