Infectious complications in the pediatric oncology patient

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Disclosures

- No financial disclosures
- Off-label use of medications will be discussed

Learning Objectives

- Review risk factors in the pediatric oncology patient for development of infectious complications
- Identify important infectious pathogens in the pediatric oncology patient
- Discuss a systematic approach for evaluating and managing common infections for the Advanced Practice Provider (APP)
- Describe risk-stratification approaches in addressing fevers in the pediatric oncology patient
- Discuss the role of preventative measures and antibiotic stewardship in this vulnerable patient population

Overview of Childhood Cancer

- In 2014: 15,780 cases of childhood cancer (0-19 years)
- Types of childhood cancer:
  - Hematologic malignancies
    - Leukemia (ALL, AML), Lymphoma
  - Solid tumors
    - CNS tumors, neuroblastoma, osteosarcoma, Ewing’s, Wilm’s, GCT, rhabdomyosarcoma, retinoblastoma
- 5-year survival rate >80%

Source: American Cancer Society, Cancer Facts and Figures (2016)
**Innate Immunity**

- Detection of microorganisms & first-line of defense
- Does not provide long-lasting immunity
- Regulation of inflammation
- Phagocytosis (neutrophils, monocytes, macrophages)
- Severe neutropenia (ANC) <500 cells/mm³
  - Risk of infection increases with decreasing ANC

**Adaptive Immunity**

- Antigen specificity (T-cells and B-cells)
- Production of antibodies (B-cells)
- Role of T-cells:
  - Kill virus-infected cells
  - Signal B-cell antibody synthesis & memory B-cell formation
  - Activate macrophages
- Development of immunological memory

**Lymphatic system**

- Spleen – major lymphopoietic organ
- Contains ~25% of total lymphoid mass of body
- Major function: remove particulates from blood stream (opsonized bacteria, antibody-coated cells)
- Important in infections with encapsulated organisms
- Functional asplenia (RT)

**Multimodal therapy**

- Chemotherapy
- Surgery
- Corticosteroids
- Radiation therapy (field, dose)
- Immunotherapy (monoclonal antibodies, interferons, interleukins, CAR-T cell therapy, oncolytic virus therapy, cancer vaccines)
- Hematopoietic stem cell transplant (HSCT)

**Other risk factors**

- Age (infants <1 year)
- Comorbid conditions (Down Syndrome)
- Intensity & length of therapy
  - Induction therapy (ALL)
  - AML therapy
  - Relapsed disease
- Presence of foreign bodies (CVLs, G-tubes, VP shunts, Ommaya reservoirs)
- Immunization status

**Other risk factors**

- Mucosal breakdown
- Skin breakdown (perianal)
- Poor nutrition
- Prolonged hospitalizations
- Antibiotic therapy
- Gastric acid suppressants
Infectious etiologies

Bacterial  Viral  Fungal

• Overall infection-related mortality rate 0.5-6.6% in pediatric fever and neutropenia

Bacterial infections

• Concern for gram negative sepsis
• Rapid progression if not identified early:
  Bacteremia → sepsis → septic shock

**All neutropenic patients who are febrile, or any patient who is toxic-appearing, are considered bacteremic until proven otherwise**

Risk factors

• Intensity of therapy (AML, ALL Induction)
• Neutropenia (duration, intensity)
• Mucositis
• Down Syndrome (DS)
• Invasive devices
• Antibiotic therapy

• Most important reduction in risk for significant bacterial infection is recovery of neutrophil count

Sources of bacterial infection

• Most commonly from endogenous flora:
  – Skin flora (CVL)
  – GI flora (mucosal breakdown)
• Nosocomial
• Community-acquired

Bacterial pathogens

• Gram-positive organisms:
  – Staphylococcus spp.* (S.epidermidis, S.aureus)
  – Streptococcus spp.* (alpha-hemolytic)
  – Enterococcus spp.* (E.faecium, E.faecalis)
  – Corynebacterium spp.* (C.jeikeium)
  – Listeria monocytogenes
  – Bacillus spp. (B.cereus, B. circulans, B.licheniformis)
  – Clostridium spp. (C.dificile, C.septicum. C.tertium)

