Management of Pediatric Hematology and Oncology Emergencies

Pediatric Grand Rounds
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Objectives

- Recognize the most common hematologic and oncologic emergencies.
- Understand the management of these emergencies.

Disclosures

- I have received a research grant from the Vidacare Corporation to fund my fellowship project, but the research will not be discussed in today's presentation.

Case Presentation

- A 3 year-old African American male presents to the ED with two week history of abdominal pain. He had been seen two other times in the ED for the same complaint. He was diagnosed with constipation and sent home with Miralax. The mother reports that the patient was less active than usual and was not eating as much.

Case Presentation

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Case Presentation

- Past Medical Hx: No hospitalizations
- Past Surgical Hx: No surgeries
- Meds: Multivitamin, Miralax
- Allergies: None
- Social History: Lives in Florida with MOC. Is on vacation visiting relatives in Texas.
- Family Hx: MGM with thrombocytopenia of unknown origin but otherwise, non-contributory. No cancers or bleeding disorders.

Physical Exam

- 2–3cm anterior/posterior cervical lymph nodes
- Inferior palpebral conjunctival pallor
- Oral mucosa pallor
- 2/6 systolic murmur
- Hepatosplenomegaly

Labs

- CBC:
  - WBC = 304,000
  - Hbg = 3
  - Platelets = 25,000
- Chemistry:
  - Na 136
  - K 5.9
  - Cl 109
  - CO2 18
  - BUN 19
  - Cr 0.8
  - Glucose 89
  - Ca 7.6
  - Uric Acid 8.8
  - LDH 2383
- DIC Panel:
  - PTT 39.1
  - PT 18.8

Problem List

- Hyperleukocytosis
- Anemia
- Thrombocytopenia
- Hyperkalemia
- Renal insufficiency
- Prolonged PT/PTT

Peripheral Smear: Blasts

Diagnostic: Leukemia

- What do you do next?
  - Call Heme/Onc
  - Start IVF at 3L/m2, no K
  - Check other labs
    - Electrolytes, Uric acid, LDH
    - DIC panel
      - PT, PTT, fibrinogen, Fibrin split products, D-Dimers
      - Type and cross blood and platelets
  - Get a Chest X-ray
  - Rule out mediastinal masses.
Worry #1: Hyperleukocytosis

- Defined as WBC >100,000/mm3
- Seen at presentation in 9–13% of children with Acute Lymphoblastic Leukemia and in 5–22% of children with Acute Myeloid Leukemia
- Associated with an adhesive reaction between abnormal endothelium and leukemic blasts → leukostasis, thrombosis and secondary hemorrhage

Clinical Features

- CNS: blurred vision, confusion, somnolence, delirium, stupor, coma, papilledema.
- Pulmonary: tachypnea, dyspnea, hypoxia.
- GU: oliguria, anuria, priapism.
- Vascular: DIC, retinal hemorrhage, MI, renal vein thrombosis.

Risk Factors

- Age < 1 year
- M4, M5 AML (higher lysozyme activity)
- Cytogenetic abnormalities 11q23, t(4,11), Philadelphia chromosome
- Blasts have higher metabolic rates and higher production of cytokines = tissue hypoxia.
- Pulmonary: Thrombi can lead to pulmonary hemorrhage and edema.
- Cerebral circulation: Presence of blasts increases the risk of cerebral hemorrhage or cerebrovascular ischemia.

What's the big deal?

- Myeloblasts are larger, less deformable and more adherent to vasculature than lymphoblasts.
- Leukostasis and thrombosis are more prevalent in AML than in ALL.
- In AML, patients more likely to have intracranial hemorrhage or pulmonary hemorrhage.
- In ALL, hyperleukocytosis is more likely to lead to metabolic disturbance from tumor lysis syndrome (TLS).

AML vs. ALL

- IVF (3,000mL/m2/day) to maintain UOP at 2mL/kg/hr
- Leukopheresis/exchange transfusions
- Blood product support
- Chemotherapy for leukemia
**Worry # 2: Tumor Lysis Syndrome**

- Arises from the rapid release of intracellular metabolites (i.e. PO₄, K, uric acid) from necrotic tumor cells in quantities that exceed the excretory capacity of the kidney.
- Can occur in patients prior to chemotherapy if there is a high tumor burden (Burkitt lymphoma, B-cell and T-cell leukemia).

**Clinical Presentation**

- Rapid onset (can occur 3 days before and up to 7 days after initiation of therapy)
- Abnormal lab values
- Abdominal pain, cramping, fullness, vomiting, ascites
- Back pain, oliguria, anuria
- Cardiac arrhythmias, tachycardia, pleural effusion
- Numbness, tingling, tetany, weakness, fatigue
- Altered mental status, seizures

**Treatment of TLS**

- Close lab monitoring (Q6–12 hours): LDH, uric acid, Na, K, BUN/Cr, PO₄, Ca, urine pH/spec gravity
- Prevention: Fluids and hydration to promote excretion of uric acid and phosphorus and to increase GFR and renal blood flow
  - IVF (no K) at rate of 3,000mL/m²/day
  - Goal UOP 2mL/kg/hr
  - Diuretics may be needed.

