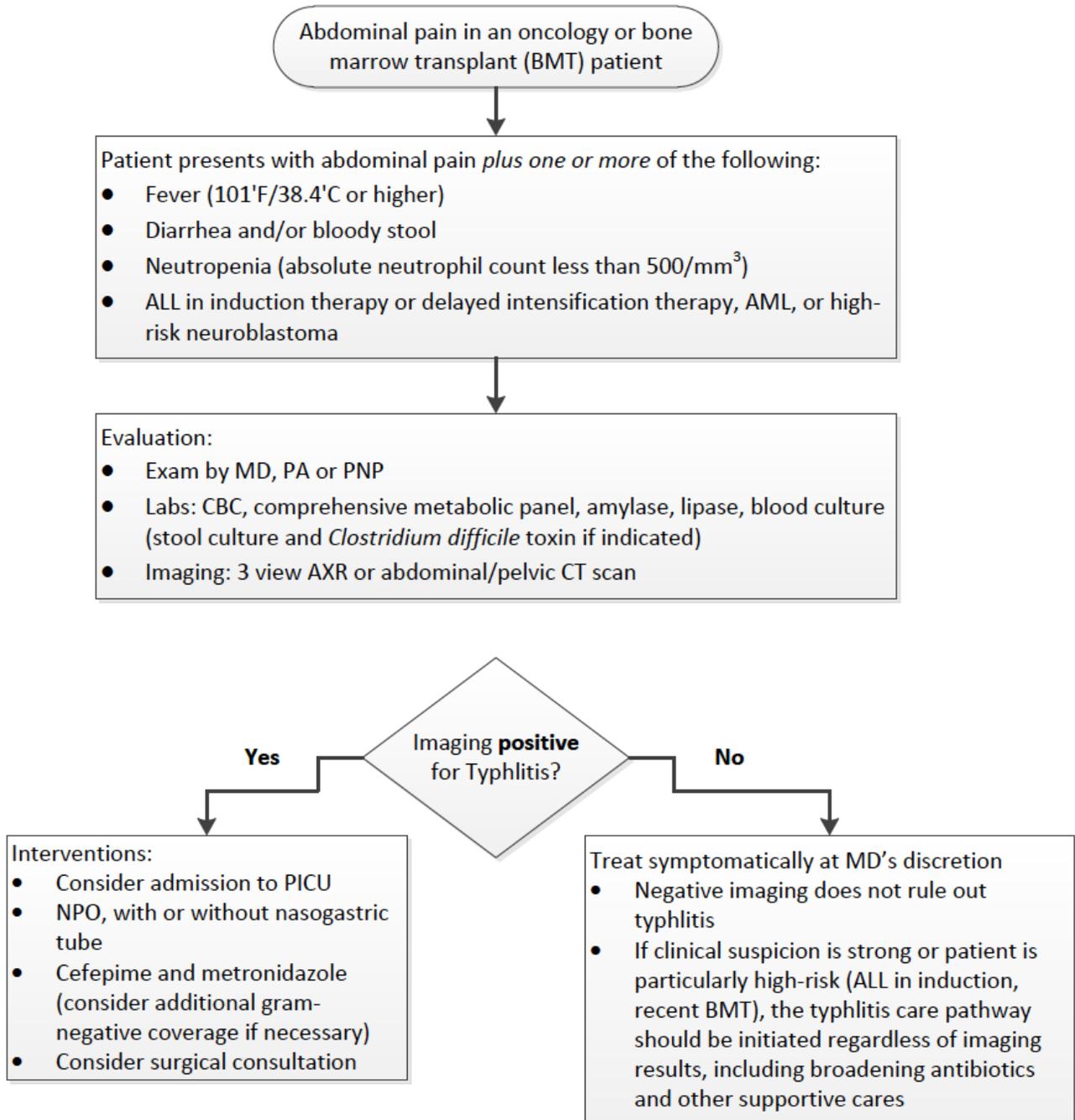


ABDOMINAL PAIN IN AN ONCOLOGY OR BONE MARROW TRANSPLANT (BMT) PATIENT (AKA TYPHLITIS)

ALGORITHM. Abdominal Pain in an Oncology or BMT Patient



OVERVIEW

- Typhlitis, also referred to as neutropenic enterocolitis, is an acute life-threatening condition, seen most commonly in children with myelosuppression.
- Mortality and morbidity rates associated with typhlitis are very high and early diagnosis and treatment is imperative as the clinical course progresses very quickly.

CLINICAL PRESENTATION

- A high index of suspicion for typhlitis should be given to oncology or BMT patients presenting with abdominal pain plus one or more of the following:
 - Fever (101°F/38.4°C or greater)
 - Diarrhea and/or bloody stool
 - Neutropenia (absolute neutrophil count less than 500/mm³)
 - Induction therapy or delayed intensification therapy for acute lymphoblastic leukemia¹ (ALL), infant ALL, diagnosis of acute myeloid leukemia¹ (AML), or high-risk neuroblastoma¹

LABORATORY | RADIOLOGIC STUDIES

- Currently there is no gold standard for diagnosing typhlitis
- **Laboratory studies should include:**
 - Complete blood cell count (CBC)
 - Comprehensive metabolic panel
 - Serum lipase
 - Serum amylase
 - Blood cultures
 - Stool cultures and *Clostridium difficile* toxin should be considered if clinically indicated
- Imaging:
 - Controversy exists regarding the ideal modality for diagnostic imaging in patients with potential typhlitis. The argument has been made that plain radiographs are nonspecific. However, abdominal x-rays along with consideration of clinical signs are sensitive enough for the diagnosis of typhlitis.

