Pediatric Head and Neck Malignancies

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Grand Rounds Presentation
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Pediatric Cancer

- 2nd leading cause of death in age range of 5-14 years
- 1/333 children diagnosed annually
- 11,000 new cases in children under 20 years of age each year
- Head and Neck Malignancies make up 5% of pediatric cancer cases = 500 kids/year
Pediatric Cancer

Albright, et al in Archives of Oto-HNS
June 2002

- Overall annual incidence of pediatric cancer
  - 1973-1975 = 11.22 cases/100,000 person/years
  - 1994-1996 = 14.03 cases/100,000 person/years
  - Increase of 25%

- Annual incidence of pediatric H&N cancer
  - 1973-1975 = 1.10 cases/100,000 person/years
  - 1994-1996 = 1.49 cases/100,000 person/years
  - Increase of 35%
Pediatric Head and Neck Malignancies

- Lymphoma = 59%
- Rhabdomyosarcoma = 13%
- Thyroid Malignancies = 10%
- Nasopharyngeal Carcinoma = 5%
- Neuroblastoma = 5%
- Nonrhabdomyosarcoma Soft-tissue Sarcoma = 4.5%
- Salivary Gland Malignancies = 2.5%
- Malignant Teratoma = 1%
- Others
Non-Hodgkin’s Lymphoma

- Lymphoma = 11.5% of all pediatric cancers
- NHL occurs in 60% of lymphoma cases
- M:F = 3:1
- Peak incidence between 7-11 years of age
- Increased risk with T-cell deficiency
  - Congenital immunodeficiency syndromes
  - Acquired immunodeficiency syndrome
  - Immunosuppressive drug therapy
Non-Hodgkin’s Lymphoma

- Low-, intermediate-, and high-grade lesions
- 90% of children with NHL have high-grade disease at presentation
- High-grade
  - Large cell lymphoma
  - Lymphoblastic lymphoma
  - Small cell noncleaved lymphoma
Non-Hodgkin’s Lymphoma

- Large cell lymphoma
  - 27% pediatric cases
  - t(2;5) anomaly
  - Rare presentation in H&N

From, Diagnostic Surgical Pathology of the Head and Neck, W.B.Saunders, p 762.
Non-Hodgkin’s Lymphoma

- Lymphoblastic lymphoma
  - 29% pediatric cases
  - t(7 or 14)
  - Mediastinal mass

From, Diagnostic Surgical Pathology of the Head and Neck, W.B. Saunders, p 759.
Non-Hodgkin’s Lymphoma

- Small cell noncleaved
  - 34% pediatric cases
  - Burkitt’s lymphoma
    - Epstein-Barr virus
    - t(8;2,14,22)
    - Mandible
    - Head and Neck

From, Surgical Pathology of the Head and Neck, Lippincott Williams & Wilkins, p 161.
Non-Hodgkin’s Lymphoma

Presentation in the H&N in 5-10% of cases

- Cervical lymphadenopathy
- Salivary gland, larynx, sinuses, orbit, scalp
- Waldeyer’s ring
  - Asymmetric tonsils-how concerning is it?
- Associated symptoms
  - Fever, night sweats, weight loss
Non-Hodgkin’s Lymphoma

Evaluation

– H&P

– Biopsy
  - Tonsillectomy
  - Lymph node

– Staging w/u
  - Blood studies
  - Lumbar puncture
  - Bone marrow biopsy
  - CT chest/abdomen/pelvis
  - Bone scan
# Non-Hodgkin’s Lymphoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Ann Arbor</th>
<th>St Jude Children’s Research Hospital</th>
<th>Memorial Sloan-Kettering Cancer Center</th>
<th>Prince of Wales Children’s Hospital, Australia</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Involvement of a single lymph node region (I) or of a single extralymphatic organ or site ($I_E$)</td>
<td>Single tumor (extranodal) or single anatomic area (nodal) excluding the mediastinum or abdomen</td>
<td>A single site</td>
<td>A single site</td>
</tr>
<tr>
<td>II</td>
<td>Involvement of two or more lymph node regions on the same side of the diaphragm or localized involvement of extralymphatic organ or site and of one or more lymph node regions on the same side of the diaphragm</td>
<td>Single extranodal site with regional lymph node involvement; two or more nodal areas on the same side of the diaphragm; two single extranodal tumors ± regional node disease on the same side of the diaphragm; primary gastrointestinal tract tumor, usually in the ileocecal area ± involvement of associated mesenteric nodes</td>
<td>Two or more sites above or below the diaphragm</td>
<td>Two or more sites above or below the diaphragm</td>
</tr>
</tbody>
</table>
| III   | Involvement of lymph node regions on both sides of the diaphragm ± extranodal involvement ± splenic involvement | Two single extranodal tumors ± regional node disease on opposite sides of the diaphragm; two or more nodal areas on opposite sides of the diaphragm; all extensive primary intraabdominal disease; all primary intrathoracic tumors | Two or more sites above and below the diaphragm; extensive intrathoracic and extensive intraabdominal involvement | Above and below the diaphragm (III-O)  
All primary intrathoracic (III-T)  
Extensive intraabdominal (III-Ab) |
| IV    | Diffuse involvement of one or more extralymphatic organs or tissues ± associated lymph node enlargement | Any of the above ± initial CNS ± bone marrow involvement | Any of the above ± initial CNS ± bone marrow involvement | Marrow infiltration by <25% tumor cells (IV-M)  
Marrow infiltration by >25% tumor cells (IV-M)  
CNS infiltration (IV-N) |
Non-Hodgkin’s Lymphoma