- Manage Hyperkalemia (EKG, CaCl₂ or Ca gluconate, Kayexelate, Insulin and glucose, NaHCO₃ to reverse acidosis, dialysis)
- Manage Hyperuricemia (allopurinol, Rasburicase)
- Manage Hyperphosphatemia (oral phosphate binder like Aluminum hydroxide or Ca Carbonate, dialysis)
Manage Hypocalcemia: if symptomatic give elemental Calcium until symptoms resolve.

Establish metabolic stability prior to initiation of chemotherapy.

The Bleeding Clotter or the Clotting Bleeder?

Petechiae
Ecchymosis
Purpuric rash
Uncontrolled bleeding

DIC
Risk factors: malignancy, infection and trauma
Promyelocytic leukemia is the most common malignancy associated with DIC at diagnosis.
Most common cause of DIC in children with cancer is gram-negative sepsis.

Symptom management
Replacement of blood products (platelets, PRBCs)
Replacement of clotting factors (FFP, cryoprecipitate)
+/− Heparin

Occurs in the microvasculature and capillaries
Consumes platelets
Consumes clotting factors
Common in AML
Labs abnormalities:
Elevated PT/PTT
Low fibrinogen and anti-thrombin III levels
Elevated fibrin split products and D-dimers
Bleeding from puncture sites
GI bleeds
Hematuria
Oliguria
Dyspnea, tachypnea
Tachycardia
Poor perfusion
Restlessness, confusion, lethargy

A 2½ year-old Caucasian female was sent to ED by PCP to rule out heart failure and cardiomegaly. Patient was recently diagnosed with a sinus infection and was on antibiotics. Patient sleeps sitting up. If she lays down, she starts breathing fast and her face becomes swollen.

Initial vitals
- BP 106/80
- Pulse 166
- RR 46
- Sats 94%

Are you worried?

BP 106/80
- 95% for age 109/65
Pulse 166
RR 46
- Age 1–3 RR 22–30
Sats 94%

Nurse’s notes
- Pallor with periods of cyanosis

Periorbital edema.
Neck Full with cervical lymphadenopathy
Respirations labored, intercostal retractions. Decreased breath sounds bilaterally with crackles.
Distant heart sounds.
Liver at 3 cm. No splenomegaly.
What do you do next?

- Chest X-ray
- Labs

A Big Heart?

What's wrong with this Picture?

Effusions

Oh, there's it is!

Superior Vena Cava Syndrome

- Consists of the signs and symptoms of superior vena cava obstruction due to compression or thrombosis.
- Frequently due to a large anterior mediastinal mass compressing the SVC.
- Rapid growth of mass = no time for development of effective collateral circulation to compensate.
**SVC Syndrome Etiology**

- Intrinsic causes: Vascular thrombosis
- Extrinsic causes: Malignant mediastinal tumors:
  - Hodgkin lymphoma
  - Non-Hodgkin lymphoma
  - Teratoma or other Germ Cell Tumor
  - Thymoma

**Clinical Features**

- Swelling, plethora, cyanosis of the face, neck and upper extremities
- Suffusion of the conjunctiva
- Engorgement of collateral veins
- Altered mental status
- Superior mediastinal syndrome (tracheal compression): cough, dyspnea, wheezing, dysphagia, chest pain, syncope. **Supine position makes symptoms worse.**

**Management**

- Extreme care handling the patient.
- Supine position (as for CT), stress and sedation can precipitate respiratory arrest.
- Diagnosis should be made quickly in the least invasive manner.

**Treatment**

- Establishing dx may not be possible.
- Empiric tx as a life-saving measure may be needed.
  - Radiation
  - Steroids (tx heme malignancies, decrease airway edema)
- Biopsy mass when patient is stable.
- Specific chemotherapy after biopsy
- Anticoagulation for symptomatic venous thrombosis (Heparin or LMWH)

**Abdominal Emergencies**

- Esophagitis: Most common GI problem in oncology patients
- Gastric hemorrhage: Patients on steroids
- Typhlitis: Neutropenic patients
- Peri-rectal abscess: Seen with prolonged neutropenia
- Hemorrhagic pancreatitis: Patients on L-asparaginase therapy

**Most Commonly Encountered in Oncology**
Necrotizing colitis localized in the cecum
Caused by bacterial or fungal invasion of the mucosa
Pathogens: Pseudomonas species, E. coli, other Gram-negative bacteria, Staph aureus, alpha–hemolytic Strep, Clostridium, Aspergillus and Candida
Can be due to cytotoxic chemotherapy causing mucosal injury.

Bacterial/fungal invasion of the mucosa → inflammation → full–thickness infarction → perforation, peritonitis and septic shock!!!

