Pediatric Hem/Onc: When to Go on a Zebra Hunt on the Boards

Terrie Tristan Flatt, DO
Hematology/Oncology
Children’s Mercy Hospital
Kansas City, MO
General Information

Pediatric cancer is rare yet it accounts for the leading cause of disease related death in children less than 15 y/o
A 2-year-old girl presents for evaluation of fussiness, low-grade fever, and what her parents describe as "growing pains." On physical examination, you palpate a nontender mass deep in the right periumbilical area and note mild purple discoloration of the eyelids. Of the following, the MOST likely diagnosis is

A. hepatoblastoma  
B. Hirschsprung disease  
C. intussusception  
D. neuroblastoma  
E. Wilms tumor
You identify a right sided mass in a 2 m/o female on routine health supervision visit. The mass is firm but not tender to palpation. US reveals a mass pushing the right kidney downward.

The most likely diagnosis is:

A. hepatoblastoma
B. Adrenocortical carcinoma
C. Neuroblastoma
D. Rhabdomyosarcoma
E. Wilm’s tumor
A parent brings in her 4 y/o son for you to evaluate a mass that she discovered while bathing him. He has remained active and not been ill. You palpate a large, non-tender mass in RUQ of the abdomen. His BP is 130/70 and HR is 80. UA reveals microscopic hematuria.

The most likely diagnosis is:

A. Hepatoblastoma

B. Wilm’s tumor

C. Renal cell CA

D. Neuroblastoma

E. Pheochromocytoma
The parents of a child who was diagnosed at birth with Beckwith-Wiedemann syndrome bring in the baby for his 2-month evaluation. They ask about future health problems and his prognosis now that his omphalocele has been repaired.

Of the following, the child is MOST at risk for

A. acute lymphocytic leukemia
B. astrocytoma
C. Hodgkin disease
D. rhabdomyosarcoma
E. Wilms tumor
Abdominal Mass: Common Types

- Wilms
- Neuroblastoma (NBL)
- Hepatoblastoma (HBL)/hepatocellular carcinoma (HCC)
- Rhabdomyosarcoma
- Sarcomas
- Other Adrenal masses: adrenocortical carcinoma (ACT)
Abdominal Mass: Clinical Presentation

- Chronic constipation
- Chronic diarrhea
- Hypertension
- Chronically distended abdomen
- Hormonal changes--virilization, acne, malar rash, etc (germinoma and adrenocortical carcinoma)
- Intussusception
Abdominal Masses By Age

- **Newborns:**
  - NBL, mesoblastic nephroma, HBL

- **Up to age 3:**
  - NBL, Wilms, HBL, rhabdomyosarcoma

- **Child 3-11:**
  - NBL, Wilms (3-5), lymphoma, HCC, rhabdomyosarcoma

- **Teenager/young adult**
  - Lymphoma, HCC, rhabdomyosarcoma, adrenal, ovarian masses (germ cell tumors)
Neuroblastoma (NBL)

- ~ 7.8% of childhood cancers in US
- 650 new cases annually in US
- Age:
  - < 1 yr—40%
  - 1-2 yrs- 35%
  - >2 yrs-25%
NBL: Clinical Presentation

- Symptoms associated with bone marrow failure—bruising, fever, infection, limp, weight loss. 50% of patients present with advanced disease to bone marrow and bone.

- 2/3 of all patients present with asymptomatic abdominal mass
NBL: Clinical Presentation

- **Other:**
  - Skin nodules (blueberry muffin)
  - Liver mets
  - Bone mets (pathological fractures)
  - Periorbital bruising known as raccoon eyes

- **Paraneoplastic syndromes:**
  - Myoclonus and opsinclonus (2%)
  - Intractable/chronic diarrhea (rare)

- **HTN and other SNS associated symptoms**
Clinical Presentation

- Other tumor sites
  - Paraspinal sympathetic ganglia: weakness, limp, paralysis, bowel/bladder dysfunction
  - Thoracic site (posterior mediastinum): no sx, to chronic cough, respiratory distress
  - Thoracic tumors to neck: Horner Syndrome or poor feeding and respiratory difficulty in an infant.
Case 1

- **HPI**: 3 y/o male with a 6 week h/o fatigue, orbital swelling, mild peri-orbital discoloration, limp, and fever. Treated for allergic rhinitis and otitis media with 3 different antibiotics and no response.

- **CT scan obtained to evaluate for sinusitis**

- **Diagnosis**: Stage 4 Neuroblastoma
Wilms Tumor

- Fifth most common pediatric malignancy
  - Most common renal tumor in children
- ~0.8 cases per 100,000 persons.
  - 500 each year in the United States
  - 6% of cases involving both kidneys
- The mean age at diagnosis is 3.5 years and is common b/t 3 to 5 yrs of age
Wilms Tumor

- The most common feature at presentation is a painless abdominal mass.

