Complications of Chemotherapy

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- BONE MARROW SUPPRESSION
  骨髓抑制

Anemia,

Neutropenia (worst 10-14days, recovery 17-21days)

Thrombocytopenia

Anemia 貧血

- Transfusion support 輸血支持

(absolute neutrophils 絕對中性粒細胞數 <0.5 x10^9/L

- Cultures 種菌/ 培植菌
- Broad-spectrum antibiotics 廣譜抗生素
- Oral ciprofloxacin/augmentin 口服環丙沙星/安奇

Versus IV antibiotics(meropenum 美羅培南, sulperazone + aminoglosides)

No change for 3-days, If febrile Consider adding vancomycin?

如果發燒三天內仍沒有變化，會否考慮加入萬古黴素？

When to stop antibiotics?
何時停止服用抗生素

- Afebrile and Neutrophils> 0.5 x10^9/L

  退燒及中性粒細胞> 0.5 x10^9/L

WHEN TO START ANTIFUNGAL DRUG?
何時開始服食抗真菌藥物？

- If fever persisted for 3-5 days and still neutopenic

  假如發燒持續３至５天和中性白血球仍然減少
- If there is characteristic X-ray changes

  假如出現X射線變化的徵狀

When to start antiviral drug?
何時開始服用抗病毒藥物？

- Clinical setting 臨床環境/ 臨床應用
- Hepatitis B carriers 乙型肝炎病毒攜帶者 (HB –s positive)- Lamuvidine prophylaxis particularly when receiving rituximab
- CMV +ve transplant recipients

  巨細胞病毒 +ve 移植患者

USE OF G-CSF- 注射白血球生長激素

- Shorten period of neutropenia 縮短中性白細胞減少的時間
- Shorter hospital stay 縮短住院時間
- No reduction in mortality 沒有降低死亡率

Causative Organisms

- Late 1960s to early 1980s
- Gram-negative bacilli (40-50% if < 0.1×10^9/L)
- 75% of the culture-positive cases
- Pseudomonas aeruginosa being the leading isolates
- Mid 1980s steady increase in gram-positive infections
- Coagulase-negative staphylococci and S. aureus are the predominant organisms
- Uniform use of long-dwelling right-atrial catheters

- Streptococcus viridans and Enterococcus spp. including vancomycin-resistant are also common

Empirical therapy

- Aminoglycosides plus anti-pseudomoas penicillins- response rates between 60% and 70%
- Tazocin (piperaciillin-tazobactem)
- Anti-pseudomonas third-generation cephalosporins (ceftazidime or cefepime, sulperazone 1-2g every 8-12 hours)
- Carbapenems (imipenem or meropenem) have been showed to be effective

Monotherapy vs Polytherapy

- Monotherapy with Tazocin, carbapenems, sulperazone, cefepime- equally effective
- Documented infection with gram-negative bacilli- Aminoglycoside-ceftazidime with synergistic

- Aminoglycoside plus ceftazidime for the first 72 hours of therapy, and discontinuing the aminoglycoside if initial cultures were negative for aerobic gram-negative bacilli

Vancomycin

- The patient is known to be at risk of methicillin resistance- those with indwelling catheter and persistant fever despite empirical therapy

ESBL

- Extended-spectrum β-lactamase (ESBL) causes resistance to most β-lactam antibiotics and often is associated with resistance to aminoglycosides, trimethoprim-sulfamethoxazole, and fluoroquinolones.
- carbapenems

Adjustment of antimicrobial therapy

- Changes in the empirical therapy will not be made in the first 3 days unless the patient's clinical status deteriorates
- Therapy will be continued until neutropenia resolves (neutrophil count >500/μL)

- If no clear infection is noted, no positive cultures found, and the patient is stable, parenteral therapy can be changed to oral therapy after two or more afebrile days

- Antibiotic therapy with ciprofloxacin and amoxicillin/ clavulanate has been suggested as reasonable oral agents for follow-up therapy.

- For neutropenic patients who remain febrile after 3 days of empirical broad-spectrum antibiotics or whose conditions deteriorate, one may consider adding vancomycin, or switching to carbapenems (ESBL)

- If vancomycin is added but there is no clear response or no isolation of a gram-positive organism, vancomycin should be discontinued and one should consider adding amphotericin B (AmB)

Fungal Infections

- Up to 20% of patients with neutropenia may experience an invasive fungal infection, and autopsy studies suggest that invasive fungal infections occur in as many as 40% of patients with hematological malignancies.