Multiagent Chemotherapy
- Cyclophosphamide
- Doxorubicin
- Vincristine
- Prednisone
- +/- Methotrexate
- XRT—not routinely used
Non-Hodgkin’s Lymphoma

Survival

- Overall Stage I and II NHL = 85-95%
- Overall Stage III and IV NHL = 65-75%
- Stage III and IV BL = 75-85%
Hodgkin’s Disease

- Less common than NHL
- More frequently in 15-20 y/o population
- 4% under 10 years
- M:F = 3:1

Association with EBV
Hodgkin’s Disease

- Nodular Sclerosing
- Lymphocyte Predominant

From, Diagnostic Surgical Pathology of the Head and Neck, W.B.Saunders, p 750 & 764.
Hodgkin’s Disease

Mixed Cellularity

Lymphocyte Depleted

From, Diagnostic Surgical Pathology of the Head and Neck, W.B.Saunders, p 750.
Hodgkin’s Disease

Presentation

– Asymmetric lymphadenopathy—90%
  - Firm, rubbery
  - Supraclavicular fossa
– Spleen, liver
– Constitutional symptoms—1/3 of cases
  - Fever, night sweats, anorexia, weakness, weight loss
Hodgkin’s Disease

Evaluation
- H&P
- Biopsy = Reed-Sternberg cells
- Staging w/u
  - Similar to NHL
  - Laparotomy
    - Controversial

From, Principles and Practice of Pediatric Oncology, Lippincott Williams & Wilkins, P 640.
Hodgkin’s Disease

**Stage I:** involvement of a single lymph node region (I) or a single extralymphatic organ (IE)

**Stage II:** involvement of two or more lymph node regions on the same side of the diaphragm (II) or one lymph node region and one extralymphatic organ on the same side of the diaphragm (IIE)

**Stage III:** involvement of lymph node regions on both sides of the diaphragm (III) plus an extralymphatic organ (IIIE), the spleen (IIIS), or both (IIISE)

**Stage IV:** diffuse involvement of one or more extralymphatic organs with or without lymph node involvement (IV)

A: no systemic symptoms

B: weight loss, fever, or night sweats
Hodgkin’s Disease

Localized disease
- Extended field XRT

Disseminated disease
- MOPP = nitrogen mustard, vinblastine, procarbazine, prednisone
- ABVD = adriamycin bleomycin, vincristine, dacarbazine
Hodgkin’s Disease

**Survival**

- Stages I, II, and III = 90%
- Stage IV = 75-80%
Rhabdomyosarcoma

- Most common soft tissue sarcoma in children
- 4.5 cases/1,000,000 children under 14 years
- Majority diagnosed before age 10
- M:F = 1.5:1
Rhabdomyosarcoma

Embryonal

- Most common in kids: 60-70% of cases
- Chromosome 11p15 deletion
- Lack of gene amplification
- Hyperdiploid DNA

From, Surgical Pathology of the Head and Neck, Lippincott Williams & Wilkins, p 157.
Rhabdomyosarcoma

- **Alveolar**
  - 20% of pediatric cases
  - Chromosomal translocation: t(2;13) or t(1;13)
  - Gene amplification
  - Tetraploid DNA

From, Surgical Pathology of the Head and Neck, Lippincott Williams & Wilkins, p 157.
Rhabdomyosarcoma

- **Botryoid**
  - 5-10% of pediatric cases
  - Grape-like tumor masses

- **Pleomorphic**
  - Rare in children

From, Diagnostic Surgical Pathology of the Head and Neck, W.B. Saunders, p 554.
Rhabdomyosarcoma

