Febrile Neutropenia Oncology Care Guideline

Inclusion Criteria:

- Central Line
- Temp ≥ 38.3°C orally/axillary or ≥ 38.0°C for longer than 1hr, ANC < 500 cells/mm³ OR ANC < 1000 cells/mm³ with a predicted decline to 500 cells/mm³ or less over the next 48 hours
- Presence of shaking chills regardless of temperature

Assessment

- Comprehensive H&P for subtle signs/symptoms, including mucositis and pain at sites most commonly infected
- Assess point in therapy and steroid use
- Vital signs, continuous pulse oximetry if respiratory signs/symptoms

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
- Blood culture q24hr while febrile
- CXR if respiratory signs/symptoms; chest CT if abnormal
- Abdominal ultrasound or CT for abdominal pain
- Heparin flush CVAD per protocol

Antibiotics – Hemodynamically Stable

- Cefepime and Meropenem - loading dose should run over 30 minutes with subsequent doses running over 3 hours
- Cefepime 50 mg/kg/dose IV q8hr (< 40kg) (Max: 2 gm/dose) ***OR*** Aztreonam 50 mg/kg/dose IV q6hr (Max: 2 gm/dose) used in conjunction with Vancomycin - if allergic to cephalosporins
- If history of ESBL, consider Meropenem
- Cefepime and Meropenem should be infused prior to Vancomycin being given

IF indications for empiric vancomycin present - *ADD*

- Vancomycin loading dose – 20mg/kg IV x 1 then, Vancomycin 15 mg/kg/dose IV q6hr x 48hrs (if ≤ 50kg) ***OR*** 1000 mg IV q8hr x 48hrs (if > 50 kg)

IF typhlitis is suspected, *and on cefepime* – *ADD*

- Metronidazole 7.5 mg/kg/dose IV or PO q6hr (Max: 2 gm/day)

Antibiotics - Hemodynamically Unstable

(requires fluid boluses or pressors)

- Meropenem - loading dose should run over 30 minutes with subsequent doses running over 3 hours
- Meropenem 40mg/kg/dose IV q8hr (Max: 2 gm/dose) – give loading dose over 30 mins

AND

- Vancomycin Loading dose – 20mg/kg IV x 1 then, Vancomycin 15 mg/kg/dose IV q6hr x 48hrs (if ≤ 50kg) ***OR*** 1000 mg IV q8hr x 48hrs (if > 50 kg)

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. (Hydrocortisone IV - 100mg/m^2/ day divided in 6 doses)
- Antibiotics to be administered within 1 hour.
- If *C. difficile* is suspected, oral vancomycin should be prescribed.
- Central vascular access device care should be performed – *please refer to CHOC Patient Care Policy F832 (Central Vascular Access Device)*

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 Education

- Review fever guidelines & temperature monitoring
- Review signs and symptoms of infection
- Review handwashing
- Review prevention of CLABSI

Continued Considerations

- Adjust antibiotics based on culture results, clinical course and serum levels.
- ***Note*** – *Continued fevers alone are not a reason to escalate to meropenem.*
- 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.**

Care Guidelines Committee – Original 7/2006
Revised: 11/18/2009; 9/27/2011, 5/15/2013
Approved Evidence Based Medicine Committee 9/19/2018
Reviewed / Revised:3/20/2024

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Evaluate overall response to empiric therapy in 2-5 days

Responding
- Afebrile
- Signs/symptoms stable or improving

Positive Culture
- Adjust antibiotics based on sensitivities
- D/C Vancomycin if no positive culture for Gram positive organisms at 36-48 hours

No Positive Culture
- Continue same antibiotic course until neutropenia resolving (ANC rising x 2 days and > 100 cells/mm^3)

OR
- Discontinue antibiotics after 7 days if remains stable
- Discontinue Vancomycin if no positive culture in 36-48 hours

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

Not Responding/ Persistent Fever

Positive Culture
- Adjust antibiotics based on sensitivities
- D/C vancomycin if no positive culture for Gram positive organisms at 36-48 hours

If patient becomes unstable

No Positive Culture

Unstable
- Consider risk mitigation/watcher status
- Consider ID Consult
- Daily reassessment of signs/symptoms and culture results
- Consider imaging
- If fever ≥5 days, consider addition of antifungal/mold active agent
- Check galactomannan and Fungitell levels
- Add empiric fluconazole/ micafungin
- If fever ≥5 days, consider addition of mold active agent
- Obtain imaging if fever ≥5 days

Stable
- Continue current therapy

OR
- 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 jeikeium, Acinetobacter, Bacillus* organisms, and VRE
- Sinusitis: 21 days
- Bacterial pneumonia: minimum 10-14 days
- Catheter removal for septic phlebitis, tunnel infection, or port pocket infection

Discharge Criteria
- Afebrile, vital signs stable x 24-48 hours
- Hemodynamically & clinically stable
- Cultures negative
- ANC increasing over 2 days and expected to continue rising
- Follow up care planned
- Antibiotics prescribed for appropriate duration

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References

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