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Paediatric oncology

Alex Outhred

HK Paediatric Infection Control Workshop 2016

Outline

- Pathogens
  - bacterial
  - fungal
  - viral
- Categories of prophylaxis
  - primary
  - secondary
  - antimicrobial prophylaxis
  - vaccination

Infection risk stratification for neoplasms

- Low- or standard-risk
  - Most solid tumours
  - Most lymphomas
  - standard-risk acute lymphoblastic leukaemia (ALL)
  - neutropenia <10 days
- High-risk
  - high-risk ALL, relapsed ALL
  - acute myeloblastic leukaemia (AML)
  - haematopoietic stem cell transplant / bone marrow transplant (allogeneic and autologous)
  - neutropenia >10 days
  - aplastic anaemia?

Infection risk stratification for neoplasms cont’d

- Remember that these risk categories are imperfect
  - some patients have low-risk malignancy but due to clinical circumstances become high-risk
    - eg. disease extent, intensive chemotherapy, prolonged neutropenia or lymphopenia, comorbidities
  - low-risk includes truly low but also moderate-risk patients
  - use guidelines but assess each patient individually

Prophylaxis for bacterial infections

- Primary prophylaxis against febrile neutropenia
  - controversial
    - probably moderately better patient outcomes in short term
    - demonstrated to lead to higher rates of antimicrobial resistance
    - cotrimoxazole as a compromise?
    - restrict to high-risk patients?
- Secondary prophylaxis against febrile neutropenia
  - cultures negative
    - standard practice to continue (oral or IV) empiric antimicrobials until neutrophil recovery
    - is this necessary? (limited evidence base to argue for or against)
  - cultures positive
    - continue directed therapy according to organism and site of infection
    - continue until neutrophil recovery unless low-risk infection (eg. CoNS)

Prophylaxis for bacterial infections: other bugs

- *Nocardia*
  - seems to be rare in children
  - cotrimoxazole (given for other reasons) likely to be effective
- *Mycobacterium tuberculosis*
  - patients with latent TB infection should receive appropriate treatment (eg. isoniazid)
  - difficult to determine LTBI status, especially in patients already immunocompromised
  - can try to screen family and use exposure history as risk indicator if lymphopenic and/or interferon gamma release assay produces invalid result
- Vaccines for primary prophylaxis
  - major limitation is impairment of immune response to vaccine during malignancy and therapy
  - vaccinate family, and patient pre-treatment if feasible
  - vaccinate patient ~6 months post completion of therapy (no live vaccines):
    - *Streptococcus pneumoniae* conjugate vaccine
    - *Haemophilus influenzae* serotype b
    - *Neisseria meningitidis* serogroups A, C, W135, Y conjugate; serogroup B OMV?
    - *Bordetella pertussis*, tetanus, diphtheria
    - no BCG, too risky

Prophylaxis for central line infections

- Central line-associated bloodstream infections (CLABSIs) must be monitored
- Total line-days should be measured as a denominator
- If your rate of CLABSIs is >1 per 1000 line-days
  - you know you could be doing better, and should try to improve
- If rate is <1 per 1000 line-days
  - focus on highest-rate units/teams to improve further, CLABSIs nearly all preventable
- Address CLABSIs with a “bundle”
  - what does that mean?
  - an array of quality improvement measures
    - patient selection
    - line selection
    - line insertion
    - line access
    - line removal
    - training/certification for all personnel involved
    - auditing, surveillance

Prophylaxis for central line infections cont'd

- Other measures:
  - antimicrobial-impregnated lines are not needed to achieve <1 CLABSI per 1000 line-days
    - can be useful for certain patients, or settings where other interventions challenging
  - taurolidine locks can be used instead of heparin
    - Handrup MM, Møller JK, Schrøder H. doi:10.1002/pbc.24482

Prophylaxis for fungal infections: yeast and mold

- Options for antifungal prophylaxis
  - Standard risk - yeast prophylaxis
    - fluconazole (eg. 8 mg/kg/day)
  - High-risk - yeast and filamentous fungus prophylaxis
    - liposomal amphotericin (eg. 1 mg/kg x3 doses per week)
    - itraconazole (eg. 2.5 mg/kg Q8h, target trough >0.5 mg/L)
    - posaconazole (eg. 5 mg/kg Q8h, target trough >0.7 mg/L)
    - voriconazole (eg. 9mg/kg Q12h, target trough >1.0 mg/L)
    - micafungin (eg. 1 mg/kg/day)
  - Monitoring and pre-emptive treatment is an alternative to prophylaxis
    - but need vigilance & capacity to monitor closely eg. with radiology plus galactomannan
- Secondary prophylaxis
  - as above, after completion of antifungal treatment, even if in “low-risk” category

