PEDIATRIC BLOOD AND MARROW TRANSPLANT PROGRAM

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Evaluation and Management of Fever in Immunocompromised Patients

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PBMT-GEN-074
EVALUATION AND MANAGEMENT OF FEVER IN IMMUNOCOMPROMISED PATIENTS

1 PURPOSE

1.1 To establish appropriate guidelines for the initial evaluation and management of pediatric transplant and cellular therapy (PTCT) patients with fever in an immunocompromised host at any point in time surrounding transplant or cellular therapy administration.

2 INTRODUCTION

2.1 Patients presenting with neutropenia or any otherwise immunocompromised state are at increased risk of developing infectious complications. Bacterial infections are of primary concern; however, fungal infections may also arise in patients with prolonged neutropenia.

2.2 Note that allogeneic hematopoietic stem cell transplant (HSCT) patients are considered at high risk of serious bacterial infection irrespective of absolute neutrophil count (ANC) through at least 100 days post-transplant, or if receiving steroids equivalent to greater than (>) 0.5 mg/kg/day of prednisone for > 5 days with functional or numeric neutropenia beyond 100 days post-transplant.

2.3 Autologous HSCT patients with a central venous line and less than (<) 50 days post-transplant are also considered high risk for serious bacterial infection.

3 SCOPE AND RESPONSIBILITES

3.1 This procedure applies to all PTCT patients with fever in immunocompromised host.

3.2 Physicians, advanced practice providers, staff nurses, and pharmacists who evaluate and treat PTCT patients with fever are responsible for adhering to the contents of this procedure.

3.3 All applicable orders by physicians or designees will be entered into the electronic medical record.

4 DEFINITIONS/ACRONYMS

4.1	ANC	Absolute Neutropenic Count
4.2	APP	Advanced Practice Providers
4.3	EBV	Epstein Barr Virus
4.4	CMV	Cytomegalovirus
4.5	HHV-6	Human Herpes Virus - 6
4.6	HSCT	Hematopoietic Stem Cell Transplant

4.7	HSV	Human Simplex Virus
4.8	PCR	Polymerase Chain Reaction
4.9	PTCT	Pediatric Transplant and Cellular Therapy
4.10	IV	Intravenous

5 MATERIALS

5.1 NA

6 EQUIPMENT

6.1 NA

7 SAFETY

7.1 NA

8 PROCEDURE

8.1 Definitions:

8.1.1 Neutropenia is defined as absolute neutrophil count of less than (<) 500/mm^3.

8.1.2 Fever is defined as a single measured temperature of greater than or equal to (≥) 101.3ºF (38.5^{0}C) or a measured temperature between 100.4ºF (38.0ºC) and 101.1ºF (38.4ºC) for four (4) consecutive hours.

8.1.3 Fever is defined as a single measured temperature of 38°C or above at ANY TIME for CAR-T cell recipients infection/fever evaluation.

8.1.4 Preferred method of measuring temperature is via tympanic thermometer for PTCT patients, unless clinically contraindicated or otherwise not tolerated.

8.1.5 Infection/fever evaluation will also be initiated with ANY CONCERNING CHANGE in clinical status, despite fever definitions, or at the discretion of the patient's provider, with special consideration given to patients who may not mount an expected febrile response (i.e. steroid recipients).

8.1.6 Physical examination by Physician or APP will be performed to look for a possible source of fever and hemodynamic instability.

8.1.7 Blood cultures from all lumens of the patient's central venous catheter(s) will be obtained with initial fever, including infusaport.

8.1.8 Further blood cultures from a patient's infusaport will be obtained at the discretion of the patient's provider, as long as initial infusaport cultures remain without growth.

8.1.9 Consider anaerobic blood culture with initial fever if suspicious for an intra-abdominal source. If not available on the unit, please request

pediatric anaerobic blood culture bottle from microbiology lab (684-2089). Do not delay antibiotic administration to collect anaerobic blood cultures.