Bacterial pathogens

• Gram-negative organisms:
  – Enterobacteriaceae (Escherichia coli*, Klebsiella spp.*, Enterobacter spp., Serratia spp.)
  – Pseudomonas aeruginosa*
  – Stenotrophomonas maltophilia
  – Anaerobes (Bacteroides spp., Clostridium spp., Prevotella spp.)
**Bacteremia**

- Transition from predominantly gram-negative organisms to gram-positive organisms since 1970s
- Contributing factors:
  - Increased use of indwelling catheters
  - Widespread use of empiric antibiotics
  - More intensive chemotherapy regimens († mucositis)
- Higher mortality rate with gram-negative bacteremia

**Presentation**

- Fever may be only presenting symptom, especially in neutropenic patient
- Other possible signs/symptoms:
  - Shaking chills
  - Altered mental status
  - Abnormal VS (†HR, ‡BP, †RR)
  - Poor peripheral perfusion
- Risk for rapid decompensation without intervention

**Diagnosis**

- Blood cultures from all catheter sites +/- peripheral cultures
  - Important to obtain aerobic & anaerobic cultures from each site with sufficient volume
- Other cultures obtained based on presenting symptoms (urine, stool, CSF, sputum, wound)

**Blood culture volume**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Total volume (1st set) (Divide into aerobic &amp; anaerobic bottles)</th>
<th>Total volume (2nd set) (Divide into aerobic &amp; anaerobic bottles)</th>
<th>Total mLs (approx. % of total blood volume)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;9 kg</td>
<td>1 mL (0.5 mL/bottle)</td>
<td>1 mL (0.5 mL/bottle)</td>
<td>2 mL</td>
</tr>
<tr>
<td>9-14 kg</td>
<td>3 mL (1.5 mL/bottle)</td>
<td>3 mL (1.5 mL/bottle)</td>
<td>6-10 mL</td>
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<tr>
<td>15-27 kg</td>
<td>5 mL (2.5 mL/bottle)</td>
<td>5 mL (2.5 mL/bottle)</td>
<td>10-20 mL</td>
</tr>
<tr>
<td>28-41 kg</td>
<td>10 mL (5 mL/bottle)</td>
<td>10 mL (5 mL/bottle)</td>
<td>20-30 mL</td>
</tr>
<tr>
<td>&gt;42 kg</td>
<td>20 mL (10 mL/bottle)</td>
<td>20 mL (10 mL/bottle)</td>
<td>&gt;40 mL</td>
</tr>
</tbody>
</table>

*% of the total blood volume is the maximum blood volume that can be drawn from a patient for each blood culture draw

Adapted from LPCH Blood Culture Procedure

**Management**

- Blood cultures first
- Prompt initiation of broad-spectrum IV antibiotics is the most important therapeutic intervention to minimize complications (within 30-60 minutes)
- Appropriate antibiotic therapy modification based on identification and sensitivity of causative organism
- Minimum treatment of 14 days after first negative blood culture; may be longer depending on organism

**Antibiotic therapy**

- Importance of early administration of IV antibiotics
- Broad-spectrum coverage (including Pseudomonas)
- Combination therapy vs. monotherapy
- Antibiotic selection based on institutional preference and local resistance patterns
- Consider I.D. consult
Antibiotic combination therapy

- Cephalosporin (Ceftazidime) + aminoglycoside
- ß-lactam (Piperacillin-Tazobactam) + aminoglycoside

**Benefits:**
- Provided expanded anti-bacterial spectrum
- Enhanced potential synergistic interaction
- Prevent emergence of resistance

**Disadvantages:**
- Potential for increased toxicity

Combination antibiotic therapy

- Considerations for use:
  - Patient instability
  - Concern for resistant pathogens (*Pseudomonas, Acinetobacter, Citrobacter, Enterobacter, Klebsiella spp.)*
  - Need for synergism for specific pathogens (*Enterococcus, Mycobacterium spp., MRSA)*
  - Certain infections (endocarditis, cryptococcal meningitis)

