A Primary Care Provider's Guide to Identifying and Treating Childhood Cancer

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Objectives

- Recognize the incidence and prevalence of childhood cancer
- Understand the cure rates of childhood cancer with modern therapy
- Identify the common forms of cancer seen in children
- Recognize common presenting clinical manifestations of cancer in children
- Understand the basic approaches to diagnosing and treating cancer in children
- Understand common complications related to cancer therapy
Incidence of Childhood Cancer

• Although cancer in children is rare it is the leading cause of death by disease past infancy among children in the United States
  – In 2017 it is estimated that 16000 children and adolescents (age <20 years) will be diagnosed with cancer
  – In 2017 it is estimated that 2000 children will die of cancer
Cure Rates of Childhood Cancer

• In 1975 just over 50% of children diagnosed with cancer before age 20 years survived at least 5 years
• In 2004-2010 more than 80% of children diagnosed with cancer before age 20 years survived at least 5 years
• The improvement has been especially dramatic for a few cancers while survival rates remain very low for some cancer types
Cure Rates of Childhood Cancer

- Children and adolescents who have been treated for cancer need regular follow-up care for the rest of their lives because they are at risk of late side effects that can occur many years later including second cancers

- As of January 1, 2010, there were approximately 380,000 survivors of childhood and adolescent cancer alive in the United States
Distribution of Cancer in Children

- Leukemia: 32%
- CNS tumors: 11%
- Lymphomas: 6%
- Neuroblastoma: 5%
- Sarcomas: 7%
- Wilms tumor: 8%
- Bone tumors: 11%
- Misc: 20%
Childhood Leukemia

• Leukemia is the most common form of cancer of childhood
  – Results from an event in a bone marrow precursor cell which gives rise to immature progeny that have lost the capacity to differentiate and proliferate in an uncontrolled manner
  – Immature progeny (blasts) expand in marrow and impair normal hematopoiesis

• Majority of childhood leukemia are acute leukemia
  – Acute Lymphoblastic Leukemia (ALL)
  – Acute Myeloid Leukemia (AML)
Conditions Associated with Increased Risk of Leukemia

• Children with Down Syndrome have 20x greater lifetime risk of developing acute leukemia compared to other children
  – ALL: 12X risk
  – AML: 46X risk

• Siblings
  – Increased risk by 2-4x in siblings of children with leukemia
  – 25% concordance in monozygotic twins <6yrs

• Genetic disorders
  – Neurofibromatosis
  – Li-Fraumeni syndrome
  – Fanconi’s Anemia
Common Presenting Signs and Symptoms

- Expanding blast population in bone marrow causes bone and joint pain
- Pallor and fatigue due to anemia
- Bruising, petechiae and bleeding due to thrombocytopenia and coagulopathy
- Fever due to infection and cytokines from leukemia
- Adenopathy, hepatomegaly and splenomegaly due to blasts migrating out of marrow
- Gingivitis/gingival hyperplasia
Lab Findings in Acute Leukemia

- CBC
  - Leukocytosis or leukopenia with or without circulating blasts
  - Anemia
  - Thrombocytopenia
  - CBC may also be completely normal

- Coagulopathy/DIC is common in AML

- Metabolic derangements due to rapid cell growth and turnover
  - Elevated creatinine, potassium, phosphorus and uric acid
  - Elevated lactate dehydrogenase
Approaching New Leukemia Cases

• Need to obtain diagnosis by flow cytometry on peripheral blood or marrow

• Need bone marrow samples for cytogenetics

• Need diagnostic LP to assess CNS status
Epidemiology of Childhood ALL

- Most common pediatric cancer
  - 25% of all childhood cancer
  - 2500-3500 cases/year in USA
  - 3-4/100,000 in white children
- 75% of pediatric leukemia
- Peak age 2-5 years
- >90% overall survival on modern therapy regimens
ALL Morphology

- Blasts are much larger than regular lymphocytes and RBCs
ALL Therapy

• Majority of therapy is outpatient
  – IV chemotherapy given in clinic and oral chemotherapy given at home
  – CNS directed chemotherapy via lumbar puncture
  – Therapy lasts 2.5 years for girls and 3.5 years for boys

• Cranial radiation used only for patients with high CNS burden at diagnosis and most T cell ALL