TREATMENT | THERAPEUTICS

- Treatment must be individualized to each patient
- Conservative treatment consists of:
 - Bowel rest with or without nasogastric suction
 - Parenteral nutrition may be considered
 - Hemodynamic support
 - Intravenous fluids, blood and platelets as needed
 - Pharmacotherapy

RISK OF RECURRENCE

Patients with a history of typhlitis are at risk for developing it again during subsequent treatment. Chemotherapy should be withheld until the patient has fully recovered and has healed completely.

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TARGET POPULATION

Inclusion Criteria

- All oncology and bone marrow transplant (BMT) patients with abdominal pain

Exclusion Criteria

- General medicine patients
- Hematology patients

CLINICAL MANAGEMENT

Overview

Typhlitis, also referred to as neutropenic enterocolitis¹, is an acute life-threatening condition, seen most commonly in children with myelosuppression. Mortality and morbidity rates associated with typhlitis are very high and early diagnosis and treatment is imperative as the clinical course progresses very quickly¹.

Telephone Triage

Use the EPIC telephone triage script named “HOB Typhlitis”. Document the disposition of the patient in the field provided.

Clinical Presentation

A high index of suspicion for typhlitis should be given to oncology or BMT patients presenting with abdominal pain² plus one or more of the following:

- Fever¹⁻³ (101°F/38.4°C or greater)
- Diarrhea^{2,3} and/or bloody stool
- Neutropenia¹⁻³ (absolute neutrophil count less than 500/mm³)
- Induction therapy or delayed intensification therapy for acute lymphoblastic leukemia¹ (ALL), infant ALL, diagnosis of acute myeloid leukemia¹ (AML), or high-risk neuroblastoma¹

Differential Diagnoses

Signs and symptoms of typhlitis often mimic other common gastrointestinal disorders including appendicitis, colonic pseudo-obstruction, diverticulitis, inflammatory bowel disease, infectious colitis, pancreatitis, and pseudomembranous colitis³.

LABORATORY | RADIOLOGIC STUDIES

Currently there is no gold standard for diagnosing typhlitis

- Laboratory studies should include:
 - Complete blood cell count (CBC)⁴
 - Comprehensive metabolic panel⁴
 - Serum lipase
 - Serum amylase
 - Blood cultures⁴
 - Stool cultures and *Clostridium difficile* toxin⁵ should be considered if clinically indicated
- Imaging:
 - Controversy exists regarding the ideal modality for diagnostic imaging in patients with potential typhlitis. The argument has been made that plain radiographs are nonspecific. However, abdominal x-rays along with consideration of clinical signs are sensitive enough for the diagnosis of typhlitis⁴.
 - Radiographic findings suggestive of typhlitis include:
 - Thumb printing
 - Fluid-filled mass like density in the right lower quadrant of the abdomen
 - Localized pneumatosis
 - Distention of adjacent bowel loops
 - CT scans can also be used for diagnosis. In cases where other pathology is a concern, this may be indicated, but abdominal x-ray has been shown to be a very sensitive test for the diagnosis of typhlitis.

TREATMENT | THERAPEUTICS

Treatment must be individualized to each patient⁴.

- Conservative treatment consists of:
 - Bowel rest³ with or without nasogastric suction
 - Parenteral nutrition may be considered
 - Hemodynamic support
 - Intravenous fluids, blood and platelets as needed
 - Pharmacotherapy³
 - Cefepime: 50 mg/kg/dose intravenously every 8 hrs. Maximum: 6 grams/day plus metroNIDAZOLE: 7.5 mg/kg/dose intravenously every 6 hrs or 10 mg/kg/dose intravenously every 8 hrs. Recommended maximum: 2 grams/day
 - Consider additional Gram-negative coverage in patients who are clinically unstable, when resistant infection is suspected^{6,7}
 - The agent to select for double coverage is controversial, as aminoglycosides are of variable benefit and increased nephrotoxicity, and fluoroquinolones increase risk of *C. difficile* disease^{6,8}
 - Discontinue double Gram-negative coverage in patients who are clinically responding after 48 to 72 hours, if there is no specific microbiologic clinical indication to continue⁶
 - Consider adding enterococcal coverage per patient risk factors and clinical severity, per National Fever and Neutropenia guidelines⁶

- Consider expanding/adding anti-fungal coverage per patient risk factors and clinical severity, per National Fever and Neutropenia guidelines⁶
- For patients with cephalosporin allergy, choices include meropenem 20 mg/kg/dose intravenously every 8 hrs (single agent) Maximum: 3 grams/day, or ciprofloxacin 10 mg/kg/dose intravenously every 12 hours (Recommended maximum: 800 mg/day) + metroNIDAZOLE 7.5 mg/kg/dose intravenously every 6 hrs or 10 mg/kg/dose orally or intravenously every 8 hrs (Recommended maximum: 2 grams/day)
 - If meropenem used, there is no clear benefit to double gram negative coverage, though exception made for patients already on meropenem (for example for BMT prophylaxis)⁸
 - Double anaerobic coverage should be avoided, as it is unnecessary and may increase risk of disease with *C. difficile*. Agents with significant anaerobic coverage used in this population include meropenem, piperacillin/tazobactam, ticarcillin/clavulanic acid, metronidazole, and clindamycin (note: clindamycin is less effective against *B. fragilis*)⁹
- Do *NOT* administer anticholinergics or antidiarrheals, as they may aggravate the condition or complicate the clinical presentation.
- Consider surgical consultation
- Immediate surgery is indicated for patients with free intra-abdominal perforation, clinical deterioration during conservative medical treatment, unrelenting intra-abdominal sepsis or abscess formation, or continued hemorrhage¹⁰.

Risk of Recurrence

Patients with a history of typhlitis are at risk for developing it again during subsequent treatment. Chemotherapy should be withheld until the patient has fully recovered and has healed completely.

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