Antibiotic monotherapy

- Found to be non-inferior to combination therapy
- Newer generation 4th generation cephalosporins
  - Cefepime
- Extended-spectrum ß-lactam Penicillin
  - Piperacillin-Tazobactam
- Carbapenems
  - Meropenem
  - Imipenem-Cilastatin
  - Ceftriaxone

Additional antibiotic coverage

- Consider adding Vancomycin in patients:
  - Presenting with hypotension, cardiopulmonary deterioration
  - Receiving high-dose ARAC (risk of alpha hemolytic strep)
  - Severe mucositis
  - Skin/soft tissue infection
  - Pneumonia
  - Clinical suspicion of CVL infection
  - History of MRSA

Addition antibiotic coverage

- Consider adding Metronidazole in patients:
  - Requiring better anaerobic coverage
  - Abdominal pain
  - Clinical suspicion of typhilitis

Severe, resistant infections

- VRE, MRSA, other gram-positive resistant organisms
  - Linezolid
  - Daptomycin
  - Quinupristin/Dalfopristin
- Usually require ID consult to use
- Not first-line therapies
- Use judiciously
CVL Infection

• Consider removal of CVL:
  – Recurrent infection
  – No response of antibiotics after 2-3 days
  – Evidence of tunnel or port-pocket infection
  – Septic emboli
  – Hypotension associated with catheter use
  – Non-patent catheter
  – Bacteremia from Bacillus spp., Pseudomonas, Stenotrophomonas maltophilia, C. jeikeium, VRE, Acinetobacter

Typhlitis (neutropenic colitis)

• Infectious and inflammatory process in the cecum
• May also involve ascending colon and ileum
• Severe and life-threatening
• Main pathologic findings:
  – Hemorrhagic necrosis
  – Ulcerations with bacterial colonization
  – Transmural inflammation
  – Thickening of bowel wall

Risk factors

• Prolonged neutropenia
• Hematologic malignancies (Burkitt’s lymphoma, AML)
• High-dose Cytarabine (ARAC) or Methotrexate (MTX)
• Mortality rates up to 20% have been reported

Presentation

• Non-specific s/s may mimic other underlying conditions
  – Fever
  – Abdominal pain (RLQ, diffuse)
  – Diarrhea
  – Abdominal distention
  – Nausea/vomiting
• High index of suspicion

Diagnosis

• Abdominal xray – low diagnostic value
• Ultrasound
• CT – higher accuracy
  – Demonstrate bowel wall thickening
  – ≥10 mm – highest risk
• Lab findings – non-specific
Treatment

- Conservative management:
  - Broad-spectrum antibiotics (gram-positive, gram-negative, & anaerobic coverage)
  - Bowel rest
  - Abdominal decompression
  - Aggressive fluid resuscitation
  - Correction of electrolyte abnormalities

- Surgical management reserved for high-risk or complicated/severe cases:
  - Evidence of bowel perforation
  - Uncontrolled bleeding after correction of cytopenia and clotting abnormalities
  - Development of abscess, appendicitis
  - Clinical deterioration
  - Perforated or necrotic appendicitis
  - Primary anastomosis not recommended

Clostridium difficile infections

- C. diff – anaerobic, gram-positive, spore-forming, toxin-producing bacillus
- Spores found in environment – metabolically dormant
- Resistant to heat, acid, antibiotics, and most disinfectants
- Can persist on hospital surfaces for months
- Increasing incidence of infection

Risk Factors

- Antibiotic exposure (esp. PCNs, cephalosporins, Cefepime, clindamycin, fluoroquinolones)
- Immunosuppression
- Use of PPIs
- Impaired intestinal mucosa
- Increased exposure to healthcare settings
- Gastrostomy/jejunostomy tubes

C. difficile

- Presentation:
  - Diarrhea with mucus or blood
  - Abdominal cramps/pain
  - Fever
- Complications:
  - Toxic megacolon
  - Intestinal perforation
  - Systemic inflammatory response syndrome
  - Death

Diagnosis

- Stool testing:
  - Glutamate dehydrogenase (GDH) antigen
  - Enzyme immunoassay (EIA)
  - PCR – Nucleic acid amplification tests (NANTs)
  - Two-step algorithms (if + GDH → PCR)
  - Cell culture cytotoxicity assay (not commonly used)
- Important to run test promptly after collection
**C.Diff treatment**

