GOOD MORNING!

July 3, 2014
OUR PATIENT

4yo Female with:
2 days of fever, sore throat, swollen nodes in neck and abdominal pain

PMH: Tonsillectomy age 2
Immunizations: UTD
NKDA
### Differential:

<table>
<thead>
<tr>
<th>Infant</th>
<th>Child</th>
<th>Adolescent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMMON CAUSES</strong></td>
<td></td>
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<tr>
<td>Syphilis</td>
<td>Viral infection</td>
<td>Viral infection</td>
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<tr>
<td>Toxoplasmosis</td>
<td>EBV</td>
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<tr>
<td>CMV</td>
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<td>HIV</td>
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<td></td>
<td>Toxoplasmosis</td>
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<td></td>
<td></td>
<td>Syphilis</td>
</tr>
<tr>
<td><strong>RARE CAUSES</strong></td>
<td></td>
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<tr>
<td>Chagas disease (congenital)</td>
<td>Serum sickness</td>
<td>Serum sickness</td>
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<tr>
<td>Congenital leukemia</td>
<td>SLE, JRA</td>
<td>SLE, JRA</td>
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<tr>
<td>Congenital tuberculosis</td>
<td>Leukemia/lymphoma</td>
<td>Leukemia/lymphoma/Hodgkin disease</td>
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<tr>
<td>Reticuloendotheliosis</td>
<td>Tuberculosis</td>
<td>Lymphoproliferative disease</td>
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<tr>
<td>Lymphoproliferative disease</td>
<td>Measles</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Metabolic storage disease</td>
<td>Sarcoidosis</td>
<td>Histoplasmosis</td>
</tr>
<tr>
<td>Histiocytic disorders</td>
<td>Fungal infection</td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td></td>
<td>Plague</td>
<td>Fungal infection</td>
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<tr>
<td></td>
<td>Langerhans cell histiocytosis</td>
<td>Plague</td>
</tr>
<tr>
<td></td>
<td>Chronic granulomatous disease</td>
<td>Drug reaction</td>
</tr>
<tr>
<td></td>
<td>Sinus histiocytosis</td>
<td>Castleman disease</td>
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<tr>
<td></td>
<td>Drug reaction</td>
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OUR PATIENT

4yo Female with:

2 days of fever, sore throat, swollen nodes in neck and abdominal pain

PMH: Tonsillectomy age 2

Immunizations: UTD

NKDA
PHYSICAL EXAM

W 17.2kg (62%)  Ht 105cm (67%)  T 98.8  P139  R15  BP 101/63  Pox 100% RA

General: well appearing, NAD

Eyes/Ears/Mouth: normal

Neck: multiple bilateral large anterior and posterior cervical lymphadenopathy

Respiratory: normal

Cardiovascular: normal

GI: +Hepatosplenomegaly

MSK: normal

Skin: normal
<table>
<thead>
<tr>
<th>LABS</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.2</td>
</tr>
<tr>
<td>253</td>
</tr>
<tr>
<td>31</td>
</tr>
<tr>
<td>26</td>
</tr>
<tr>
<td>2S/4L/1M/93 Blasts</td>
</tr>
<tr>
<td>CRP: 0.5/ESR: 5</td>
</tr>
<tr>
<td>137</td>
</tr>
<tr>
<td>103</td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td>73</td>
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<tr>
<td>6.5</td>
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<tr>
<td>23</td>
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<tr>
<td>0.3</td>
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<tr>
<td>Ca 9.5</td>
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<tr>
<td>7.8/3.7/1.2/400/310/62</td>
</tr>
<tr>
<td>Pt 18.2/PTT 30.7/INR 1.55</td>
</tr>
<tr>
<td>LDH: &gt;4400 Uric Acid: 8.3</td>
</tr>
<tr>
<td>Bone Marrow Biopsy: T-ALL, 95% blasts</td>
</tr>
<tr>
<td>LP: 59% lymphocytes 5% monocytes 36% blasts</td>
</tr>
</tbody>
</table>

Strep: negative
Mono: negative
VP: + Parainfluenza
INCIDENCE AND EPIDEMIOLOGY:

Cancer: 1 case per 7,000 children age 15 years and younger

40% are hematologic malignancies (leukemia and lymphoma)
- Leukemia most frequent malignancy during childhood (30% of all childhood cancers)

ALL accounts for 77% of all cases of leukemia in children
- Children 2-5 years of age
- Boys > Girls
- Hispanic > Caucasian >>>>> African American

Majority of cases are from B-cell progenitors
- 15% from T-cells
- 1-2% from mature B-cells
The genetic disorder most commonly associated with an increased risk of leukemia is:

