Goals for Today

Review Presenting Signs & Critical Diagnostic Tests

Leukemia

Lymphoma

Bone Tumors

Brain Tumors
A 5-year old with anemia

At home:
Pale X 2 weeks with bags under her eyes
Vomiting qod X one week, no blood or bile; GM with pneumonia
DOA temp 99.7, not eating, diarrhea, cough & green sputum

At the doctor’s office:
Pale, alert, active, no bruising or petechiae, no adenopahty, no HSM
Hgb 5.3; retic 0.6%; ANC 1100; platelets 306,000

Differential Dx:
Iron deficiency anemia
Viral suppression
Leukemia or aplastic anemia a distant 3rd and 4th
When to think about ordering a bone marrow

Two cell lines down and child looks ill

WBC > 20,000 OR uric acid >5

Blasts on peripheral smear

Anemia with low reticulocyte count

Before giving steroids for new asthma or new arthralgia
When to think about ordering a bone marrow

Two cell lines down and child looks ill

WBC > 20,000 OR uric acid >5

Blasts on peripheral smear

Anemia with low reticulocyte count

Before giving steroids for new asthma or new arthralgia

Our patient had blasts on the peripheral smear and 97% in BM

Was in remission by Day 29 of induction.

Why is this child being treated as high risk?
Cytogenetics and MRD in B-cell Acute Lymphocytic Leukemia

Low Risk Favorable
ETV6/RUNX1 (TEL/AML1) fusion
double trisomy of chromosomes 4 and 10

High Risk Unfavorable
iAMP21 on FISH
MLL rearrangement on FISH
Hypodiploidy and/or DNA index <0.81
Ph+ chromosome: BCR-ABL1 on FISH or t(9;22)(q34;q11) cytogenetics

Minimal Residual Disease
Immunophenotyping to look for original B-cell leukemic clone
T-Cell: CD3.
B-Cell: CD19, CD20, CD22, CD79a, PAX5, Kappa, Lambda.
Myeloid: CD13, CD15, CD33.
Other: CD10, CD34, CD45, TdT.
**Why does our patient have High Risk B-cell Acute Lymphocytic Leukemia?**

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Favorable/Unfavorable</th>
<th>Description</th>
</tr>
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</table>
| Low Risk Favorable | NO | ETV6/RUNX1 (TEL/AML1) fusion  
double trisomy of chromosomes 4 and 10 |
| High Risk Unfavorable | NO | iAMP21 on FISH  
MLL rearrangement on FISH  
Hypodiploidy and/or DNA index <0.81  
Ph+ chromosome: BCR-ABL1 on FISH or t(9;22)(q34;q11) cytogenetics |
| Minimal Residual Disease | YES | Immunophenotyping to look for original B-cell leukemic clone  
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Myeloid: CD13, CD15, CD33.  
Other: CD10, CD34, CD45, TdT. |
Current Risk Stratification for Acute Lymphocytic Leukemia

Low Risk
- favorable cytogenetics and CNS1
- day 8 blood & day 29 BM are minimal residual disease (MRD) negative

Standard Risk
- 12 mos to 10 yrs at dx; <50,000 wbc in peripheral blood, and CNS1/2
  A) no favorable cyto; day 8 PB MRD <1% & Day 29 BM MRD < 0.01%
  B) no favorable cyto; day 29 BM MRD < 0.01%; day 8 PB MRD ≥ 0.01% or CNS2

High Risk
- 10-13 yrs at diagnosis
- unfavorable genetics with day 8 PB and day 29 BM MRD negative
- no unfavorable genetics with day 8 PB MRD≥1%

Very High Risk
- >13 yrs at diagnosis
- induction failure with day 29 BM MRD≥0.01% or hypodiploidy or CNS3
## Risk Stratification in B-cell ALL

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>5-year survival</th>
<th>Therapy Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td>&gt;95%</td>
<td>no anthracyclines, no alkylating drugs, few intrathecal (IT) treatments, prednisone, L-asparaginase, vincristine, methotrexate, mercaptopurine</td>
</tr>
<tr>
<td><strong>Standard</strong></td>
<td>90-95%</td>
<td>Low dose anthracyclines, moderate alkylating agents, moderate IT, prednisone, L-asparaginase, vincristine, methotrexate, mercaptopurine</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>88-90%</td>
<td>High dose anthracyclines &amp; alkylating agents, frequent IT, IV methotrexate, prednisone, L-asparaginase, vincristine, methotrexate, mercaptopurine</td>
</tr>
<tr>
<td><strong>Very High</strong></td>
<td>&lt;80%</td>
<td>intense chemo, frequent IT, XRT, BMT if matched sibling donor</td>
</tr>
</tbody>
</table>
Eleven-year old with mumps