Diagnosed clinically when a neutropenic patient presents with RLQ pain
Physical Exam: absent bowel sounds, bowel distention, tenderness on palpation in RLQ or palpable mass in RLQ
Imaging: Abdominal X–ray, ultrasound or CT (bowel wall thickening, pneumatosis intestinalis, free air in bowel wall or peritoneum)

NPO
Nasogastric tube suctioning
Broad–spectrum antibiotics (anaerobic and Gram–negative coverage)
IV fluids and electrolytes
PRBC and platelet transfusions
Vasopressors, as needed (**Hypotension is associated with a poor outcome).

Indications for surgery:
- Persistent GI bleeding
- Bowel perforation (free air in abdomen)
- Clinical deterioration requiring fluid and vasopressor support

Mortality is related to bowel perforation, bowel necrosis and sepsis.

Septic Shock
- A systemic response to pathogenic microorganisms and endotoxins in the blood
- Usually Gram–negative organisms and arise from endogenous flora
- Sepsis with hypotension despite adequate fluid resuscitation
- Leads to decreased perfusion, cellular hypoxia and death
Septic Shock

- Risk Factors
  - ANC < 100mm3
  - Prolonged neutropenia
  - Breaks in the skin/mucous membranes
  - Use of invasive devices
  - Malnutrition
  - Asplenia

Sepsis

- Patient with a known or suspected infection + 2 or more of the following:
  - Fever or hypothermia
  - Unexplained tachycardia or tachypnea
  - Signs of peripheral vasodilation
  - Leukocytosis or leukopenia
  - Altered mental status

Clinical Presentation

- Compensated shock
  - Tachycardia, poor perfusion
  - Normal blood pressure
- Decompensated shock
  - Weak central pulses
  - Altered mental status
  - Oliguria
  - Hypotension

Treatment

- Early recognition is key!!
- Volume resuscitation (Most Important)
  - 20ml/kg NS boluses over 5-20 minutes (up to 60ml/kg in first hour)
- Vasopressors
- Broad-spectrum antibiotics

Neurologic Emergencies

Occur in > 10% of Oncology Patients

- Seizures
- Altered mental status (AMS)
- Cerebrovascular accidents (CVA)
- Spinal cord compression
- Increased intracranial pressure (ICP)
Spinal Cord Compression

- Occurs in 3–5% of children with cancer
- Sarcomas account for about half the cases of spinal cord involvement in kids.
- Others: neuroblastoma, germ cell tumors, lymphoma, leukemia and metastasis of CNS tumors
- Usually not life threatening

Clinical Presentation

- Back pain with localized tenderness (80% of patients)
- Loss of strength and sensory deficits
- Incontinence, urinary retention and other abnormalities of bowel/bladder are late findings.
- Children with cancer + back pain = spinal cord involvement until proven otherwise.

Evaluation

- History and neurologic exam
- Spinal radiographs (useful if vertebral mets are present but will miss 50% of epidural disease)
- MRI +/- contrast
- Cerebrospinal fluid analysis (important when evaluating subarachnoid disease)

Treatment

- Immediate initiation of treatment is crucial!!
- Dexamethasone (decrease local edema)
- Chemotherapy, radiation or surgical decompression

Hematology Emergency
An 11 year-old African American male with sickle cell disease (HgbSS) and asthma presents to PCP with 2 day history of chest pain and cough. Physical exam revealed diffuse wheezes bilaterally and oxygen saturation of 86%. EMS was called, and patient was transferred to ED.

- BP 106/65
- HR 110
- RR 28
- SaO2 88% on room air
- T 102.7°F

Physical Exam: Inspiratory and expiratory wheezes throughout all lung fields, nasal flaring but no retractions.

What do you do next?
- Call Heme Onc
- Start oxygen
- Obtain Labs (CBC, type and screen, retic, blood culture)
- Give antibiotics (IV Cephalosporin)
- Obtain Chest X-ray

Lab Results
- WBC 15.4
- Hgb 6.5 (baseline = 6–7)
- Platelets 405K
- Retic Count 21.4%

Definition:
- New radiologic density on CXR in patient with SCD and 2 or more of the following:
  - Fever, cough, chest pain, hypoxia, tachypnea, dyspnea or respiratory distress
  - Infiltrate development lags behind other symptoms
  - Leading cause of premature death
  - Second most common reason for hospitalization
  - Affects approximately 50% of patients at least once

Treatment

- Antibiotics: IV abx and oral macrolide
- Cautious hydration: Can easily tip into worsening pulmonary edema
- Blood transfusions: Simple or exchange
- Steroids: For patients with asthma
- Incentive spirometry

Summary

- Survival in children with cancer and blood disorders has increased dramatically during the past five decades.
- The progress is not only due to advances in specific hematologic and oncologic therapies, but also to advances in supportive care and improved ability to manage life-threatening complications.


References

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