• Bone marrow transplant (BMT) reserved only for certain very high risk patients and in relapse
B precursor ALL

- 80-90% of childhood ALL
- Cure rate >90%
- Use age, cytogenetic risk factors and response to therapy to define risk groups that affect prognosis

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Occurrence</th>
<th>Overall Survival</th>
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<tbody>
<tr>
<td>Low risk</td>
<td>15%</td>
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<td>Standard risk</td>
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<td>90-95%</td>
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<tr>
<td>High risk</td>
<td>30%</td>
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<tr>
<td>Very high risk</td>
<td>10%</td>
<td>70-80%</td>
</tr>
<tr>
<td>Infant</td>
<td>5%</td>
<td>50%</td>
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</table>
T Cell ALL

• Accounts for 15-20% of ALL
• Patients frequently have WBC >100K, are male (4X more than female), and >10 years old
• Anterior mediastinal mass is often present at diagnosis and can cause severe cardio-respiratory compromise so often have to make diagnosis from peripheral blood or from biopsy done under minimal sedation
• Cure rates >85% with more intensive therapy
AML Morphology

• 15-20% of childhood leukemia
• Malignant precursors of the myeloid, monocyte, erythroid and megakaryocytic cell lineages
• Most common leukemia seen in children with bone marrow failure syndromes like Fanconi’s Anemia
• Can result from exposure to chemotherapy
• 50-60% overall survival on modern therapy regimens
  – 5-10% toxic death rate
  – High risk of relapse
Epidemiology of Childhood AML

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<tr>
<th>FAB</th>
<th>Leukemia</th>
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<tbody>
<tr>
<td>M0</td>
<td>Acute myeloid leukemia, minimal differentiation</td>
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<tr>
<td>M1</td>
<td>Acute myeloid leukemia without maturation</td>
</tr>
<tr>
<td>M2</td>
<td>Acute myeloid leukemia with maturation</td>
</tr>
<tr>
<td>M3</td>
<td>Acute promyelocytic leukemia</td>
</tr>
<tr>
<td>M4</td>
<td>Acute myelomonocytic leukemia</td>
</tr>
<tr>
<td>M5</td>
<td>Acute monocytic leukemia</td>
</tr>
<tr>
<td>M6</td>
<td>Acute erythrocytic leukemia</td>
</tr>
<tr>
<td>M7</td>
<td>Acute megakaryoblastic leukemia</td>
</tr>
</tbody>
</table>

- Blasts are larger with more cytoplasm and granules than lymphoblasts
- Auer rods are common in APML
- M7 AML is seen 400-500X more often in Trisomy 21 than in other children
Pediatric AML Therapy

- 4-5 cycles of high-dose IV chemotherapy given inpatient every 4-5 weeks
  - Associated with lengthy periods of severe neutropenia and mucositis
  - Remain hospitalized for most of therapy due to high risk of life threatening bacterial infections

- APML
  - Use differentiating agents like ATRA and arsenic trioxide often without chemotherapy
  - Much better outcomes with OS >85%

- BMT
  - Used frequently in kids who have a sibling match, have poor response to Induction or have unfavorable cytogenetics
  - Almost always used in cases due to bone marrow failure syndromes or chemotherapy exposure
AML and Trisomy 21

• Transient Myeloproliferative Disorder (TMD)
  – Seen in 20-30% of neonates with Trisomy 21
  – Can have leukocytosis with circulating blasts
  – Typically will self resolve by 90 days age
  – May need to treat with low-dose chemotherapy if there is liver or pulmonary dysfunction
  – 20-30% of neonates with TMD will develop AML

• AML is the most common leukemia in young children with Trisomy 21
  – Is associated with better outcomes than other children with less intensive therapy and without BMT
  – Majority are M7 (megakaryocyte precursor)
  – OS >90% in children <4 years old
Lymphomas

• Lymphomas are malignant proliferation of white blood cells derived from peripheral lymphoid tissue
• 15% of childhood cancers are lymphomas
  – 3rd most common malignancy after acute leukemia and malignant brain tumors.
• In the US 1700 kids (less than 20 years old) diagnosed with lymphomas yearly
  – 850-900 with Hodgkins
  – 750-800 with Non Hodgkins Lymphoma (NHL)
When to Worry About Lymphadenopathy