- Vancomycin (PO) preferred for severe or complicated infection
  - Usual duration 10-14 days (tailored to clinical response)
  - Recurrent infections can be treated with longer courses of Vancomycin (up to 7 weeks with taper)
- Metronidazole for mild/moderate infection
  - PO treatment for 10-14 days
  - IV Metronidazole in unable to tolerate POs

**C.Diff prevention**

- Strict infection control
  - Isolation (contact plus+ precautions) as soon as symptoms present
  - Good hand hygiene (soap & water only)
  - Environmental cleaning (bleach solution)
- Antibiotic stewardship

**Viral infections**

- Varicella zoster (VZV)
- Herpes Simplex (HSV)
- Influenza A & B
- Respiratory Syncytial Virus (RSV)
- Parainfluenza
- Adenovirus
- Human metapneumovirus
- Cytomegalovirus (CMV)
- Epstein-Barr Virus (EBV)
- Human Herpes Virus-6 (HHV6)

**Varicella zoster virus (VZV)**

- Human herpesvirus 3
- Varicella (disseminated) and herpes zoster (localized) infections
  - Zoster infections can disseminate in immunocompromised patients
- Highly contagious
- Contact with upper respiratory tract mucosa or conjunctiva
- Person-to-person transmission by airborne route from direct contact with VZV lesions

**Varicella zoster virus (VZV)**

- Patients are contagious 1-2 days prior to onset of rash, until all lesions have crusted over
- Usual incubation period 14-16 days (range 10-21 days)
- Risk factors:
  - Immunosuppressive therapy
  - Corticosteroids
- Immunocompromised patients are at increased risk of severe disease
Zoster infection

Diagnosis

- VZV PCR* (vesicle swab/scraping, crusted lesion, tissue biopsy, CSF)
- VZV DFA (vesicle, lesion base)
- Viral culture (vesicular fluid, CSF, tissue biopsy)

- Not useful:
  - VZV IgG (serum)
  - VZV IgM (serum)

Treatment

- Maximum benefit if started within 24 hours of rash onset
- Anti-viral agents:
  - IV Acyclovir
  - PO Valacyclovir (may consider in low-risk patients)
- VariZig
  - Administered ASAP after exposure
  - Ideally given within 96 hours
  - Can be given up to 10 days after exposure
- IVIG (if VariZIG unavailable)

Isolation

- Airborne and contact precautions (localized or disseminated disease) in immunocompromised patients
- For duration of illness
- Important to identify potentially exposed patients

Varicella complications

- Secondary infection of skin lesions (strep, staph)
- Immunocompromised patients at risk for:
  - Cutaneous dissemination
  - Visceral organ involvement
    - Pneumonia
    - Hepatitis
    - Encephalitis
- Primary VZV – ~10% mortality rate in untreated children with leukemia

Fungal infections
Types of fungus

- Yeast ➔ single cell, reproduce by budding
- Mold ➔ characterized by development of hyphae

Candida

- Most common causative species – *Candida albicans*
- Found on skin, mouth, intestinal tract & vagina
- Person-to-person transmission is rare
- Incubation period – unknown

Risk factors

- Myelosuppresive chemotherapy
- Prolonged neutropenia (AML therapy)
- Corticosteroids
- TPN/IL
- Treatment with broad-spectrum antibiotics
- Long-term CVLs

Candida infections

- Oral/Esophageal/Laryngeal candidiasis
- Vaginal candidiasis
- Candidemia*
- Disseminated/Invasive candidiasis*

Diagnosis

- Culture from sterile body site (blood, CSF, BM) or tissue biopsy
- Negative culture does not exclude infection in immunocompromised host

Treatment

- Echinocandin
  – Micafungin (Disseminated or esophageal candidiasis)
  – Caspofungin (Candidemia)
- Liposomal Amphotericin B
- Fluconazole
- Treat for minimum of 14 days
Invasive Aspergillosis