- Abdominal pain occurs in only 30-40% of cases.

- Other signs and symptoms include hypertension, fever from tumor necrosis, hematuria, and anemia.
Wilms Tumor & Syndromes

- **Beckwith-Wiedemann syndrome**
  - Macroglossia
  - Organomegaly (liver, kidneys, pancreas, heart)
  - Omphalocele, umbilical hernia or diastasis recti
  - Hemihypertrophy
  - Chrom 11p, increased production IGF-2

- **Denys-Drash (11p13)**
  - Wilms tumor,
  - Pseudohermaphroditism
  - Glomerulopathy
Wilms Tumor & Syndromes

- **WAGR Syndrome**
  - Wilms' tumor
  - Aniridia (lack or defect of the iris)
  - Genitourinary Anomalies (gonadal dysgenesis, hypospadias, cryptorchidism, duplication of collecting system)
  - Mental Retardation
  - Deletion of chromosome 11p13
  - Tumor develops at a younger age
  - Increased incidence of bilateral tumor
Wilms Tumor & Syndromes

- Trisomy 18—Edward syndrome
Surveillance: Beckwith-Wiedemann syndrome

- Abdominal US every 3-4 months until 8 yrs of age
- Alpha-fetal protein level every 3-4 months until 4 yrs of age
- **Vary from center to center**
A 4 y/o male presents with several “masses” over the skull (see XR). The lesion was biopsied and the following finding was present (see photo).

Of the following, the child is MOST at risk for
A. Ewing’s Sarcoma
B. Langerhan’s cell histiocytosis
C. Osteosarcoma
D. Aneurysmal bone cyst
E. Wiskott-Aldrich Syndrome
- Stain CD1a & S-100 positive
- Birbeck Granules
Osteosarcoma

- The incidence is 400 cases per year (4.8 cases per million persons <20 y)
- The incidence increases steadily with age; a relatively dramatic increase in adolescence corresponds with the growth spurt.
- The incidence is slightly higher in African Americans than in Caucasians
Osteosarcoma

- **Location**
  - femur (42%), with 75% of tumors in the distal femur
  - tibia (19%), with 80% of tumors in the proximal tibia
  - humerus (10%), with 90% of tumors in the proximal humerus
  - jaw (8%) and pelvis (8%)
  - ALWAYS think METHAPHYSEAL portion of long bones
Osteosarcoma

- Radiographic Buzz Words
  - characteristic Codman triangle
Osteosarcoma

- Radiographic Buzz Words
  - Sunburst lesion: *hair-on-end* appearance when new bone is laid down perpendicular to cortex along Sharpey’s fibers
Ewing Sarcoma

- The annual incidence of Ewing sarcoma family tumors from birth to age 20 years is 2.9 cases per million.
- Incidence peaks in the late teenage years (64%) in the 2nd decade of life.
- The incidence in whites is at least 9 times higher than that in blacks.
Ewing Sarcoma

- Patients usually present with pain.
- Patients often have a palpable mass.
- Patients with lesions of the long bones can present with a pathologic fracture.
- Back pain may indicate a paraspinal, retroperitoneal, or deep pelvic tumor.
Ewing Sarcoma: Buzz Words

- **Translocation t(11;22)** or one of a series of related translocations occurs in more than 95% of Ewing sarcoma.

- Radiographic Buzz words
  - Onion Skin lesion (laying down of lamellar bone)
  - THINK **DIAPHYSEAL**
Aneurysmal bone cyst

