Febrile Neutropenia
Oncology Care Guideline

Inclusion Criteria:
- Central Line
- Temp \( \geq 38.3^\circ C \) orally or \( \geq 38.0^\circ C \) for longer than 1 hr, ANC < 500 cells/mm\(^3\) OR ANC < 1000 cells/mm\(^3\) with a predicted decline to 500 cells/mm\(^3\) or less over the next 48 hrs
- Presence of shaking chills regardless of temperature

Assessment
- Comprehensive H & P for subtle signs/symptoms, including pain at sites most commonly infected
- Vital signs, continuous pulse oximetry if respiratory signs/symptoms

Recommendations/Considerations
- Thoroughly assess common sites of infection: GI tract, groin, skin, lungs, sinuses, ears, perineum, perirectal, intravascular access sites.
- Consider stress doses of IV steroids for hypotension if currently receiving steroids or was recently tapered off steroids.
- Administer antibiotics within 1 hour of arrival.
- Central vascular access device care should be performed – please refer to CHOC Patient Care Policy F832 (Central Vascular Access Device)

Interventions
- CBC with differential, CMP
- Blood cultures from each CVAD lumen/port, urinalysis & urine c/s (no cath) for UTI symptoms, stool for C. difficile for GI symptoms, RP/PCR if URI signs/symptoms
- Keep all lines open and running
- Assess CVAD site for presence of infection & perform dressing change within 4 hours of admission
- Blood culture q 24 hours while febrile
- CXR if respiratory signs/symptoms; chest CT if abnormal
- Abdominal ultrasound or CT for abdominal pain
- Heparin flush CVAD per protocol
- Assess CVAD site for presence of infection & perform dressing change within 4 hours of admission

Antibiotics – Hemodynamically Stable
- cefepime 50 mg/kg/dose IV q8hrs (<40kg) (Max: 2 gm/dose) OR aztreonam 50 mg/kg/dose IV q 6 hrs (Max: 2 gm/dose) used in conjunction with vancomycin - if allergic to cephalosporins
- If history of ESBL, consider meropenem

If indications for empiric vancomycin present - ADD
vancomycin 15 mg/kg/dose IV q 6 hrs x 48 hrs (if < 50kg) OR 1000 mg IV q 8hrs x 48 hrs (if > 50 kg)

If typhlitis or C. difficile is suspected – ADD metronidazole 7.5 mg/kg/dose IV or PO q 6hrs (Max: 2 gm/day)

Antibiotics - Hemodynamically Unstable
(required fluid boluses or pressors)
- meropenem 40mg/kg/dose IV q 8hrs (Max: 2 gm/dose)
- vancomycin (x 48 hrs) 15 mg/kg/dose IV q 6 hrs if \( \leq 50 \)kg or 1000 mg IV q 8h if > 50 kg

If C. difficile is suspected – ADD metronidazole 7.5 mg/kg/dose IV or PO q 6hrs (Max: 2 gm/day)

Continued Considerations
- Adjust antibiotics based on culture results, clinical course and serum levels.
- Consider Vancomycin levels after 48 hours
- Perform daily site specific exam, review of lab tests & cultures, response to therapy (fever trends & signs/symptoms of infection)
- Evaluate drug toxicity including end-organ toxicity (LFTs/renal function tests 2x/wk)
- For follow up therapy, duration algorithms & discharge criteria, see page 2.

Indications for Empiric Vancomycin Use:
- Blood culture positive for Gram positive bacteria prior to final ID & susceptibility testing
- Known colonization with penicillin/cephalosporin resistant pneumococci or MRSA
- Hypotension or septic shock w/o an identified pathogen
- Received high dose cytarabine recently
- AML
- Soft tissue infection
- Mucositis
- Suspected meningitis
- Cephalosporin allergic

Patient/Family Education
- Review fever guidelines & temperature monitoring
- Review S&S infection
- Review handwashing
- Review prevention of CLABSIs
Evaluate overall response to empiric therapy in 2-5 days

Responding
- Afebrile
- Signs/symptoms stable or improving

Positive Cultures
- Continue same antibiotic course until neutropenia resolving (ANC 250-500) OR
- Discontinue antibiotics after 7-14 days if remains stable (ANC <250)
- Discontinue vancomycin if no positive culture at 48 hrs
- Adjust antibiotics based on sensitivities
- D/C vancomycin if no positive culture for Gram positive organisms at 48 hrs

No positive culture
- Adjust antibiotics based on sensitivities
- Consider vancomycin if no positive culture for Gram organisms at 48 hrs
- Consider risk mitigation/watcher status
- Consider ID Consult

Receiving biologicals likely to cause fever (i.e. ATG, Ara-C, interferon)
- Review ANC
- Consider discontinuing antibiotics when afebrile x 48 hrs
- Consider imaging

Positive Cultures
- Adjust antibiotics based on sensitivities
- D/C vancomycin if no positive culture for Gram positive organisms at 48 hrs
- Obtain imaging if fever > 5 days

No positive culture
- Consider broadening coverage for anaerobes, i.e. add metronidazole to cefepime, if clinical change (i.e. GI symptoms)
- If continued fever > 5 days, consider addition of antifungal/mold active agent
- Consider imaging

Suggested Duration of Therapy
- Bloodstream infection (uncomplicated)
  * Gram-negative: min 10 days after 1st negative culture
  * Gram-positive: min 10 days after 1st negative culture
  * S. aureus: min 14 days after 1st negative blood culture
- ID Consult & catheter removal for BSI with Candida, Pseudomonas aeruginosa, atypical mycobacteria, molds, Stenotrophomonas maltophilia
- Consider catheter removal for BSI with S. aureus, Corynebacterium jeikium, Acinetobacter, Bacillus organisms, and VRE
- Sinusitis: 21 days
- Bacterial pneumonia: minimum 14 days
- Catheter removal for septic phlebitis, tunnel infection, or port pocket infection
- Discharge Criteria
  - Afebrile, vital signs stable x 24-48 hrs
  - Hemodynamically & clinically stable
  - Cultures negative
  - ANC 250 - 500 and increasing
  - Follow up care planned
  - Antibiotics prescribed for appropriate duration

Reassess the appropriateness of Care Guidelines as condition changes and 24 hrs after admission. This guideline is a tool to aid in clinical decision making. It is not a standard of care. The physician should deviate from the guideline when clinical judgment so indicates.
References
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