- Mostly commonly caused by *Aspergillus fumigatus*, then *Aspergillus flavus*
- Route of transmission – inhalation of spores
- Common sources:
  - Soil
  - Dust (e.g., construction or demolition)
  - Plants, vegetables
  - Water supplies (e.g., shower heads)

Risk Factors

- New onset AML
- Relapse of hematologic malignancy
- Prolonged neutropenia
- T-lymph suppressive therapy (corticosteroids)

Diagnosis

- Not usually isolated from blood
- Lung, sinus, skin biopsy usually needed
- Galactomannan testing
- Imaging:
  - Chest xray
  - Chest CT

Galactomannan

- Molecule found in *Aspergillus* cell wall
- Serum or bronchoalveolar lavage (BAL)
- False positives:
  - food sources
  - cross-reactivity with fungal-derived antibiotics
- Negative test does NOT exclude diagnosis
- Use in conjunction with clinical & radiologic findings

Voriconazole

- Treatment of choice for *Aspergillus*
- *Minimum* treatment – 12 weeks
- Close monitoring of serum trough concentrations
- High interpatient variability in metabolism
- Need to individualize dosing
- Significant drug-to-drug interactions
Alternative treatments

- Severe disease in high-risk patients
  - May consider combination therapy
  - Voriconazole + echinocandin (Caspofungin, Micafungin)
- Liposomal Amphotericin B
  - *Aspergillus terreus* fully resistant
  - Not available orally
- Surgical debridement or excision of localized lesion (if possible)

Treatment of refractory aspergillosis

- Azoles:
  - Posaconazole
    - Erratic absorption
    - Patient must be tolerating PO or enteral feeds
  - Itraconazole
- Echinocandins:
  - Caspofungin
  - Micafungin
- Limited data on combination therapy:
  - Broad-spectrum azole or liposomal ampho + echinocandin

Environmental measures

- Barriers between construction sites and patient care areas
- Laminar flow rooms, HEPA filters
- Routine cleaning of air-handling systems
- Repair of faulty air flow
- Replacement of contaminated air filters
- Minimize environmental exposure

Approaches to management of the febrile oncology patient

- All neutropenic patients who are febrile, or any patient who is toxic-appearing, are considered bacteremic until proven otherwise
- The afebrile, neutropenic patient presenting with:
  - localizing pain (especially abdominal pain)
  - hemodynamic instability
  - altered mental status
  - new s/s suggesting infection
  
  *should be evaluated and treated as high-risk patient*

Important caveats

- Neutropenic patients may not display the same inflammatory responses to infection as non-neutropenic patients
- Fever may be the only presenting sign of serious infection in the immunocompromised patient
- Not all febrile patients will have a documented infection
- Not all patients with a serious infection will present with fever
### Management
- Detailed history and comprehensive review of systems
- Thorough physical examination
- Understanding recent therapies
- Labs to obtain
- Neutropenic or not?
- Importance of prompt initiation of therapy, if indicated

### History
- Type of malignancy
- Treatment regimen/most recent therapy
- Fever (t.max, duration, associated chills/shaking/ribors)
- Potential exposures/sick contacts
- Current medications
- History of previous febrile infections

### Review of Systems
- Headache
- Myalgias
- Orthostatic symptoms
- Cough, rhinorrhea, SOB
- Sore throat, ear pain
- Chest pain
- Abdominal pain
- Vomiting, diarrhea
- PO intake
- Pain with urination
- Skin lesions, rashes

### Physical Exam
- Vital signs (Temp, BP, HR, RR, SpO2, weight)
- Thorough head-to-toe exam
- Particular attention to:
  - Oral mucosa
  - Abdomen
  - Perineum
  - CVL site
  - Surgical sites
  - Pain

### Labs
- CBC with differential
- Blood cultures from all catheter sites +/- peripheral cultures
- Chemistry panel (lytes, Cr, LFTs)
- Urine culture +/- UA (non-cath)
- *Lactate*

### Additional studies
- Based on symptoms:
  - Respiratory → CXR, respiratory virus panel, CT scan
  - GI → Stool cultures, KUB, US, CT scan, amylase/lipase
  - CNS → LP (CSF studies and culture), CT scan
  - Skin → culture (bacterial, viral)
  - Oral → throat cultures; viral or fungal cultures
### Treatment