• History:
  – Rapidly growing
  – Stay enlarged >2 months
  – No response when treated with antibiotics
  – Shrinks with steroids but then grows again
  – Associated fever, weight loss, fatigue
  – Causing respiratory distress bad enough to consider steroids

• Physical:
  – Supraclavicular nodes always require more evaluation
  – >3 cm is worrisome
  – Hard, immobile, non-tender or irregular are worrisome

• Labs:
  – High LDH and uric acid are worrisome
Evaluating For Lymphoma

- Radiology imaging
  - CT: Look at size, location and extent
  - PET CT: Looks at metabolic activity
- Complete blood count
  - Can see cytopenias if marrow is involved
- Electrolytes
  - Can see elevated LDH, hyperuricemia and hyperphosphatemia
- Biopsy
  - Establishes diagnosis
  - Look at lymph nodes and marrow
Incidence of Lymphoma by Age

- Majority of lymphomas in younger children are NHL
- Incidence of Hodgkin’s Lymphoma increases with age
Hodgkin’s Lymphoma Presentation

• Usually painless adenopathy (80%) commonly in the supraclavicular or cervical area
  – The enlarged nodes are typically firmer than inflammatory nodes and have a rubbery texture.
  – Many have some mediastinal involvement at presentation
• May present with systemic “B” symptoms indicative of advanced disease (25%)
  – Fever
  – Night sweats
  – Weight loss
Hodgkin’s Lymphoma Therapy

- Standard Treatment includes combination chemotherapy ± low dose involved-field XRT
- Current therapies are designed to minimize long-term toxicities especially sparing low risk patients XRT
- Most chemotherapy regimens are predominantly outpatient
- Survival rates in the >90%
- Late effects
  - Increased risk of thyroid and breast cancer with chest radiation
  - Increased risk of infertility in males
  - Increased risk of heart and lung disorders
Non-Hodgkin’s Lymphomas (NHL)

• 800 new cases of NHL diagnosed each year.
• Incidence is approximately 10 per 1,000,000
  – Incidence increases steadily with age
  – Most commonly in the second decade of life
• Most frequent malignancy in children with AIDS
• Several subtypes in children
  – Lymphoblastic Lymphomas
  – Burkitt’s Lymphomas
  – Large Cell Lymphomas
• Generally treated with chemotherapy without radiation
Lymphoblastic Lymphoma

- 30% of childhood NHL

- 85-90% are Precursor T-Cell Origin

- ~75% present with anterior mediastinal mass
  - Frequently initially diagnosed with “Asthma”
  - Pre-treatment with steroids is common
    - Can make diagnosis difficult
    - Can precipitate severe Tumor Lysis Syndrome

- Therapy is based on high risk ALL treatment
  - Current regimens with >85% EFS at 5 years
Burkitt’s Lymphoma

• 40% to 50% of childhood NHL
  – Most rapidly growing lymphoma
  – Frequently have electrolyte issues at presentation

• Endemic Form – primarily in Africa
  – Associated with EBV infection
  – Majority localized to Jaw or Head/Neck

• Sporadic Form – most common in US
  – No clear association with EBV
  – ~ 90% are intra-abdominal.

• OS >90% with inpatient chemotherapy
Large Cell Lymphomas

• B lineage LCL
  – Similar to Burkitt’s Lymphoma but more indolent
  – Most often localized, frequently involves the mediastinum

• T-lineage LCL (rarer)
  – Anaplastic LCL
  – Peripheral T-cell lymphomas
Childhood Brain Tumors

• 2nd most common cancer in children
  – Most common solid neoplasm
  – 2500-3000 new diagnoses/year

• Types of tumors and location are different than adults
  – Children have more low-grade gliomas and embryonal tumors while adults have more high-grade gliomas and meningiomas
  – Nearly 2/3 of pediatric brain tumors are infrarapatentorial while the majority of adult brain tumors are supratentorial
Localized Symptoms of Brain Tumors

• Brainstem and cerebellum
  – Cranial neuropathies
  – Ataxia

• Pituitary gland
  – Tunnel vision
  – Endocrine dysfunction

• Cerebrum
  – Hemiparesis
  – Early handedness/change in handedness
  – Seizures
  – Personality changes
Symptoms of Increased Intracranial Pressure