- The most common fungal infections in this group include superficial and invasive infections due to Candida species and invasive aspergillosis.

Invasive candidiasis

- The presence of the central catheters, use of corticosteroids, broad-spectrum antibiotic exposure, mucositis, and longer duration of neutropenia.

- Candida albicans, followed by C. tropicalis, C. glabrata and C. parapsilosis overall mortality among patients with invasive Candida infections approaches 60%
- Some patients may develop endophthalmitis and chronic disseminated hepatosplenic candidiasis
- These complications may present after neutrophil recovery

Invasive Aspergillosis

- High mortality (up to 80%) in neutropenic patients

- The lungs are the portals of entry, and risk factors include long duration of neutropenia, use of glucocorticosteroids and other immunosuppressive agents, and chronic graft-versus-host disease.

- Parenteral itraconazole and caspofungin are indicated for cases of refractory aspergillosis that are unresponsive to or intolerant of initial therapy with an AmB formulation.

- A characteristic appearance on high-resolution computed tomography scan of the lung, the so-called “halo sign”, is particularly suggestive of invasive aspergillosis, and – less commonly – nocardiosis and mucormycosis.

- Determination of fungal antigens (eg Aspergillus galactomannan), fungal metabolites (eg arabinito), or polymerase chain reaction-based assay can detect yeast and mould infection.
- Febrile patients who are positive for fungal antigens or have suggestive x-ray findings should be given preemptive antifungal therapy.

- If no fungal organism is isolated, antifungal treatment should continue until neutropenia resolves

- G-CSF or GM-CSF shortens the duration of neutropenia, but with no clear reduction in morbidity and mortality.

- Transfusion of white blood cells for febrile neutropenic patients have not yielded conclusive results.
- Transfusion is recommended for patients with proven bacteria infections who have not responded to appropriate antibiotics.

Out patient Management of Patients with Neutropenic Fever

- Low risk patients are candidates for outpatient management – these are patients with solid tumors receiving conventional chemotherapy, with expected duration of neutropenia for 7 days or less, who are clinically stable and have simple infections such as cellulitis or no obvious focus of infection.

- Oral outpatient regimens generally include a quinolone (ciprofloxacin 500-750 mg twice daily) in combination with amoxicillin/clavulanate (375 mg three times a day), or a macrolide.

- High-risk patients with severe (ANC <100) and prolonged neutropenai (>14 days), recipients of allogeneic bone marrow/ stem cell transplants, clinically unstable patients, and patients with a poor performance status or complex infection such as pneumonia or meningitis.

Thrombocytopenia 血小板減少症

- If Bleeding, transfuse when platelet counts <50x 10^9/L

  如果出血、輸血時血小板數量<50x 10^9/L
- Prophylactic transfusion for platelet counts ,10 x10^9/L

  血小板數量的預防性注射

Special blood products 特殊的血液制品

- Irradiated blood products to prevent Graft versus Host Disease (bone marrow transplant recipents) 受照射的血液制品以預防 移植體對主反應 (骨髓移植接受者)
- Patents receiving Fludarabine 患者接受福達樂靜脈凍晶注射劑

CMV negative blood products
巨細胞病毒陰性血液制品

- CMV negative patients who are candidate for bone marrow transplant.

患有陰性巨細胞病毒的骨髓移植輪候者

Filtered (Leucocytes depleted) blood products
去除白細胞血制品/ 濾除白細胞血制品

- Prevent febrile non-hemolytic transfusion reactions 預防非溶血性輸血反應
- Reduce allo-immunisation 減少免疫系統變異
- Reduce CMV transmission 減低巨細胞細菌傳輸/ 感染

Other side effects 其他副作用

- Nausea/Vomiting- 噁心/ 嘔吐
- Alopecia 脫髮
- Specific toxicity 特殊毒性
- Anthracyclines-cardiotoxicity
  阿霉毒引起的心臟毒性
- Bleomycin/ Bulsulphan-pulmonary fibrosis
  博萊霉素/ 肺臟纖維化毒性
- Cis-platinum –renal toxicity
  順鉑- 腎毒性反應
- Secondary malignancy
  次發性惡性腫瘤