- **Prompt** initiation of broad-spectrum antibiotic therapy (30-60 minutes)
- Close inpatient monitoring (minimum 48 hours)
- Intensive supportive care
  - Aggressive IV fluids
  - Monitor s/s septic shock
  - Monitor mental status changes
  - Vasopressor support

### Ongoing management

- Close monitoring for changes in clinical status
  - Monitor closely after initial dose of IV antibiotics
- Aggressive IV fluid support
- Hemodynamic support, if needed
- +/- daily blood cultures, if febrile
- Repeat blood cultures if change in clinical status
- Follow chemistries, LFTs, BUN/Cr
- Monitor drug levels

### Ongoing management

- Consider therapy modifications:
  - Changes in clinical status
    - Broaden coverage (aminoglycoside, Vanco, Metronidazole)
  - Persistent fevers first 3-5 days
    - +/- Broaden coverage based on clinical status
    - Consider adding anti-fungal coverage (by day 5)
  - Pathogen identified
    - Narrow coverage based on sensitivity, if possible

### Duration of treatment

- Broad-spectrum IV antibiotic coverage for minimum of 48 hours
- Criteria for discharge:
  - Negative cultures after 48 hours
  - Afebrile >24 hours
  - ANC > 500 (or ANC >200 for 2+ days and rising)
  - Clinically stable
- If positive cultures, length of antimicrobial treatment will be based on pathogen identified & response to therapy

### Home antibiotics?

- No uniform treatment recommendations
- Requires close outpatient follow-up
- Considerations:
  - Frequency of therapy
  - Family dynamics
  - Availability of home support services
  - Outpatient support

### Fever in non-neutropenic patient

- Work-up same in all febrile oncology patient
  - Detailed history and review of systems
  - Thorough physical examination
  - Labs (CBCd, CMP, blood culture, urine culture +/- additional studies, if indicated)
- Antibiotic coverage
  - Ceftriaxone vs. no abx?
- If stable, close outpatient follow-up
Consequences of aggressive management of febrile neutropenic patients

- Emergence of anti-microbial resistance (MRSA, VRE, ESBL, CRE)
- In-hospital complications (e.g., catheter dysfunction, nosocomial infections)
- Disruption of quality of family life
- Increased medical costs

Risk stratification

- Not all neutropenic children with fever are alike
- ~10-30% of F/N patients have documented bacteremia
- Is it possible to differentiate high-risk vs. low-risk neutropenic patients?

Pediatric risk-stratification

- No consensus on criteria has been established to date
- Possible factors associated with risk of severe infection:
  - High risk of prolonged neutropenia (>7-10 days)
  - Underlying malignancy (AML, relapsed disease, BM involvement, multiple malignancies)
  - Comorbidities (hypotension, shaking chills, FNA on XR, evident bacterial or fungal infection, severe mucositis, requiring ICU care)
  - Treatment with HD ARAC
  - Age <1 year
  - CRP >90 mg/L
  - Platelet count <50k

PO antibiotic step-down therapy

- No standardized guidelines
- May be considered for selected low-risk, stable patients
- Amoxicillin-Clavulanate + fluoroquinolone
- Considerations:
  - Family reliability
  - Distance to medical center
  - Close follow-up available

Role of Prevention

- Meticulous hand hygiene
- CLABSI initiatives
- Neutropenic precautions
- Avoid known sick contacts
- Full immunization of close contacts
- Prompt notification of infectious disease exposure (esp. VZV)
- Good oral hygiene

Role of anti-microbial prophylaxis

- Select high-risk patients (e.g., AML, infant leukemia) with periods of profound & prolonged neutropenia
- Antibiotic therapy
  - Fluoroquinolones
  - Levofloxacin
  - Ciprofloxacin
- Antifungal therapy
  - Fluconazole (Candida)
  - Caspofungin (Candida & Aspergillus)
  - Posaconazole (Candida & Aspergillus)
- Pneumocystis carinii/jiroveci prophylaxis
  - Sulfamethoxazole-TMP, Pentamidine, Dapsone, Atovaquone
**Case Study**