- Painless swelling
- ABCs most commonly affect the long, tubular bones, followed spine/flat bones
- 70-86% occurring in patients younger than 20 years
15 m/o female of Southeast Asian ancestry presents for well child exam. She is well appearing and exam is unremarkable. CBC is significant for Hgb 8, MCV 66, RBC 6.5 million and RDW 13. All other cell lines are normal. She drinks 16oz of cow’s milk/day.
What is the next step in management
a) Iron supplementation
b) Osmotic fragility test
c) Hgb Electrophoresis
d) G6PD levels
## Iron Deficiency vs. Thalassemia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Iron Deficiency Anemia</th>
<th>Thalassemia Trait</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCV</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>RDW</td>
<td>High</td>
<td>NL</td>
</tr>
<tr>
<td>RBC</td>
<td>Low</td>
<td>Normal to High</td>
</tr>
<tr>
<td>Hb Electrophoresis</td>
<td></td>
<td>β-Thal Trait: Elevated HbA2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>α-Thal Trait: Low HbA2</td>
</tr>
<tr>
<td>FEP</td>
<td>Elevated</td>
<td>NL</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Low</td>
<td>NL</td>
</tr>
<tr>
<td>Serum Iron</td>
<td>Low</td>
<td>NL</td>
</tr>
<tr>
<td>Transferrin sat.</td>
<td>Low</td>
<td>NL</td>
</tr>
<tr>
<td>Mentzer index (MCV/RBC)</td>
<td>&gt;13.5</td>
<td>&lt;11.5</td>
</tr>
</tbody>
</table>
A 3 y/o Caucasian male presents with jaundice and fatigue. Splenomegaly is present on examination. Hgb is 6.3, MCV 77, and MCHC is 39 (elevated). He had significant jaundice at birth as well anemia that resolved. There is a family history of anemia and cholecystectomy.
How is this disorder most often inherited:
- a) autosomal recessive
- b) autosomal dominant
- c) X-linked
- d) never inherited
A 3 y/o male presents to his PCP with new onset bruising and “rash” on his neck. He has h/o recent URI. He is well appearing and examination is only remarkable for petechiae on neck and bruising to shins and arms. CBC is remarkable for platelet count of 6000 and all other cell lines are normal. Blood chemistries, ESR and uric acid are normal. No family history of blood disorders or deaths from cancer or infection before 40 years of age.
What is the most likely diagnosis:
- a) Acute lymphoblastic leukemia
- b) Immune thrombocytopenia purpura
- c) Fanconi anemia
- d) Wiskott Aldridge syndrome
The most common cause of bacteremia in a patient with the above blood smear is:
- a) Salmonella
- b) Staphylococcus areus
- c) *Strep. Pneumoniae*
- d) Pseudomonas species
An 18 m/o boy presents with pallor, decreased activity and appetite but he always tends to be a picky eater. He has been limping and complaining of leg pain for 2 weeks. On exam you note bruising to the legs, arms and one on his back. He is ill-appearing but non-toxic. He is sallow appearing, oral mucosa is pale, conjunctivae are pale and he has several small mouth sores. He has several 1-2 cm hard nodes in the inguinal area. His HR is 170.

The most likely diagnosis is:
A. ITP
B. Child abuse
C. ALL
D. iron-deficiency anemia
E. Transient erythroblastopenia of childhood
A 12-year-old girl presents to the emergency department with nausea, vomiting, and abdominal pain of 1 month's duration. Physical examination reveals a large, smooth mass encompassing almost the entire lower abdomen. Computed tomography scan confirms a mass, and biopsy documents Burkitt lymphoma. She immediately begins receiving chemotherapy, and 12 hours later she develops the classic electrolyte and urinary findings consistent with tumor lysis syndrome (TLS).

Of the following, the laboratory findings MOST consistent with TLS are

A. Serum Potassium: Elevated; Serum Phosphorous: Elevated; Serum lactate dehydrogenase: Normal; Serum sodium: Elevated
B. Serum Potassium: Elevated; Serum Phosphorous: Normal; Serum lactate dehydrogenase: Elevated; Serum sodium: Normal
C. Serum Potassium: Normal; Serum Phosphorous: Elevated; Serum lactate dehydrogenase: Elevated; Serum sodium: Elevated
D. Serum Potassium: Normal; Serum Phosphorous: Normal; Serum lactate dehydrogenase: Elevated; Serum sodium: Normal
E. Serum Potassium: Elevated; Serum Phosphorous: Elevated; Serum lactate dehydrogenase: Elevated; Serum sodium: Normal
Tumor Lysis

- Definition: Break down (lysis) of fragile tumor cells that contain increased quantities of potassium, phosphorous, and protein (uric acid).
Risk for Tumor Lysis

- ***Burkitt’s Lymphoma
- Leukemia, esp lymphoblastic
- AML is less associated with this
- Lymphoma
- High WBC with high blast count
- Large spleen, liver, bulky nodes
Tumor Lysis

- Lab Findings:
  - K↑, Phos ↑, Uric Acid ↑
  - Ca↓ to normal
  - LDH ↑
Treatment

- IV Hydration (1.5 to 2 x maintenance fluids WITHOUT K+).
- Allopurinol or Rasburicase for uric acid
- Phosphorous binders if Phos extremely elevated
- Some use NaHCO3 in IVF but must exercise caution b/c if ca x phos ratio is >50, then it will increase the risk of precipitation and phos will often continue to rise.  HCO3 is most beneficial with high uric acid as it makes it more soluble for excretion.  HCO3 decreases the solubility of Phos
“When you hear hoof beats beneath your window, think ponies for there are far fewer zebras in our presence.”

HOWEVER, there will always be zebras when you hunt for them.