• May be due to intrinsic mass lesion in brain or ventricular obstruction
• Altered mental status
• Headache and vomiting
  – Mainly in the mornings and then improves
  – No associated diarrhea
• Cranial nerve abnormalities
  – Esotropia
  – Abnormal pupil response
• Ataxia
Symptoms of Increased Intracranial Pressure

- Papilledema
- Bulging fontanelle
- Cushing’s Triad signals impending herniation
  - Hypertension
  - Bradycardia
  - Abnormal Respirations
Imaging for CNS Tumors

CT scan can quickly assess for presence of a mass, hydrocephalus and bleeding

MRI is best tool for localization especially for cerebellum and brain stem tumors
Frequency and Survival in Pediatric Brain Tumors

- 5 year survival overall 60-70%
- Good prognosis
  - Low grade gliomas: >90%
  - Medulloblastoma: >80% for standard risk
  - Germinomas/Germ cell tumors: >80%
- Poor Prognosis
  - High grade gliomas: 10-30%
  - ATRT: 30-40%
  - Diffuse intrinsic brainstem glioma: 0%
## Treatment of Pediatric Brain Tumors

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Surgery</th>
<th>Radiation Therapy</th>
<th>Chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medulloblastoma</td>
<td>Yes</td>
<td>Cranio-spinal</td>
<td>Yes</td>
</tr>
<tr>
<td>Pilocytic Astrocytoma</td>
<td>Yes</td>
<td>Focal</td>
<td>For unresectable or recurrent tumors</td>
</tr>
<tr>
<td>Glioblastoma Multiforme</td>
<td>Yes</td>
<td>Focal</td>
<td>For recurrence</td>
</tr>
<tr>
<td>Brain Stem Glioma</td>
<td>No</td>
<td>Focal</td>
<td>For progressive disease</td>
</tr>
<tr>
<td>Germ cell Tumors</td>
<td>No</td>
<td>Focal +/- Cranio-spinal</td>
<td>Yes</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>Yes</td>
<td>Focal</td>
<td>For recurrence</td>
</tr>
</tbody>
</table>

• Significant late effects from surgery, chemotherapy and radiation
Non-CNS Solid Malignancies in Children

• Need tumor specimen to confirm diagnosis
• Evaluation at diagnosis requires CT/MRI of primary tumor as well as CT chest
• Some tumors require further metastatic evaluation
  – Bone scan
  – PET CT
  – Bone marrow aspirate and biopsy
Solid Tumor Staging (Generalization)

• Stage I - Completely resected
• Stage II - Grossly resected with microscopic residual disease
• Stage III - Partially resected tumor, lymph node involvement
• Stage IV - Distant metastatic disease
• [Stage V - Bilateral Wilms tumor]
Metastases in Solid Tumors

Lungs are the most frequent sight of metastatic disease.
Metastases in Solid Tumors

PET CT showing disseminated disease

Bone scan showing diffuse bony metastases

Tumor cells forming clumps in bone marrow aspirate
General Approach to Solid Tumor Therapy

• Chemotherapy
  – Shrink primary tumor to make surgical resection more feasible
  – Treat microscopic and radiographic metastatic disease
• Surgery and/or radiation for local control of primary tumor site
• Surgery and/or radiation to metastatic sites
Abdominal Tumors in Children

• Common types
  – Neuroblastoma
  – Wilms Tumor
  – Hepatoblastoma

• Common presenting symptoms
  – Abdominal pain and distension
  – Constipation
  – Vomiting and weight loss
  – Hematuria
  – Jaundice

• Frequently asymptomatic with mass incidentally discovered by family member or PCP
Beckwith-Wiedeman Syndrome

• Complex multi-genic disorder
• Incidence: 1/10,000 births
• Clinical features
  – Macroglossia
  – Macrosomia
  – Hemihypertrophy
  – Omphalocele
  – Neonatal hypoglycemia
• Increased risk of tumors: 7.5%
  – Neuroblastoma: RR 197
  – Wilms Tumor: RR 816
  – Hepatoblastoma: RR 2280
• Require screening as young children with abdominal ultrasound
Neuroblastoma

- #1 extra cranial solid tumor in children
  - 8-10% childhood cancers
  - 600 new cases per year in the US
  - 15% of childhood cancer mortality
- Median age at diagnosis is 22 months
  - Most common cancer diagnosed in infancy
  - 98% of cases diagnosed by age 10
- Primary tumors occur in abdomen (65%) and along thoracic or cervical spine
  - Metastatic sites-lymph nodes, bone marrow, bone, liver, skin
- Prognosis depends on risk group assignment
Neuroblastoma Presentation