At home:
Lump in left neck; some pain with swallowing
More swelling and pain over the week

At the doctor’s office 10 days later:
Alert, active, swelling in left neck
No immunizations for religious reasons; likely mumps

At the surgeon’s office 17 days later:
More swelling in neck; CXR shows widening mediastinum
Biopsy taken and steroids started

In the Pediatric ICU 24 days later:
Cough, difficulty breathing, air hunger
Massive lymphadenopathy in neck bilaterally

Differential Dx:
Viral Infection vs Hodgkin’s vs Non-Hodgkin’s vs Leukemia
Superior Vena Cava Syndrome and/or Tumor Lysis Syndrome
....
Initial Chest Xray
Superior Vena Cava Syndrome

• Major Causes in Children
  – Thrombosis following cardiac surgery
  – Cancer with mediastinal mass

• Why is it a problem?
  – SVC thin walled; low intraluminal pressure
  – SVC surrounded by thymus, lymph nodes
  – Mediastinal mass can impinge on bronchus
Anatomy of SVC Syndrome
Neck CT in Non-Hodgkin’s Lymphoma

Face & Neck show supraclavicular node and massive adenopathy
Tumors that cause SVC syndrome

• Non-Hodgkin’s Lymphoma
  – 70% have mediastinal mass

• Hodgkin’s Disease
  – 30% have mediastinal mass

• Acute Lymphocytic Leukemia
  – 8% have mediastinal mass (but many more children have ALL compared to NHL)
Signs of SVC syndrome

- Cough/dyspnea 68%
- Dysphagia 63%
- Orthopnea 63%
- Pleural effusion 50%
- Wheezing 31%
- Hoarseness 19%
- Facial edema 12%
- Pericardial effusion 19%
Tumors that cause SVC syndrome

• Non-Hodgkin’s Lymphoma
  – 70% have mediastinal mass

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• Acute Lymphocytic Leukemia
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Care of child with SVC syndrome

- Sit up and give oxygen
- Upright chest xray
- Transfer to PICU
- No conscious sedation or anesthesia
- Call hematologist/oncologist to
  - Obtain biopsy of lymph node or bone marrow
  - Treat with chemotherapy or irradiation
A 10-year old soccer player

At the game:
Kicked in the leg; got up and played again

At home 5 days later:
Left leg still painful with some swelling; no bruising

At the doctor’s office:
Mild pain for several months
Mild swelling on lateral left leg, 4 cm below knee; tender to palpation
Plain x-ray: “...mixed sclerotic and permeative pattern with soft tissue bone formation and distal periosteal reaction involving approximately 9 cm of the proximal metadiaphysis portion of the fibular shaft. The proximal portion appears sclerotic and extends to the growth plate.

Differential Dx:
Osteogenic sarcoma
Ewing’s sarcoma
....
Xray of Painful, swollen leg

Fibula lesion
Sunburst appearance
Periostial reaction
Codman triangle
A 10-year old farmer

On the lawn mower:
Lower back pain for 3 months
Bilateral leg pain for 2 weeks

At school the next day:
Unable to participate in gym
Left school to be able to lie supine

At the doctor’s office:
Unable to sit upright
Bilateral leg weakness

Differential Dx:
Osteogenic sarcoma
Ewing’s sarcoma
....
# Osteogenic and Ewing Sarcomas

<table>
<thead>
<tr>
<th></th>
<th>Osteogenic</th>
<th>Ewing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: Female</td>
<td>1.5 : 1.0</td>
<td>1.2 : 1.0</td>
</tr>
<tr>
<td>Age</td>
<td>10 – 30</td>
<td>10 - 20</td>
</tr>
<tr>
<td>Primary Sites</td>
<td>Long bones</td>
<td>Long &amp; skeletal bones</td>
</tr>
<tr>
<td>Metastases</td>
<td>lungs</td>
<td>adjacent tissue</td>
</tr>
<tr>
<td>5-yr survival</td>
<td>10-20% if metastatic</td>
<td>15-30% if metastatic</td>
</tr>
<tr>
<td>Genetics</td>
<td>p53, del9p21</td>
<td>T(11;22)  EWSR1/FLI1</td>
</tr>
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</table>
An irritable infant