A. Ataxia telangiectasia
B. Down Syndrome
C. Fanconi Anemia
D. Klinefelter syndrome
E. Neurofibromatosis
PATHOGENESIS:

Results from expansion of malignant hematopoietic or lymphoid cells
- Cellular proliferation is usually monoclonal

Casual factors unknown

Tobacco smoke, organic solvents, and pesticides, increase relative risk of childhood leukemia

No viral agent demonstrated in causing the more frequent subtypes of ALL

Conditions with an increased risk:
- Down Syndrome**
  - 1% of children with Down Syndrome develop leukemia by 5 years of age
- Ataxia Telangiectasia
- Immunodeficiencies
- Fanconi Anemia
- Klinefelter syndrome
- Neurofibromatosis
A previously healthy 5-year old girl presents with pallor and bone pain of 3 weeks’ duration. PE reveals pallor, increased bruising, and scattered petechiae. She is afebrile and has neither LAD nor HSM. Her Hgb is 3.5g/dl, WBC 1.1x10^3/mcl, and platelet count is 17x 10^3/mcl. No blasts are seen on her peripheral blood smear. You are most concerned about acute leukemia and aplastic anemia. Pending a bone marrow examination, which should establish the diagnosis, the clinical feature that is most helpful in pointing to the correct diagnosis is:

A. Absence of blasts on the peripheral blood smear
B. Absence of hepatosplenomegaly
C. Presence of bone pain
D. Presence of fever
E. Presence of petechiae and purpura
**CLINICAL PRESENTATION:**

Initially nonspecific symptoms:
- Low-grade fevers, anorexia, fatigue, and irritability.

As bone marrow is replaced with malignant cells, clinical features of marrow failure develop:
- Pallor, bruising, epistaxis, petechiae, and recurrent infections
- Severe bone pain and tenderness may be seen (25% present this way) → limp/refusal to walk

Infiltration most commonly of lymph nodes, spleen and liver

Can affect any organ!

<table>
<thead>
<tr>
<th>Leukemia Abnormality</th>
<th>Clinical Signs, Symptoms, or Complications</th>
</tr>
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<tbody>
<tr>
<td>Anemia</td>
<td>Pallor, fatigue, decreased appetite; congestive heart failure with extremely severe anemia</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>Fever; risk of overwhelming infection increases with severity of neutropenia</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Petechiae, ecchymoses, mucosal and other bleeding</td>
</tr>
<tr>
<td>Coagulation factor deficiencies</td>
<td>Increased bleeding; disseminated intravascular coagulation with severe factor deficiencies occurs frequently in the acute promyelocytic subset of acute nonlymphocytic leukemia</td>
</tr>
<tr>
<td>Leukemia in bone</td>
<td>Bone pain</td>
</tr>
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</table>
An 18-year-old boy comes to your office with complaints of fatigue, pallor, bruising, cough, and difficulty doing any exercise. His physical examination reveals pallor, mild bruising, occasional petechiae, and moderate respiratory distress. He is afebrile, but his respiratory rate is 35 breaths/minute. His chest is clear. He has diffuse cervical adenopathy and moderate hepatosplenomegaly. The results of a complete blood count are hemoglobin of 8.9 g/dL, white blood cell count of 44 x10^3/mcL, and platelet count of 19x10^3/mcL. The most likely cause of his respiratory distress is:

A. Congestive heart failure due to anemia

B. Intrapulmonary hemorrhage

C. Mediastinal lymphadenopathy

D. Pneumonia.

E. Pulmonary hyperleukocytosis
PRESENTATION COINCIDING WITH WORKUP:

Proliferation in marrow results in decreased WBCs, RBCs, platelets on CBC
- Malignant blasts are frequently (but not always!) observed in blood
- Bone marrow biopsy is essential to distinguish leukemia from other conditions that involve marrow

Airway obstruction with respiratory distress secondary to mediastinal lymphadenopathy
- Chest X-Ray can reveal mediastinal mass
- Risk is greatest with T-cell ALL

Metabolic abnormalities
- Kidney function compromised secondary to infiltration, hyperuricemia can impair function itself

Hyperleukocytosis (>100x10^3) can damage vital organs in kids with ANLL
- These cells are like “sludge” → infarction
- ALL has much risk because cells are more deformable
6 year old girl presents with 3-week history of low-grade fever, malaise, bruising, and pallor. Her PE reveals pallor, mild generalized LAD, and a spleen palpable 2cm below the left costal margin. She is afebrile. You suspect leukemia and obtain further studies. WBC 86, diff: 95% blasts, 5% lymphocytes, Hgb 7.6, Plts 49, NA 145, CI 105, BUN 8, Crt 0.6, UA 9.9, LDH 1200, Phos 4.5, Ca 9.2. At this time you should start:

A. Allopurinol and hydration
B. Broad spectrum ABX coverage
C. Platelet transfusion
D. Prednisone
E. Red cell transfusion
TUMOR LYSIS: AN ONCOLOGIC EMERGENCY!