• Signs and symptoms depend on location
  – Abdomen
    • Fullness, fixed/hard mass
  – Cervical/high thoracic
    • Horner syndrome (ptosis, miosis, anhydrosis)
    • SVC syndrome
    • Spinal cord or nerve root compression
  – Orbital mets
    • Proptosis and periorbital ecchymoses (Raccoon eyes)
  – Bone and bone marrow
    • Pain and cytopenias
Neuroblastoma Evaluation

- Masses frequently have calcifications
- 90-95% of cases have elevated urine catecholamines
  - Homovanillic acid (HVA)
  - Vannilylmandelic acid (VMA)
- Bilateral bone marrow aspirate and biopsy
- MIBG scan (meta-iodobenzylguanidine)
  - 90% of neuroblastoma are MIBG avid
Neuroblastoma Risk Factors

• Favorable vs. unfavorable histology
• Age: <18 months age at diagnosis is favorable while >18 months age at diagnosis is unfavorable
• Higher stage disease is unfavorable
• Myc-N Amplification
  – Amplification occurs in about 25% of neuroblastomas
  – Associated predominately with advanced stages of disease, rapid tumor progression and a poor prognosis
Neuroblastoma Therapy

• Low-risk disease (40% of cases): OS >90%
  – Surgical removal of primary tumor
  – No chemotherapy or radiation

• Intermediate-risk (20% of cases): OS >90%
  – Surgical removal of majority of primary tumor
  – Moderate dose chemotherapy avoids radical surgery and radiation in most

• High-risk disease (40% of cases): OS 40-60%
  – Induction chemotherapy and surgery to reduce tumor bulk
  – Consolidation- high-dose chemo with autologous stem cell rescue and radiation
  – Immunotherapy to treat minimal residual disease
Wilms Tumor

• Most common renal tumor in children
  – 6% of all childhood cancer
  – 500 new cases per year in U.S.
• 80% of cases in children ages 1-5 years old
• Most are unilateral but 5-10% are bilateral
• 10-15% of cases are in children with congenital anomalies
  – Beckwith-Wiedeman Syndrome
  – WAGR: Wilms Tumor, Aniridia, GU malformation, Retardation
  – Denys-Drash: Pseudohermaphroditism, Renal disease, Wilms Tumor
  – Hemihypertrophy
• Overall cure rates of 85-90%
Wilms Tumor Presentation

• Palpable abdominal mass
  – Most common presentation
  – Often asymptomatic and incidentally noted while bathing child
• Hematuria
• Hypertension
• Less common
  – Obstipation
  – Weight loss
• CT scans shows “claw sign”
Wilms Tumor Therapy

• Surgery
  – Attempt nephrectomy at presentation and avoid biopsy if possible
  – For initially unresectable tumors attempt nephrectomy after chemotherapy

• Chemotherapy
  – Given post-nephrectomy to prevent metastatic relapse
  – Based on histology and extent of disease
  – Give chemotherapy first for bilateral tumors and then remove

• Radiation for higher stage tumors and lung metastases
Wilms Tumor Outcomes

• Favorable histology
  – 90-95% of cases
  – Well differentiated
  – Excellent EFS and OS

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<tr>
<th>Stage</th>
<th>EFS</th>
<th>OS</th>
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<tr>
<td>I</td>
<td>87-98%</td>
<td>97-100%</td>
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<tr>
<td>II</td>
<td>84.4</td>
<td>97.2</td>
</tr>
<tr>
<td>III</td>
<td>86.5</td>
<td>94.4</td>
</tr>
<tr>
<td>IV</td>
<td>75.1</td>
<td>85.2</td>
</tr>
<tr>
<td>V</td>
<td>66.4</td>
<td>87.7</td>
</tr>
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• Anaplastic histology
  – 5-10% of cases
  – Only unfavorable histology
  – Poorer EFS and OS

