Objectives

- To discuss the cancers most often seen during infancy.
- To define developmental delay and how it is determined.
- To understand the causes of developmental delay in infants with cancer.
- To explore the role of physical therapy in the management of developmental delay in this population.

Statistics \(^1,^2\)

- Cancer in childhood is RARE
  - 1% of all cancer diagnoses
  - 15,780 estimated cases in 2014
- Occurs less likely during infancy — the first year of life
  - 23:100,000 infants diagnosed annually

Infant Cancers \(^3,^4\)

- Different epidemiological, clinical and genetic characteristics than cancers seen in older children
- Diagnostic challenge to identify malignancy
- Treatment decisions must take into account
  - Inherent vulnerability of infants
  - Small size
  - Potential toxicity

Disclosure

This presenter has no conflict of interest to report regarding any commercial product/manufacturer that may be referenced during this presentation.
Neuroblastoma is a cancer of neuroblasts in the sympathetic nervous system. It represents 6% of all pediatric cancers, with 700 new cases diagnosed annually. It affects 1/3 of all malignancies seen in infants. The average age of diagnosis is 1-2 years of age, with 90% of cases occurring before age 5.

Risk factors include age and genetic predisposition. Common locations include the adrenal gland, abdominal sympathetic nerve ganglia, spinal sympathetic nerve ganglia (chest, neck, pelvis), and bone marrow.

Symptoms of neuroblastoma include a lump/swelling, bone pain, weakness, and Blueberry muffin sign. Other symptoms include opsoclonus-myoclonus.

Methods of diagnosis include imaging tests such as ultrasound, CT scan, MIBG scan, and PET scan. Laboratory tests include blood and urine catecholamine. Biopsy methods include surgical and bone marrow biopsy.

Tumor staging includes:
- **Stage 1**: No spread, unilateral tumor involvement, complete surgical removal
- **Stage 2A**: No spread, unilateral tumor involvement, incomplete surgical removal
- **Stage 2B**: Unilateral tumor involvement, complete or incomplete surgical removal, lymph node involvement
- **Stage 3**: Unilateral or bilateral tumor involvement, complete or incomplete surgical removal, midline tumor involvement, possible LN involvement
- **Stage 4**: Metastatic disease
- **Stage 4S**: Less than 1 year old

Treatment includes surgery, chemotherapy (carboplatin, cisplatin, cyclophosphamide, doxorubicin, etoposide, ifosfamide, topotecan), radiation (MIBG), immunotherapy, and stem cell transplant.
Neuroblastoma

- Prognosis

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>5-Year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>95%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>90-95%</td>
</tr>
<tr>
<td>High Risk</td>
<td>40-50%</td>
</tr>
</tbody>
</table>

Leukemia

- Leukemia is a cancer of blood-forming cells
  - Most common cancer seen in children
  - Represents 26% of all pediatric cancers
  - Second most common cancer in infants
- Risk factors
  - Genetic predisposition, radiation, chemotherapy

Leukemia

- Types
  - Acute lymphoblastic leukemia (ALL)
  - Acute myelogenous leukemia (AML)
  - Hybrid/mixed leukemia
  - Juvenile myelogenous leukemia (JMML)
  - Chronic forms of leukemia are uncommon in childhood

Leukemia

- Symptoms
  - Cutaneous infiltration
  - Fatigue
  - Pallor
  - Easy bruising
  - Weakness
  - Infections

Leukemia

- Methods of diagnosis
  - Laboratory tests
    - Blood tests (CBC)
  - Biopsy
    - Bone marrow aspiration/biopsy
    - Lumbar puncture
Leukemia\textsuperscript{9,11}

**ALL Classification**
- Based on immunotype
  - B-cell ALL (80-85%)
  - Early precursor B-cell ALL
  - Common ALL
  - Pre-B ALL
  - Mature B-cell ALL
  - T-cell ALL (15-20%)

**AML Classification**
- Based on morphology
  - M0, M1, M2, M3, M4, M5
  - Starts in immature forms of WBC
  - M6
  - Starts in immature forms of red blood cells
  - M7
  - Starts in immature forms of cells that make platelets

Leukemia\textsuperscript{9,12}

**Treatment**
- Chemotherapy
  - Vincristine
  - Daunorubicin
  - Doxorubicin
  - Cytarabine
  - L-asparaginase
  - Etoposide
  - Methotrexate
  - Cyclophosphamide
  - Prednisone
  - Dexamethasone

- Stem cell transplant
  - High risk disease
  - Relapsed disease

- Radiation
  - CNS involvement
  - Testicular involvement
  - Pre-SCT

**Prognosis**

<table>
<thead>
<tr>
<th>Leukemia Type</th>
<th>5-Year Survival Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>85%</td>
</tr>
<tr>
<td>AML</td>
<td>60-70%</td>
</tr>
<tr>
<td>JMML</td>
<td>50%</td>
</tr>
</tbody>
</table>