- Most common site of presentation is H&N--40% of cases
- 1/3 of cases involve the orbit
- Oral cavity & oropharynx, face & neck, middle ear & mastoid, nose & paranasal sinuses
- Localized swelling, proptosis, nasal obstruction, epistaxis, otorrhea, hearing loss, fetor and cranial nerve deficits
Rhabdomyosarcoma

Evaluation

- H & P
- Biopsy
- CT/MRI of primary
- Metastatic w/u
  - Chest CT
  - Bone scan
  - Bone marrow biopsy
Rhabdomyosarcoma

Intergroup Rhabdomyosarcoma Study Clinical Grouping Classification (IRSCGC)

<table>
<thead>
<tr>
<th>Group</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Localized disease, completely resected</td>
</tr>
<tr>
<td>II</td>
<td>Compromised or regional resections with microscopic residual disease</td>
</tr>
<tr>
<td>III</td>
<td>Incomplete resection or biopsy with gross residual disease</td>
</tr>
<tr>
<td>IV</td>
<td>Distant metastatic disease present at onset</td>
</tr>
</tbody>
</table>
## Rhabdomyosarcoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sites</th>
<th>T</th>
<th>Size</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Orbit</td>
<td>T1 or T2</td>
<td>a or b</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Head and neck (excluding parameningeal area)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Bladder/prostate</td>
<td>T1 or T2</td>
<td>a</td>
<td>N0 or NX</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Extremity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cranial parameningeal sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other (includes trunk, retroperitoneum)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Bladder/prostate</td>
<td>T1 or T2</td>
<td>a</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>Extremity</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Cranial parameningeal sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other (includes trunk, retroperitoneum)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>All</td>
<td>T1 or T2</td>
<td>a or b</td>
<td>N0 or N1</td>
<td>M1</td>
</tr>
</tbody>
</table>

- **Stage 1**: Orbit, Head and neck (excluding parameningeal area)
- **Stage 2**: Bladder/prostate, Extremity, Cranial parameningeal sites, Other (includes trunk, retroperitoneum)
- **Stage 3**: Bladder/prostate, Extremity, Cranial parameningeal sites, Other (includes trunk, retroperitoneum)
- **Stage 4**: All
Rhabdomyosarcoma

Treatment

- Surgery
  - Goal = complete excision with margin
  - Consider morbidity of surgery
    - Cranial nerves
    - Cosmesis
  - Debulking

Exception is orbital rhabdomyosarcoma—surgery offers no advantage over chemo/XRT
Rhabdomyosarcoma

Treatment

– Chemotherapy

Low-risk: vincristine, dactinomycin, +/- cyclophosphamide

Intermediate- and High-risk: vincristine, dactinomycin and cyclophosphamide
Rhabdomyosarcoma

Treatment

- Radiation Therapy
  - Postoperative microscopic disease
    - 4,000-4,500 cGy
  - Gross disease
    - 4,500-5,000 cGy
  - Hyperfractionated XRT
  - Brachytherapy
Rhabdomyosarcoma

Survival
- Before 1970 = 33%
- Currently = 70%
- Intergroup Rhabdomyosarcoma Study
- Prognostic factors
  - Tumor size
  - Regional node status
  - Margins after surgery
  - Genetic factors
Neuroblastoma

- Most common extracranial solid tumor in children
- 8-10% of childhood cancers
- 90-95% of cases diagnosed before age 10
- More common in boys and Caucasians
- ? Genetic or environmental factors
Neuroblastoma

- “Small blue round cell” tumor
- Immunohistochemical stains: neurofilament proteins, synaptophysin, NSE
- Electron microscopy: neurosecretory granules, microtubules and filaments
- Chromosome 1 deletions or \( N\)-myc oncogene amplification

From, Principles and Practice of Pediatric Oncology, Lippincott Williams & Wilkins, p 903.
Neuroblastoma

- 2-5% in the H&N region—most often as lateral neck mass
- Airway obstruction, aspiration, dysphagia, Horner’s syndrome, proptosis, periorbital ecchymosis, ophthalmoplegia, conjunctival or eyelid edema, papilledema
- Heterochromia irides
Neuroblastoma

Evaluation
- H & P
- Biopsy
- Urine catecholamine studies
- Metastatic w/u
  - CXR
  - Bone marrow biopsy
  - Bone scan
  - CT or MRI
## Neuroblastoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Primary tumor $\leq 5$ cm; no evidence of regional node disease; no evidence of distant disease</td>
</tr>
<tr>
<td>II</td>
<td>Primary tumor $&gt;5$ but $\leq 10$ cm; no evidence of regional node disease; no evidence of distant disease</td>
</tr>
<tr>
<td>III</td>
<td>Stage I or II with evidence of regional node disease or primary tumor $&gt;10$ cm ± regional node disease; no evidence of distant disease</td>
</tr>
<tr>
<td>IV</td>
<td>Primary single tumor ± regional node disease; evidence of distant metastases</td>
</tr>
<tr>
<td>V</td>
<td>Multicentric tumors ± regional node disease ± distant metastases</td>
</tr>
</tbody>
</table>
Neuroblastoma