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<thead>
<tr>
<th>Stage</th>
<th>EFS</th>
<th>OS</th>
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<tr>
<td>I</td>
<td>69.5%</td>
<td>82.6%</td>
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<tr>
<td>II</td>
<td>82.6%</td>
<td>81.5%</td>
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<tr>
<td>III</td>
<td>64.7%</td>
<td>66.7%</td>
</tr>
<tr>
<td>IV</td>
<td>33.3%</td>
<td>33.3%</td>
</tr>
<tr>
<td>V</td>
<td>25.1%</td>
<td>41.6%</td>
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Renal Cell Carcinoma (RCC)

- 5-6% of pediatric renal neoplasms
  - Makes up 2/3 of renal tumors in 15-19 year olds
  - Most common adult renal cancer
- Risk factors
  - Smoking, obesity, HTN, heavy metals, chlorinated solvents, asbestos
  - Von Hippel Lindau--up to 45% may have RCC in lifetime
  - Tuberous Sclerosis
- Prognosis is poor when disease has spread beyond kidney
  - Stage I (33% cases)--92.4% 5 year survival
  - Stage II (11% cases)--85% 5 year survival
  - Stage III (27% cases)--73% 5 year survival
  - Stage IV (30% cases)--14% 5 year survival
Hepatoblastoma

- Third most common intra-abdominal neoplasm
  - 66% of hepatic malignancies in age <20 years
  - 91% of patients are < 5 years age at diagnosis

- Prematurity and low birth weight (<2500 grams) is associated with increased risk
  - RR 15.64 for BW <1000g
  - RR 2.53 for BW 1000-1499g
  - RR 1.21 for BW 1500-2499g

- Elevated alpha-fetoprotein in >90% of cases

- Distant metastases in ~20% of cases mostly to lung
Hepatoblastoma Therapy

- Surgery alone is an option for resectable pure fetal histology tumors
- Majority require chemotherapy in addition to surgery
- May need liver transplant
- Outcomes poorer with advanced stage disease

Fuchs et al. Cancer 2002
Hepatocellular Carcinoma

• >95% of liver tumors in age >15 years
• Risk factors
  – Hereditary Tyrosinemia, Biliary cirrhosis, Glycogen storage diseases, α-1 antitrypsin deficiency, Hemochromatosis
  – Hepatitis B & C, Alcohol consumption, Anabolic steroids
• Elevated alpha-fetoprotein in 75-80% of cases
• Treatment
  – Chemotherapy+Surgery
  – Only 35-40% of patients are able to have complete resection
  – 5yr OS: 28%

Katzenstein et al. J Clin Oncol 2002
Czauderna et al. J Clin Oncol 2002
Soft Tissue Sarcomas in Children

• Present with pain +/- associated soft tissue mass
  – Pelvic tumors: Urinary and stool retention or incontinence
  – Chest/rib tumors: respiratory distress
  – Orbital tumors: Proptosis
  – Biliary tract: Jaundice

• Can present with pathologic fracture due to minimal trauma

• Can have diffuse pain due to metastatic disease
Osteosarcoma

• Most common malignant bone tumor
  – 400 new diagnoses each year
  – Peak incidence in 2nd decade of life
• Predilection for metaphyseal portion of growing bones
  – Distal femur
  – Proximal tibia
  – Proximal humerus
• Associated with radiation exposure, bilateral retinoblastoma, p53 tumor suppressor mutations (Li-Fraumeni)
• X-ray often shows a destructive sclerotic lesion with periostial elevation (Codman’s triangle)
• MRI often shows a destructive intra-osseous lesion with extra-osseous soft tissue component
Osteosarcoma Therapy

- Chemotherapy x10 weeks followed by resection of primary tumor
  - Amputation vs limb salvage
  - Try to remove metastatic disease as well if possible
  - No role for radiation
- Continue chemotherapy post-op
- Prognosis is poor in metastatic disease (OS <30%)
  - Localized disease: OS 65-70%
  - 15-20% have metastatic disease
  - Metastasize to lungs and bones
Ewing Sarcoma

- Second most common malignant bone tumor
- More than half of patients are adolescents
- Most common sites
  - Pelvic bones
  - Diaphysis of long bones of legs
  - Chest wall and rib
- Predilection for Caucasians (6x> African Americans)
Ewing Sarcoma Therapy

- Chemotherapy
- Local control to primary tumor site (surgery, radiation or both)
- Radiation to metastatic sites
- Prognosis is poor in metastatic disease (OS <30%)
  - Localized disease: OS 70-75%
  - 20% have distant metastasis
  - Metastasize to lung, bone marrow, and bone
Rhabdomyosarcoma