Brain Tumors\textsuperscript{3,13,14}

- Brain tumors are abnormal growths in the brain (benign and malignant)
  - Second most common cancer seen in children
    - Most common solid tumor seen in children
  - Represents 19% of all pediatric cancers
  - Third most common cancer seen in infants

Brain Tumors\textsuperscript{14}

- Histology Classification - WHO
  - Gliomas
    - Astrocytomas
    - Oligodendrocytomas
    - Ependymomas
  - Primitive neuroectodermal tumors
    - Medulloblastomas
    - PNET
    - Malignant teratoid rhabdoid tumors
  - Cranial nerves
  - Meninges
Brain Tumors 14

<table>
<thead>
<tr>
<th>Location Classification</th>
<th>ICCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supratentorial</td>
<td></td>
</tr>
<tr>
<td>• Four lobes</td>
<td></td>
</tr>
<tr>
<td>• Cerebrum</td>
<td></td>
</tr>
<tr>
<td>• Ventricle</td>
<td></td>
</tr>
<tr>
<td>Infratentorial</td>
<td></td>
</tr>
<tr>
<td>• Cerebellum</td>
<td></td>
</tr>
<tr>
<td>• Brainstem</td>
<td></td>
</tr>
<tr>
<td>Brainstem</td>
<td></td>
</tr>
<tr>
<td>• Cranial nerves</td>
<td></td>
</tr>
<tr>
<td>• Meninges</td>
<td></td>
</tr>
</tbody>
</table>

Brain Tumors 3,13,14

General Symptoms
- Macrocephaly
- Irritability
- Nausea/Vomiting
- Headache
- Seizures
- Motor weakness

Site Specific Symptoms
- Cerebrum
  - Hemiparesis
  - Sensory loss
  - Speech and memory disturbances
- Posterior fossa
  - Abnormal gait
  - Incoordination
- Brainstem
  - Cranial nerve deficits

Brain Tumors 13,14

Risk factors
- Radiation, genetic predisposition
- Neurofibromatosis (1, 2), Li-Fraumeni syndrome

Brain Tumors 13

Methods of diagnosis
- Imaging Tests
  - MRI
  - CT scan
- Biopsy
  - Stereotactic
  - Craniotomy
  - Lumbar puncture

Brain Tumors 13,16

Treatment includes:
- Surgery
  - Craniotomy
  - Shunt placement
    - Ventriculoperitoneal (VP) shunt
    - External ventricular drain (EVD)
  - Ommaya reservoir
- Chemotherapy
  - Carboplatin
  - Carmustine
  - Cisplatin
  - Cyclophosphamide
  - Etoposide
  - Lomustine
  - Methotrexate
  - Temozolomide
  - Thiopeta
  - Vincristine
- Radiation
Brain Tumors

- Prognosis

<table>
<thead>
<tr>
<th>Tumor Types</th>
<th>5-Year Survival Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilocytic Astrocytoma</td>
<td>~95%</td>
</tr>
<tr>
<td>Fibrillary Astrocytoma</td>
<td>~80-85%</td>
</tr>
<tr>
<td>Anaplastic Astrocytoma</td>
<td>~30%</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>~20%</td>
</tr>
<tr>
<td>Oligodendroglioma</td>
<td>~90-95%</td>
</tr>
<tr>
<td>Ependymoma/Anaplastic Ependymoma</td>
<td>~75%</td>
</tr>
<tr>
<td>PNETs (Medulloblastoma, Pineoblastoma)</td>
<td>~60-65%</td>
</tr>
</tbody>
</table>

Retinoblastoma

- Retinoblastoma is a cancer of the eye, starts in the retina
  - Most common eye cancer seen in children
  - Represents 2% of all pediatric cancers
    - 200-300 cases diagnosed annually
  - 11% of cancers diagnosed in the 1st year of life
- Average age of diagnosis is 2

Retinoblastoma

- Risk factors
  - Age, genetic predisposition
    - RB1 gene

- Types of retinoblastoma
  - Congenital (hereditary)
  - Sporadic
- Can be unilateral, bilateral or trilateral

Retinoblastoma

- Symptoms include
  - Leukocoria
  - Strabismus
  - Pain
  - Decreased vision

Retinoblastoma

- Methods of diagnosis
  - Imaging tests
    - Ultrasound
    - MRI
  - Ophthalmologic exam
Retinoblastoma

