Neutropenia with and without fever

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Introduction

- History and Definition of neutropenia
- Work-up of neutropenia
- Work-up of febrile neutropenia
- Risk Stratification
- Initial Antibiotic Treatment
- On-going management/inpatient management
- Summary

Definition of Neutopenia

- **Neutropenia** $<0.5 \times 10^9$ (or <1.0 with predicted decline to <0.5)
- Typically secondary to treatment effect (eg chemo, radiation) or bone marrow infiltration of tumour (which usually results in low hemoglobin and platelets)
- Main concern is risk for serious or atypical infections – usually indicated by fever

Neutropenia secondary to Chemo

- Generally we expect some neutropenia
- If patient develops **febrile neutropenia** or a **dose delay** they will be considered for GCSF (Granulocyte Colony Stimulating Factors)
- May be some cases where primary prevention (start following first chemo) is indicated

Neutropenia secondary to Tumour

- This is often treated with chemotherapy
- Patients may require dose delays and must be assessed carefully

Neutropenia secondary to Radiation

- Usually occurs when a large area of bone marrow is radiated (pelvis)
- Usually will resolve but while neutropenic must be followed carefully for infection

Definition of Febrile Neutropenia

- **Febrile** - >38 on 2 occasions or >38.3 on one occasion (not necessarily febrile in ER) AND
- **Neutropenia** <0.5 (or <1.0 with predicted decline to <0.5)
- Chemo induced FN first identified in the 1970's – mortality rate was >50%
- Currently mortality rate <5% with proper identification and management
- Only 30-50% of patients have identified source of infection

Watch for

- FN generally occurs 7-10 days after chemo but some chemotherapy (eg taxanes) can occur <3 days after treatment
- Patients taking tylenol/prednisone
- Patients on GCSF (neupogen, neulasta) and those on prophylactic antibiotics
- Other non-infectious causes such as PE, drug reaction, tumour fever

Work-up

- **All patients on chemo** (or those with hematologic tumours regardless if on chemo) **with fever** should be considered **febrile neutropenia until proven otherwise**
- **They must be assessed by a physician urgently**
- 'complete physical exam' looking for atypical sites (mouth, IV sites) – NO rectal exam
- Investigations – CBC/diff, blood cultures x 2 sets (one peripheral and one per lumen of catheter), culture of any other suspected sites, CR, lytes, LFT's, CXR

Risk Stratification – who to discharge

- 70% of patients are low risk – well identified risk stratification

Low risk: clinically stable (HR, BP)
solid tumour(not lymphoma/leuk)
duration of Neut expected <7d
no serious co morbid illness
adequate renal/hepatic fcn
geographically accessible for f/u
suitable home circumstances

Who to admit to hospital

- If unstable
- Transplant patient/leukemia/lymphoma/bone marrow involvement by cancer
- Obvious source of infection (esp catheter infection, evidence of neutropenic enterocolitis)
- Febrile for more than 48 hours
- Does not meet criteria for low risk

- Some of these patients **may be sent home by heme/onc** on oral antibiotics on **a case by case basis** after assessment

Out-patient Antibiotics

- Cipro 750 mg po q 12 h and amoxicillin/clavulanate 875/125 mg po q 12h
- If **PEN allergic** then cipro 750 mg po q 12 h and clindamycin 450 mg po q 8h
- Suggest 5 day supply – optimal to give first dose in ER
- **If patient already on cipro (or allergic) should not be considered low risk**

On-going management

- Patients are seen daily in cancer centre until neutrophils recover and are afebrile
- If they continue to spike temps, become clinically unstable or have a positive blood culture they are brought into hospital for IV antibiotics
- Generally we do not start neupogen unless they are in ICU or very unwell, general **first line IV antibiotic is ceftazidime 1-2 gm IV q8h**

Summary of Outpatient Protocol

- 70% of patients are low risk and can be treated as an outpatient safely (<5% risk of complication and <1% risk of death)
- Need to be appropriately assessed and treated with ongoing follow-up until neutrophils and fever recover
- In high risk patients or those not treated appropriately the risk of serious medical complication and death can be as high as 20%

Inpatient Management

- Start on **broad spectrum** antibiotic (Ceftazidime)
- If the patient has a positive culture the antibiotics are adjusted to treat this organism
- If **fevers continue** consider coverage for line infection (Vanco), PCP (Septra), Aspergillous (Amphoteracin), Herpes (Acylovir), Candida (Fluconazole), CMV (Gancylovir) – and ID consult

Summary

- Neutropenia results in a high risk of developing serious infections
- Fever in these patients is an oncologic emergency and they must be urgently assessed by a physician
- A subgroup of patients are low risk and may be managed as outpatients