Treatment

– Surgery

– Chemotherapy
  - Intermediate- or High-risk
  - Low-risk with recurrence
  - Cyclophosphamide, ifosfamide, doxorubicin, teniposide, etoposide, cisplatin or carboplatin

– Radiation Therapy
  - Limited use
Neuroblastoma

Prognostic Factors
- Age at diagnosis
- Stage at diagnosis

Overall, Stage I or II = 75-90%

Infants: Stage III = 80-90%; Stage IV = 60-75%

Children: Stage III = 50%; Stage IV = 15%
Esthesioneuroblastoma

- 100 pediatric cases in the literature
- Teenagers, boys > girls
- Presentation
- Histology
- Staging
- Treatment
Esthesioneuroblastoma

Histology

From, Surgical Pathology of the Head and Neck, Lippincott Williams & Wilkins, p 86.
Esthesioneuroblastoma

- 100 pediatric cases in the literature
- Teenagers, boys > girls
- Presentation
- Histology
- Staging
- Treatment
Nasopharyngeal Carcinoma

- 5% of pediatric H&N malignancies
- Teenagers, M=F, African Americans
- Significantly higher incidence in Chinese
  - HLA-A2, HLA-B-Sin 2
  - Smoke, dust, nitrosamine rich salted fish
- EBV

From, Diagnostic Surgical Pathology of the Head and Neck, W.B. Saunders, p 43.
Nasopharyngeal Carcinoma

WHO Classification
- Type I – squamous cell carcinoma
- Type II – non-keratinizing squamous cell carcinoma
- Type III – undifferentiated or lymphoepithelioma

From, Diagnostic Surgical Pathology of the Head and Neck, W.B. Saunders, p 43
Nasopharyngeal Carcinoma

**Presentation**

- Neck mass and hearing loss
- Nasal obstruction, rhinorrhea, epistaxis, headache, otalgia
- Cranial neuropathy
  - Abducens palsy
  - CN III, IV, V
  - CN IX, X, XII
Nasopharyngeal Carcinoma

**Evaluation**
- H & P
- Endoscopy
- Biopsy
- CT/MRI for local extent
- Metastatic w/u
  - CT chest/abdomen
  - Bone scan
Nasopharyngeal Carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1</th>
<th>N0</th>
<th>M0</th>
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</thead>
<tbody>
<tr>
<td>Stage II A</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II B</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
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<td>T2a</td>
<td>N1</td>
<td>M0</td>
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<tr>
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<td>T2b</td>
<td>N0-1</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0-2</td>
<td>M0</td>
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<td>Stage IVA</td>
<td>T4</td>
<td>N0-2</td>
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<tr>
<td>Stage IV B</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV C</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
Nasopharyngeal Carcinoma

Treatment

- Radiation Therapy
  - Primary and local lymphatics
  - 6,500-7,000 cGy

- Chemotherapy
  - Advanced disease
  - Vincristine, doxorubicin, cyclophosphamide, cisplatin, 5-fluorouracil

- Surgery
Nasopharyngeal Carcinoma

Survival
- Overall 5-year = 40%

- Prognostic Factors
  - Positive
    - Locally confined disease
    - Ipsilateral nodes
  - Negative
    - Bilateral nodes
    - CNS penetration
Soft-tissue Sarcomas

4.5% of pediatric H&N malignancies

Diverse group of tumors

- fibrosarcoma
- synovial sarcoma
- dermatofibrosarcoma protuberans
- osteosarcoma
- hemangiopericytoma
- liposarcoma
- epitheloid sarcoma
- chondrosarcoma
- leiomyosarcoma
- clear-cell sarcoma
Soft-tissue Sarcomas

- Presentation
- Evaluation
- Staging
- Treatment
- Survival
Primitive Neuroectodermal Tumors

- Rare
- 42% involve the H&N region
- “small blue round cell” tumor

From, Diagnostic Surgical Pathology of the Head and Neck, W.B. Saunders, p 527.
Primitive Neuroectodermal Tumors

- Presentation
- Evaluation
- Staging
- Treatment
- Survival
Conclusion

- Rare diseases
- Broad differential diagnosis
- High index of suspicion
- Early diagnosis
- Accurate staging
- Multimodality therapy
- Improved prognosis