Prophylaxis for fungal infections: *Pneumocystis*

- High-risk patients - *Pneumocystis* prophylaxis
  - cotrimoxazole (eg. 25/5 mg/kg 3 times per week, or 12.5/2.5 mg/kg/day)
    - may also act as primary prophylaxis for bacterial infections
  - dapsone? (few advantages)
  - nebulised pentamidine (eg. 300 mg every 4 weeks via special inhaler)
  - intravenous pentamidine (eg. 4 mg/kg every 4 weeks)
  - atovaquone (complex dosing, eg. ~30 mg/kg daily)
- Same for low-risk patients if lymphopenia, prolonged course of therapy
  - generally low threshold for giving cotrimoxazole prophylaxis

Prophylaxis for parasites: *Toxoplasma*

- Patients who are seropositive and:
  - high-risk
  - low-risk with prolonged lymphopenia
- Options:
  - cotrimoxazole
  - dapsone-pyrimethamine
  - atovaquone

Prophylaxis for parasites: *Strongyloides*

- *Strongyloides* hyperinfection is devastating with high mortality rate
- *Strongyloides* subclinical infection is very common in low-resource settings
- How to test for *Strongyloides*?
  - serology is not always available, and has modest sensitivity (~70-80%)
  - *Strongyloides* culture
    - not always available
    - hazardous to lab staff
    - more sensitive than serology when testing serial specimens
    - may still miss infections that are revealed after immune suppression
- Think about patient background, if *Strongyloides* risk elevated:
  - can test (serology or culture) up-front, or
  - culture regularly during immunosuppression
- Ivermectin is drug of choice for treatment
  - generally retreat after ~2 weeks
  - (hyperinfection requires aggressive treatment, ~50% mortality)

Prophylaxis for viral infections: cytomegalovirus (CMV)

- Big topic, worth it's own lecture?
- For high-risk patients who are seropositive, consider:
  - ganciclovir (eg. 5 mg/kg/day)
  - valganciclovir (eg. 7mg x BSA x eGFR daily)
  - SOT and HSCT patients are highest risk
- Another strategy is to monitor CMV load
  - commence preemptive therapy when viral load is rising
- Should be evaluated as potential cause of fever in low-risk patients
- Secondary prophylaxis is indicated after clinical CMV disease
- Resistance to antivirals can be a major problem

Prophylaxis for viral infections: Epstein-Barr virus (EBV)

- No antivirals proven to work as prophylaxis or treatment
- For patients post-transplant (solid organ or HSCT):
  - monitor EBV load
  - need to reduce immunosuppression if rising viral load
  - risk of post-transplant lymphoproliferative disease (PTLD)
  - treatment targets B lymphocytes, not EBV

Prophylaxis for viral infections: HHV-1 (HSV)

- All high-risk patients and all leukaemia patients
  - check serology before treatment
  - if IgG positive, give aciclovir prophylaxis (eg. 10-20 mg/kg Q12h)
  - regardless of risk level, secondary HSV prophylaxis recommended after HSV disease
  - valaciclovir and famciclovir used in adults, but used less in paediatrics

Prophylaxis for viral infections: influenza

- Vaccination
  - live attenuated intranasal vaccine is a good option in general, but for patients already immunocompromised use standard haemagglutinin vaccine
- Antiviral prophylaxis is available
  - need to explain to family so they'll know to use it if there is an exposure

Prophylaxis for viral infections: RSV

- Palivizumab
  - very expensive
  - modest efficacy
    - high number needed to treat (NNT) to prevent one bad outcome
  - need to find a compromise that you can afford
    - in my institution, it’s hardly ever used
    - if it cost $50 per dose we’d use it all the time, starting with high-risk infants

Prophylaxis for viral infections: misc respiratory

- Cause significant morbidity in paediatric oncology patients
- No specific prophylaxis available
- High-risk patients can wear masks when leaving room
  - (challenging for infants!)
- Isolate patients to prevent hospital transmission
  - syndromic basis first and foremost
  - testing for respiratory viruses may facilitate cohorting patients with the same virus
  - repeat testing generally unhelpful as test of cure / noninfectious status
- Droplet plus standard precautions (hand hygiene)

Prophylaxis for viral infections: vaccine preventable

- Similar recommendations to vaccines for bacterial infections
- Check vaccine history and antibodies before starting therapy
- Ensure family members are fully vaccinated
- Vaccinate the donor if possible
- Killed or component vaccines can be given >2w pre-transplant and >6 months post-transplant
  - eg. Salk polio, HBV, HAV, influenza haemagglutinin
- Live vaccines are more complicated
  - Sabin polio is not recommended at any time
  - Measles, mumps, rubella and VZV
    - can give >4 weeks pretransplant to most patients (after assessment)
    - can give at 24 months posttransplant (but not if GVHD, significant immunosuppression)

Summary

- Bacteria, fungi, parasites, viruses
- Primary and secondary prophylaxis
- Use of antimicrobials and vaccines
- Patient risk stratification