Tumor Staging

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
<th>Group E</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3 mm or less, confined to the retina</td>
<td>&gt;3 mm or small and close to optic disc or fovea</td>
<td>Well defined, small subretinal or vitreous seeding</td>
<td>Large or poorly defined, widespread subretinal or vitreous seeding, possible retinal detachment</td>
<td>Large, extends forward, bleeding or causing glaucoma</td>
</tr>
</tbody>
</table>

Retinoblastoma

- Treatment includes:
  - Surgery
    - Enucleation
  - Radiation
    - External beam
    - Brachytherapy
  - Cryotherapy
  - Thermotherapy
  - Photocoagulation
  - Stem cell transplant

Retinoblastoma

- Chemotherapy
  - Carboplatin
  - Cisplatin
  - Cyclophosphamide
  - Doxorubicin
  - Etoposide
  - Vincristine
  - Topotecan

Retinoblastoma

- Prognosis

<table>
<thead>
<tr>
<th>Type</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>94% (5-year)</td>
</tr>
<tr>
<td>Metastatic</td>
<td>50%</td>
</tr>
<tr>
<td>Trilateral</td>
<td>44% (pineal)</td>
</tr>
<tr>
<td>Trilateral</td>
<td>57% (non-pineal)</td>
</tr>
</tbody>
</table>

Wilms Tumor

- Wilms tumor is a primary cancer of the kidneys
  - Most common kidney cancer in children
  - Represents 5% of all pediatric cancers
    - 500 cases diagnosed annually
  - Average age of diagnosis is ~3-4 years of age
  - Risk factors
    - Age, gender, race, genetic predisposition

Wilms Tumor

- Types of Wilms tumor
  - Favorable histology
  - Unfavorable histology
- Can be unilateral or bilateral
- Symptoms
  - Abdominal mass/swelling, fever, decreased appetite, nausea

Wilms Tumor

- Methods of diagnosis
  - Imaging tests
    - Ultrasound
    - CT scan
    - MRI
  - Biopsy
Wilms Tumor \(^{19,21}\)

**Tumor Staging**

<table>
<thead>
<tr>
<th>Stage I (40-45%)</th>
<th>Stage II (20%)</th>
<th>Stage III (20-25%)</th>
<th>Stage IV (10%)</th>
<th>Stage V (5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral, complete surgical removal, intact renal capsule</td>
<td>Tumor extension into fatty tissue or blood vessels, complete surgical removal, no lymph node involvement</td>
<td>Tumor extension, involvement of the abdomen</td>
<td>Metastatic spread beyond the kidney</td>
<td>Bilateral kidney involvement at diagnosis</td>
</tr>
</tbody>
</table>

**Treatment**
- Surgery
  - Radical nephrectomy
  - Partial nephrectomy
- Radiation

**Chemotherapy**
- Actinomycin D
- Vincristine
- Doxorubicin
- Cyclophosphamide
- Etoposide
- Irinotecan
- Carboplatin

**Prognosis**

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>Favorable Histology</th>
<th>Unfavorable Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>99%</td>
<td>83%</td>
</tr>
<tr>
<td>Stage II</td>
<td>98%</td>
<td>81%</td>
</tr>
<tr>
<td>Stage III</td>
<td>94%</td>
<td>72%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>86%</td>
<td>38%</td>
</tr>
<tr>
<td>Stage V</td>
<td>87%</td>
<td>55%</td>
</tr>
</tbody>
</table>

**Severe Combined Immunodeficiency (SCID) \(^{22,23}\)**

**Primary immunodeficiency**
- Heterogeneous group of disorders which arise from a disturbance in the development and function of immunity
  - T cells
  - B cells
- “Severe” - lead to early death from significant infections
Severe Combined Immunodeficiency (SCID)\textsuperscript{22,23}

- **Symptoms**
  - Recurrent infections
- **Diagnosis**
  - Newborn screen
- **Treatment**
  - Stem cell transplant
  - Enzyme replacement therapy

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**Developmental Delay**

- Defined as “a significant delay in the process of development”
- Can occur as a result of various causes
  - Pre-natal
    - Maternal infection
    - Genetic syndromes
  - Peri-natal
    - Difficult childbirth
  - Post-natal
    - Brain injury

---

**Developmental Areas\textsuperscript{25}**

- **Gross Motor**
  - Use of large muscles
- **Fine Motor**
  - Use of small muscles
- **Speech/Language**
  - Producing and understanding speech
- **Cognitive**
  - Learning and problem solving
- **Social/Emotional**
  - Interaction with others, self-control

---

**Developmental Delay\textsuperscript{25}**

- Can be seen across several domains/areas of development
  - Physical
    - Gross motor
    - Fine motor
    - Feeding
  - Cognitive
    - Speech
    - Learning
    - Communication