Hyperkalemia
Hyperphosphatemia
Hyperuricemia
Secondary hypocalcemia

Who’s at risk:
- High proliferative rate
- Large tumor burden (>50K per microL)
- Organ infiltration/Marrow involvement
- Pre-treatment LDH >2x upper limit of normal
- Pre-treatment hyperuricemia
- Dehydration
- Highly sensitive to chemo
TUMOR LYSIS- CLINICAL PICTURE AND TREATMENT

Symptoms:
- Nausea, Vomiting, Diarrhea, Anorexia, Lethargy, Hematuria, Heart failure, Cardiac dysrhythmias, Seizures, Muscle cramps, Tetany, Syncope, Possible sudden death

Prevention/Treatment:
- Aggressive hydration is key!
- Allopurinol- hypoxanthine analog that inhibits xanthine oxidase → blocks metabolism to uric acid (decreases the incidence of obstructive uropathy)
- Rasburicase- promotes degradation of uric acid by administration of urate oxidase
- NaBicarb- Urinary alkalinization to increase uric acid solubility
- Correct Electrolyte abnormalities
A patient in your practice was diagnosed with acute lymphoblastic leukemia 2 weeks ago and is undergoing treatment at the regional pediatric oncology center. His parents are concerned that the oncologists are being too optimistic in stating his prognosis. The overall 5-year survival rate for newly diagnosed acute lymphoblastic leukemia in developed countries is best described as being at least:

A. 40%.
B. 50%.
C. 60%.
D. 70%.
E. 80%.
Before chemo - median survival 3 months

Now - 5 year survival rate for children receiving new diagnosis of ALL in the US is > 80%

LPs for diagnosis of meningeal involvement and to administer medications

Chemo regimen 3 phases: induction, intensification, maintenance

- Want to achieve a complete remission
- >94% probability of this occurring in 4 weeks if have ALL
- Remission defined by less than 5% blasts in the bone marrow

Main therapy is given for 2-3 years
An 18-year old girl is coming to you because of left-sided hip pain. The pain began approx. 4 months ago initially with exercise only, but has worsened. She now has pain with weight bearing. She denies pain elsewhere. She has a history of ALL diagnosed at 11 months and was treated based on a high risk status because of her age and initial WBC of 65. She completed chemo and has remained in remission. A CBC today is normal. The most likely cause of her hip pain is:

A. Aseptic necrosis of the femoral head due to corticosteroids and chemo
B. Hip fracture due to chronic calcium loss as a result of her chemo
C. Osteogenic sarcoma as secondary malignancy
D. Osteomyelitis related to her immune suppression.
E. Recurrent ALL
**PROGNOSIS**

CNS and testes most common sites for recurrence

**Risk of ALL recurrence highest if:**
- Less that 1 yr and older than 10 yrs
- Higher concentration of leukemia cells in blood (WBC >50K)
- Presence of Philadelphia chromosome abnormality (3-5% of children with ALL)

Starting antibiotics immediately in a neutropenic febrile child has helped reduce morbidity and mortality

Radiation therapy/Intensive therapy for relapsed leukemia most likely to develop long term complications:
- Growth abnormalities, precocious puberty
- Secondary malignancies after radiation, CNS most frequent
- Cardiomyopathy
- Impaired fertility

Avascular necrosis of femoral head secondary to prolonged corticosteroid use
CONCLUSIONS PER CONTENT SPECS:

✓ Recognize bone pain as a symptom of leukemia

✓ Understand that most patients with acute lymphoblastic leukemia will be cured of their disease using current treatment strategies

✓ Identify the central nervous system and testes as important sites of relapse of acute lymphoblastic leukemia

✓ Identify Down syndrome as a disease with an increased risk of leukemia

✓ Know that overwhelming sepsis is a serious complication in patients with leukemia

✓ Recognize that renal function and serum electrolytes should be assessed in patients who have suspected leukemia or lymphoma to exclude tumor lysis syndrome

✓ Understand that aplastic anemia and childhood leukemia may both present with purpura, pallor, and fever

✓ Know that the absence of blasts in the peripheral blood of a patient with pancytopenia does not rule out the diagnosis of leukemia
OUR PATIENT:

Leukopheresis x 2 days

Rasburicase x 5 days
Allopurinol
Bicarbonate in fluids

Blood Cultures negative

1 month of induction chemo-
intrathecal MTX, Daunorubicin,
VCR, Solumedrol

Prophylactic Bactrim

CXR: 6/20
HAVE A GREAT DAY!

NOON CONFERENCE: DR. BARKEMEYER “NICU EMERGENCIES”