At home 11 months old:
- Fussy when waking up
- Spits up frequently
- Starting to walk around furniture

At the doctor’s office for 12 month checkup:
- Growing well
- Standing alone
- Fussy child
- All labs normal and immunizations up to date

At home 13 months old:
- Fussy every morning
- Vomiting before breakfast
- Not standing or walking
- Falling frequently

Differential Dx:
- Failure to thrive
- Neurological disorder
- Brain tumor...
Signs of Increased ICP

• Infant and toddler
  – Irritability, lethargy, personality changes
  – Head holding or banging
  – Vomiting
  – Loss of motor skills
  – seizures

• Pre-teen and Adolescent
  – Headache, occipital, occur in morning
  – Vomiting occurring in morning
  – Blurred vision, strabismus, nystagmus
Increased Intracranial Pressure

- Obstructive hydrocephalus
  - Mass lesion blocks flow of CSF
  - Shunt malfunction

- Compression of cerebellum and brainstem forces brain through foramen
  - Mass lesion in cerebellum or brainstem
  - Brain swelling
  - Infection (meningitis or abscess)
  - Pseudotumor cerebri
  - Meningeal metastases
Pediatric Brain Tumors

**Supratentorial**
- Astrocytoma
- PNET
- Ependymoma
- Glioblastoma

**Infratentorial**
- PNET
- Astrocytoma
- Glioblastoma
Brain Herniation

- **Supratentorial**
  - Cingulate (1)
  - Transtentorial (2)
  - Uncal (3)

- **Infratentorial**
  - Tonsillar (4)
  - Transtentorial
Pre-surgical MRI in Medulloblastoma

Khanna et al., Ped Blood Cancer 2008
Brain Herniation

• **Downward herniation**
  – Displacement of brain through tentorium and/or tonsils
  – Progressive failure of diencephalic & brainstem functions
  – Decorticate posturing

• **Lateral (cingulate or uncal) herniation**
  – Frontal lobe across falx
  – Rapid shift of temporal lobe brain tissue
  – Compression of CNIII and lateral midbrain

• **Upward herniation**
  – Ventriculostomy placed for cerebellar mass
  – Shunt blockage removed
  – Cerebellum upward through tentorium
Response to Increased ICP

• Prevent further swelling
  – Dexamethasone, 2 mg/kg, then 0.5mg/kg q 6 hrs
  – Mannitol, 2 gm/kg over 30 – 60 min
  – Intubate & hyperventilate to pCO$_2$ of 30-35 mmHg

• Obtain imaging
  – CT without contrast shows bleed, abcess, hydrocephalus, tumor (except posterior fossa)
  – MRI with contrast for suspected brain tumor
  – MRI diffusion for ischemia of thrombotic CVA
  – MRA for locating hemorrhagic CVA origin
Neurologic emergencies due to tumors

- Increased IntraCranial Pressure
- Spinal Cord Compression
- Seizures
# Pediatric Brain Tumors

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Age</th>
<th>Location</th>
<th>5-year survival</th>
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<tbody>
<tr>
<td>Medulloblastoma</td>
<td>6 mos-21 yrs</td>
<td>Cerebellum</td>
<td>70% with XRT</td>
</tr>
<tr>
<td>ST PNET</td>
<td>2 mos-2 yrs</td>
<td>Supratentorial</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>2-18 yrs</td>
<td>Ventrices</td>
<td>60% with XRT</td>
</tr>
<tr>
<td>Pilocytic Astro</td>
<td>12 mos-10 yrs</td>
<td>Optic n, brain stem, cerebellum</td>
<td>85%</td>
</tr>
<tr>
<td>Anaplastic Astro</td>
<td>5-30 yrs</td>
<td>Frontal, parietal</td>
<td>60% with XRT</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>2-30 yrs</td>
<td>Brain stem, frontal, parietal</td>
<td>&lt;20%</td>
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