Febrile Neutropoenia in Paediatric Oncology

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Aims & Objectives

- Be able to:
  - Define terms
  - Describe groups at risk
  - Assess patients rapidly and safely
  - Outline initial assessment & management
  - Understand further treatment

APPHON GUIDELINES

- www.apphon-rohppa.com/en/guidelines

Definitions - Oncology

- **Neutropoenia**
  - ANC < $1.0 \times 10^9/L$
- **Severe neutropoenia**
  - ANC < $0.5 \times 10^9/L$
- **Profound neutropoenia**
  - ANC < $0.1 \times 10^9/L$

Definitions - Oncology

- **Fever:**
  - >38.3^{o}C x 1 reading
  - >38.0^{o}C over 1 hour persistently
  - Tympanic or oral preferred
  - Axillary acceptable (threshold 37.5^{o}C)
  - **NEVER RECTAL**

Why so aggressive?

RISK OF OVERWHELMING SEPSIS AND DEATH

Why so aggressive?

- 10-20% cases have positive bacterial cultures
- ~20% develop septic shock
  - sepsis + sustained hypotension needing fluid resuscitation
  - Can be culture pos or neg
- Mortality ~5%

Which patients at risk?

- Patients on active chemotherapy
- Patients post HSCT/BMT
- Other immunosuppressed patients
- Neutropoenia – other causes
  - Congenital neutropoenia (e.g. Kostmann's)
  - Autoimmune neutropoenia
  - Infection-related suppression

Who is at "High risk"?

- Age < 1 year
- Post Stem Cell Transplant
- AML on therapy *
- Bone Marrow infiltration
- Immunodeficiency (e.g. Down Syndrome)
- Sepsis (or previous sepsis)
- Typhlitis
- Prosthesis
- Possible Staphylococcal infection

Who is at "low risk"?

- Expected neutropoenia <7 days
- No comorbid symptoms (e.g. rigors)
- Negative blood cultures
- In remission
- No significant mucositis/organ failure
- > 1 year old
- Rapid resolution of fever

Beware!

- SICK, SEPTIC CHILD 39.5^{o}C
  - Persistent Hypotension
  - Capillary refill > 3 seconds

Beware!!

- AFEBRILE SEPSIS
  - On high dose/prolonged dexamethasone + anthracyclines
  - ANC < 0.1 x 10^9/L

Beware!!!

- Can be septic without positive cultures
- May have meningitis with minimal signs
- Sepsis often with gram -ve organisms and/or mixed organisms
- Rigors & fever with line flushing suggests CVL infection

Beware!!!!

- REMEMBER:
  - Cannot make pus without neutrophils
  - Signs of infection may be very soft
  - Check perineum and perianal pain

Organisms

- Gram negative
  - E coli
  - Pseudomonas spp
  - Klebsiella spp
- Gram Positive
  - Streptococcus spp
  - Staphylococci - aureus & coag negative

Initial Assessment

- NEEDS RAPID ASSESSMENT & MANAGEMENT
- Be in ER within 1 HOUR of fever
- Be assessed, CBC & diff and start antibiotics within 1 HOUR of arrival

History

- Current symptoms & duration
- Date of start of last cycle chemo
- Exposure to infections
  - Colds/flu
  - chickenpox
- Recent drugs & antibiotics given
- Ask for Treat Promptly card

Signs and Symptoms

- Fever
  - Irritable/listless
  - Rigors
    - Esp with line flush
  - Tachycardia
  - Flushed & unwell
  - Cold & clammy

Other signs/symptoms

- Mucositis
- Abdominal pain +/- diarrhoea
- Perianal pain
- Cough/respiratory symptoms
- Rashes
- Altered conscious state
- urinary symptoms

Examination

- Full physical examination please
- Include
  - Skin
  - Perianal/genital area
  - Ears & throat
  - Mouth
  - Signs of meningism
  - Fundi

Examination !

- Please:
  - **NO rectal temperatures**
  - **NO rectal exams**

Investigations

- CBC & Diff immediately
- Blood cultures (aerobic/anaerobic/fungal)
  - All lumens of CVL immediately
  - Peripheral culture only if no CVL
- Culture any suspect site
  - Urine
  - Throat
  - Respiratory/NPA etc
- +/- CXR
  - Only if lower respiratory signs/symptoms

Treatment - initial

- ABC
  - Initial resuscitation if needed
- Antibiotics - immediately after cultures
  - Broad spectrum IV – e.g.
    - Tobramycin & Piperacillin/Tazobactam
    - Ceftazidime & Tobramycin
  - Add:
    - Vancomycin if high risk or symptoms suggest CVL infection
    - Metronidazole if significant GI symptoms
    - Aciclovir IV if chickenpox or oral herpes

Treatment - supportive

- IV fluids
  - ~ 100 ml/m^2/hour or 1.5 x maintenance
- Blood as necessary
  - Hb < 70 g/L
- Platelets as necessary
  - Plt < 20 x 10^9/L
- Continue Cotrimoxazole (prophylaxis)
- Call Haematologist/Oncologist on call

Uncomplicated course

- Antibiotics minimum 48 hours
- Fever settles
- Low risk
- Cultures negative
- Neutrophils recovering (~0.5 x 10^9/L)

Next Steps

- Antibiotics - minimum 48 hours
- Persisting fever
  - Re-culture q24h
- Additional symptoms/complicated
- Re-consult haematologist/oncologist
  - Consider transfer to sub-speciality site
  - Change/add antibiotics/antifungals

Positive Cultures

- Bacterial culture
  - Tailor antibiotics to sensitivities
  - 14 days treatment
  - Consult Paediatric ID also
  - Consider removal of CVL

Treatment – Fungal

- Persistent fever or positive culture
  - Add Amphotericin B lipid formulation
    - e.g. 3 mg/Kg/day AmBisome
    - Minimum 7 days or until ANC >0.5 x 10^9/L
  - Other antifungals as appropriate
    - Fluconazole prophylaxis indicated for some patients
    - 5-Flucytosine
    - Voriconazole
    - Caspofungin

Viral Infections

- Chickenpox/shingles/oral herpes
  - Aciclovir
    - 5 - 15 mg/Kg TID IV
    - Consider change to oral when improving
- CMV (rare)
  - IV Ganciclovir

Pneumocystis jirovekii

- All oncology patients on prophylaxis

  BUT IF:

- Documented or clinical suspicion
  - Tachypnoea & cough
  - Bilateral infiltrates on CXR
  - IV Cotrimoxazole 30 mg/Kg TID
    - (120 mg/Kg/day)

Summary

- Febrile neutropoenia is major risk
- Treat promptly
  - Assess within 1 hour of fever
  - CBC, diff & Culture
  - Start antibiotics within 1 hour of arrival

Guilty

until proven innocent

Questions?