- 17 yo female with Ph+ pre-B ALL calls at @ 2030 with fever to 102.1°F (38.9°C) & shaking chills
- s/p platelet transfusion earlier same day
- s/p chemotherapy 8 days prior (Etoposide & Cyclophosphamide x5 days)
- On daily Dasatinib
- Started GCSF on Day 6

**History**

- Diagnosed ~9 months prior, treated as per COG AALLo622
- Therapy complications to date:
  - h/o prolonged QTc 2o therapy (Dasatinib & Doxorubicin)
  - h/o renal toxicity 2o high-dose Methotrexate therapy
- Infectious complications to date:
  - h/o Klebsiella sepsis x2
  - h/o Coag-negative staph bacteremia x2
  - h/o Enterococcus UTI x2
  - h/o C.diff colitis x1

**Presentation**

- Arrives ED ~2100
- ROS:
  - Fever with chills
  - Mild headache
  - Nausea with 1 episode NBNB emesis
  - Diarrhea
  - “Achy”
- No recent illnesses, no sick contacts

**Presentation**

- Admit VS:
  - BP: 115/75, HR: 152, RR: 20, T: 102°F, O2 sat: 100%
- Exam:
  - Neuro: A&O x3, slightly confused, word searching, speech slurred
  - CV: tachycardic, flow murmur, 1 sec. central cap refill, cool extremities
  - No focal findings concerning for infection

**Labs**

- Labs: CBCd, CMP, blood culture x2
- CBCd (ANC ~0)

  | <0.1 | 10.2 | 28.0 | 36k |

**Labs**

- CMP normal except:
  - Na 134 (L)
  - BUN 20 (H)
  - Cr 0.93 (H)
  - T.Bili 1.4 (H)
  - AST 90 (H)
  - ALT 190 (H)
  - Anion gap 13 (H)
- Blood cultures pending
**Treatment**

- IV Cefepime @ 2130, IV Tobra ordered
- NS bolus (20 mL/kg) IV
- Tylenol
- Transferred to ward

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**Hospital course**

- 2200: BP: 93/39, HR 164, T: 101.7
- 2300: BP: 94/39, HR 160
- Now confused, dizzy, agitated with decreasing BP to 65/35
- Transferred to PICU
  - Multiple NS boluses with minimal improvement in BP
  - Started on Dopamine gtt @ 5 mcg/kg/min
  - Increased to 7 mcg/kg/min overnight
  - Added IV Vancomycin

**Hospital course**

- Additional studies:
  - Head CT (negative)
  - Coag significant for mildly elevated PT, PTT, & INR with D.Dimer 4.17 (normal <0.5)
  - Concern for DIC
  - Venous B.G. with pH 7.31 (L), HCO3 15.2 (L), Lactate 4.0 (H)
    - Concern for metabolic acidosis
  - Received IV Sodium bicarbonate
  - Peripheral IV placed

**Hospital course Day #2**

- By morning, more lucid & alert with appropriate behavior
- Improving VS, Dopamine weaned off by 1600
- Received PRBC and platelet transfusion
- Creatinine increasing (max. 1.33)
- Dopamine restarted at 1830 (BP 87/43)
- Blood cultures positive for gram-negative rods

**Hospital course Day #3**

- Defeveresced, Dopamine weaned off by 1430
- Lactate normalized – 0.87
- Blood cultures ID – *Klebsiella pneumoniae*
- Vancomycin stopped, continued Cefepime & Tobramycin

**Continued hospital course**

- Repeat blood cultures Days 2 & 3 – negative
- Day 6 – Hickman catheter removed
- Day 7 – ANC 168
- Day 8 – low-grade temp to 100.6, ANC 468
  - No therapy changes
- Continued on 14 days of IV Cefepime & Tobramycin (through Day 15)
- Day 12 – new Hickman catheter placed
- Day 16 – discharged home, ANC 1302
Questions?

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Stanford Children’s @ CPMC

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Pediatric Infectious Diseases  
Stanford Children’s @ CPMC

References


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