---

**Developmental Milestones**

- A skill that a child achieves within a specific time frame
- Occurs in a sequential fashion
- Can be used as an indication of potential delay
Developmental Milestones

Standardized Assessments

- Quantifies amount of delay
- Provides specific information for clinician and parent
- Justifies need for services
- Tracks progress over time

Standardized Assessments

- Alberta Infant Motor Scales (AIMS)
- Peabody Developmental Motor Scale (PDMS)
- Developmental Assessment of Young Children (DAYC)

AIMS

- Norm-referenced test
- Birth to 18 months
- Purpose
  - Identify children with delayed motor development
  - Evaluate motor development/maturation over time

PDMS

- Norm-referenced test
- Birth to 5 years old
- Purpose
  - Qualitative and quantitative assessment of fine and gross motor development
  - Recommends activities to address problems
PDMS

Subtests

- Reflexes
- Stationary
- Locomotion
- Object Manipulation
- Grasping
- Visual-Motor

DAYC

- Norm-referenced test
- Birth to 5 years
- Purpose
  - Identify normal and delayed development
  - Determine specific strengths/weaknesses
  - Document progress related to intervention

DAYC

Subtests

- Cognitive
- Communication
- Social-Emotional
- Physical Development
- Adaptive Behavior

Developmental Delay in Infant Cancers

Causes of Developmental Delay in Infant Cancers

- Treatment side effects
  - Chemotherapy
    - Myelosuppression → decreased energy/activity tolerance, infection
    - Mucositis → impaired oral feeding, impaired weight gain
  - Radiation
    - Fatigue → decreased energy/activity tolerance
  - Surgery
    - Pain → faulty posturing/alignment, impaired reaching/ROM

Causes of Developmental Delay in Infant Cancers

- Line placement
  - Can impede “tummy time” and tolerance of prone positioning, limited UE reaching
    - Central lines
      - Mediport
      - Broviac
    - Feeding tubes
      - PEG/PEG
Causes of Developmental Delay in Infant Cancers

- Prolonged positioning
  - Impaired alignment
  - Decreased ROM
- Environment
  - Home vs. hospital
    - Limited consistency
  - Impaired sleep/wake cycle
  - Isolation (masks, gloves, gowns)
  - Decreased interaction with peers/social interaction

Role of Physical Therapy

PT Intervention

- Assessment
  - Strength/ROM
  - Muscle tone
  - Alignment
  - Neurological function
  - Resting position
  - Balance
  - Transitions
  - Skill acquisition
  - Play/mobility in supine, prone, sitting, standing

- Goals
  - Based on current and expected skill level
  - Consider various positions and transitions
  - May require increased time to achieve
  - Involve parents and caregivers

- Frequency
  - Things to consider
    - Amount of delay
    - Activity tolerance
    - Parental wishes/input
    - Medical treatment needs

- PT Treatment
  - Strengthening
  - Tolerance of positioning (tummy time, sitting, standing)
  - Balance
  - Gross motor skill acquisition
  - Transitions
  - Ambulation
  - Sensory integration
  - Endurance/cardio Pulmonary
**Intervention – Team Approach**

**Case Studies**

- **Case Study**
  - Diagnosed via newborn screen with SCID
  - Treatment
    - SCT x 2
  - Complications
    - Transplant failure
    - Multiple infections (respiratory, bacterial/viral)
    - Hemolytic anemia requiring multiple transfusions
    - Impaired feeding

- **Case Study**
  - Multiple hospital admissions
    - Extended time
    - Consistently on isolation
    - Transfers to PICU for escalated care
  - Rehab history
    - Initially evaluated at 3 months
    - Currently receives PT 3x/wk at 2 years old
    - Inpatient, outpatient, early intervention

- **Case Study**
  - A few developmental milestones...
    - Head lag, cervical rotation and tilt, hands fisted at 3 months
    - Rolled at 5-6 months
    - Sat independently at 7 months
    - Maintained quadruped at 9 months
    - Showed regression of skills at 11 months
    - Took first independent steps at almost 2 years old
Literature Review

“Physical Functioning in Pediatric Survivors of Childhood Posterior Fossa Brain Tumors” – Piscione, et al
• Cross-sectional assessment of physical functioning using the Bruininks-Osteretsky Test of Motor Performance (BOT-2)
  – Statistically significant differences noted in survivors observed in bilateral coordination, balance and running speed/agility

References


Literature Review

“Motor Development of Infants with Positional Plagiocephaly” – Kennedy, et al
• Compared the motor development of infants with positional plagiocephaly (PP) and matched peers without using the AIMS and PDMS
  – Young infants placed predominately in the supine position tend to posture their heads preferentially to one side
  – Infants with PP who spent less awake time in prone had lower motor scores