8.1.10 Obtain surface or drainage cultures of any lesions, if present.

8.1.11 Obtain infectious stool studies with any presence of unexpected increase in stool frequency, volume or change in consistency.

8.1.12 Consider urinalysis and urine culture (only if clean catch specimen can be obtained) as clinically indicated. Do not delay antibiotic administration for urine specimens. Note that neutropenic patients with a urinary tract infection may not demonstrate pyuria on urinalysis.

8.1.13 Chest radiograph with extended respiratory viral panel should be obtained with new respiratory symptoms, new or increasing oxygen requirement, or if otherwise clinically indicated as ordered by the patient's provider.

8.1.14 Complete blood count with differential should be obtained at fever onset.

8.1.15 Serum chemistries, including electrolytes, creatinine, and liver function tests will be obtained with other laboratory studies at time of fever onset.

8.1.16 Additional studies should be obtained as indicated by the patient's clinical stability, at the discretion of the patient's provider.

8.1.17 In the outpatient setting, the evaluation and treatment may be initiated in the clinic, but the patient may require admission to the hospital for ongoing evaluation and management, if appropriate.

8.1.18 In the inpatient or outpatient setting, with any concern of hemodynamic instability or acute decompensation in a patient with neutropenic fever, a Pediatric Rapid Response should be initiated.

8.2 Management:

8.2.1 Empiric administration of broad-spectrum antibiotics should be initiated as soon as possible, but no later than 1 hour following fever onset.

8.2.1.1 For outpatients, the initial empiric regimen will be ceftriaxone IV every 24 hours pending clinical stability of the patient (unless contraindicated).

8.2.1.2 For hemodynamically stable inpatients, the initial empiric regimen will include cefepime IV every 8 hours (unless contraindicated).

8.2.1.3 For hemodynamically unstable inpatients, vancomycin IV will be added to the initial empiric regimen (unless otherwise contraindicated).

8.2.1.4 If the patient is allergic to cephalosporins, an alternative antibiotic therapy will be ordered.

8.2.1.5 Antibiotic dosing will be adjusted for renal dysfunction and pharmacokinetics if available.

8.2.1.6 Antibiotic approval will be obtained from the Pediatric Transplant Infectious Disease Service, as indicated per Duke policy.

8.2.1.7 Antibiotic use will be re-evaluated daily based on culture results, imaging findings and the patient's clinical trajectory.

8.2.2 If fevers persist after 48 hours on broad-spectrum antibiotics:

8.2.2.1 Consider starting vancomycin at a dose appropriate for weight and renal function, if not already initiated.

8.2.2.2 Consider consulting Pediatric Transplant Infectious Disease team if not already done.

8.2.2.3 Consider evaluation for viral infection with CMV, EBV, adenovirus, HHV-6, HSV PCRs.

8.2.3 If fever persists after 96 hours on broad-spectrum antibiotics:

8.2.3.1 Consider broadening antifungal coverage or increasing prophylactic dosing to treatment dosing, if different. Please note approval by the Pediatric Transplant Infectious Disease Service is required for specific medications.

8.2.3.2 Consider CT chest/ abdomen/ pelvis and sinuses to evaluate for invasive fungal infection or other occult source of infection.

8.3 Reportable conditions:

8.3.1 Intolerance or allergy to therapeutic regimen, persistent fevers with unidentified source, hypotension or other signs of hemodynamic instability, any cultures with positive growth, or signs and symptoms of infection.

9 RELATED DOCUMENTS/FORMS

9.1 NA

10 REFERENCES

10.1 Hughes WT, Armstrong D, Bodey GP, Bow EJ, Brown AE, et al. 2002 Guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clin Infect Dis 2002; 34:

10.2 Gilbert C, Meisenberg B, Vredenburgh J, Ross M, Hussein A, et al. Sequential prophylactic oral and empiric once-daily parenteral antibiotics for neutropenia and fever after high-dose chemotherapy and autologous bone marrow support. J Clin Oncol 1994;12: 1005-11.

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