• Malignant muscle tumor
• 3% of childhood cancer
  – 350 new cases each year
  – 2/3 diagnosed <6yrs,
  – Smaller peak in mid-adolescence (usually males)
• More common in caucasians
• Most occur sporadically but may arise with NF1 and Li-Fraumeni
Rhabdomyosarcoma Therapy

• Chemotherapy
• Local control
  – Surgery only if function and cosmesis are not impaired
  – Radiation is used in most cases unless tumor was completely resected at diagnosis
• Prognosis depends on histology and disease extent
  – Localized disease and embryonal histology: OS 85%
  – Localized disease and alveolar histology: OS 60%
  – Metastatic disease with embryonal histology in young children: OS 50%
  – Metastatic disease in older children and metastatic alveolar histology: OS 20%
Germ Cell Tumors

• 3% of childhood cancer
• Arise from primordial cells involved in gametogenesis
  – 41% Gonadal vs. 59% Extragonadal
  – Age <15 years: Extragonadal > Gonadal
  – Age >15 years: Gonadal > Extragonadal
  – Extragonadal sites: Sacro-coccyx, Mediastinum, Abdomen, Brain
• Increased risk with Turner’s and Klinefelter’s syndromes as well as cryptorchidism
• Tumor markers vary by histology
  – Yolk sac tumor: Elevated AFP
  – Choriocarcinoma: Elevated B-HCG
  – Seminoma: Normal AFP and B-HCG
Germ Cell Tumor Presentation

- Ovarian: abdominal pain, palpable abdominal mass
- Testicular: Irregular, non-tender mass
- Extragonadal tumors
  - Sacrococcygeal: Constipation, urinary retention
  - Mediastinal: Chest pain, respiratory distress
  - Brain: Precocious puberty, Diabetes insipidus, SIADH
- Diagnosis
  - Biopsy
  - Tumor markers
  - CT/MRI of primary
  - Metastatic work-up: Bone scan, Chest CT
Germ Cell Tumor Treatment

- Surgery
- Chemotherapy
- Radiation for brain disease
- Prognosis depends on extent of disease, location of primary tumor, and histology
  - Localized disease: OS >95%
  - Metastatic disease: OS 90-95%
  - Thoracic primary: <80%
  - Choriocarcinoma: <50%
Common Complications of Chemotherapy

• Bone marrow suppression
  – Require blood product transfusions
  – Increased risk of infection when neutrophil count is low
• GI symptoms
  – Nausea/Vomiting, Constipation, Mucositis
• Liver and renal toxicity
• Alopecia
• Myositis
• Neurotoxicity
Vaccinations During Treatment

• Hold all vaccines during therapy except inactivated seasonal flu vaccine
• Continue to vaccinate family members
• Safe to administer live vaccines to siblings but advise patient not to change diapers
• Resume vaccinations 6 months after therapy
• Complete re-vaccination not needed unless receiving BMT
• When in doubt check CDC website
Fever During Treatment

• Fever: Temperature >38.3°C or 101°F
• Severe neutropenia: ANC <500
  – ANC: WBC count X (% segs and bands)
• Obtain blood cultures x2 from central line as well as CBC
  – OU Policy is to give Ceftriaxone 75mg/kg x1 while awaiting CBC results
• ANC <500:
  – Immediately give very broad spectrum antibiotics like Cefepime, Ceftazadime or Zosyn and
  – Admit to OU
• ANC >500: Can discharge home if looking well
Pneumocystis jiroveci/carinii

- Ubiquitous fungus that causes interstitial pneumonia in immunocompromised patients
- Physical Exam
  - Non-productive cough
  - Hypoxia, Dyspnea, Tachypnea
- Imaging
  - Bilateral reticular infiltrates
  - “Angel Wings” appearance on CT
- Preventable with prophylaxis
  - Bactrim 3 days a week
  - Weekly Dapsone
  - Monthly Pentamadine
  - Continue until 6 months off therapy
Long Term Effects of Cancer Therapy

- Cardiac dysfunction
- Renal dysfunction
- Liver dysfunction
- Infertility
- Abnormal growth
- Osteoporosis
- Secondary malignancies
- Neurocognitive dysfunction
Any Questions?

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