**Common Pediatric Malignancies**

Deepak Viswanath, DN Umashankar, R Mahesh Kumar

**ABSTRACT**

Childhood cancer is not a single disease, but includes a variety of malignancies in which abnormal cells divide in an uncontrolled manner. Childhood cancers vary by type of histology, site of disease origin, race, sex, and age. The axiom that ‘children are not little adults’ has long been applied to the management of pediatric patients, and it certainly applies to cancer patients. Most pediatric cancers differ quite significantly from adult cancers in several important ways including: (1) incidence, (2) underlying etiopathogenesis, (3) response rates, (4) outcomes and (5) biology. Unlike adult cancers, childhood cancer remains a rare event, affecting approximately 15 per 100,000 children annually. The most common pediatric solid tumors include brain tumors (25%), lymphomas (10%), neuroblastoma (8%), Wilms tumor (6%), and bone tumors (5%).

**Keywords:** Pediatric malignancies, Lymphoma, Leukemia.

**How to cite this article:** Viswanath D, Umashankar DN, Kumar RM. Common Pediatric Malignancies. J Indian Aca Oral Med Radiol 2013;25(2):126-130.

**Source of support:** Nil

**Conflict of interest:** None

**INTRODUCTION**

Cancer is a relatively rare disease in children with an annual frequency of 13 to 14 in 100,000 children up to 15 years.\(^1\) It accounts for less than 1% of all cancer in industrialized countries. However, cancer represents the second leading cause of childhood death in children 1 to 14 years old in developed countries, following accidents. Leukemia and lymphoma represent the most frequent pediatric malignancies (about 35 and 12%), followed by tumors of the central nervous system (CNS) (about 17%). All other entities are less frequent—bone tumors (5%), soft tissue tumors (7%), neuroblastoma (8%), nephroblastoma (7%), and germ-cell tumors (about 4%).\(^1,2\) Several types of these malignancies are specific to children, in particular the ‘blasto’-type.

**CLASSIFICATION OF CHILDHOOD CANCERS**

It has been established firmly that, for children, classification of tumors should be based on morphology rather than, as in adults, the primary site of origin. Ever-improving diagnostic methods, based on genetic studies and pathologic studies, have prompted a third edition of the ICD-O (ICD-O-3),\(^3\) to bring forth the new classification.

**The Classification**

Refer Table 1.


**LEUKEMIA**

The leukemias of childhood are cancers of the hematopoietic system, involving in most cases, and malignant transformation of lymphoid progenitor cells\(^4\) and less commonly transformation of myeloid progenitors.\(^5\) Following are the different types of leukemia with their specific diagnosis:

<table>
<thead>
<tr>
<th>Diagnostic group</th>
<th>Specific diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia: Lymphoid leukemia</td>
<td>• Lymphoid leukemia • Acute lymphoblastic • Subacute lymphoid • Chronic lymphocytic • Aleukemic lymphoid • Prolymphocytic • leukemia • Burkitt’s cell leukemia • Adult T-cell • Lymphosarcoma</td>
</tr>
<tr>
<td>Ib: Acute nonlymphocytic</td>
<td>• Erythroleukemia • Acute erythremia • Acute myeloid • leukemia • Aleukemic myeloid • Acute promyelocytic • Acute myelomonocytic • Acute monocytic leukemia • Aleukemic monocytic • Chronic myeloid leukemia • Chronic myelomonocytic</td>
</tr>
<tr>
<td>Ic: Chronic myeloid leukemia</td>
<td>• Plasma cell leukemia • Chronic erythremia • Myeloid leukemia • Basophilic leukemia • Eosinophilic leukemia • Monocytic leukemia • Chronic monocytic • Mast cell leukemia • Myeloid sarcoma • hairy cell leukemia</td>
</tr>
<tr>
<td>Id: Other specified leukemias</td>
<td>• Acute leukemia • Subacute leukemia • chronic leukemia</td>
</tr>
<tr>
<td>Ie: Unspecified leukemias</td>
<td>• Acute lymphocytic leukemia is a cancer of WBC’s and is of three types, L1, L2 and L3. The most common oral manifestations of this type of leukemia are: • Spontaneous gingival bleeding • Oral candidiasis, due to suppressed immune levels</td>
</tr>
</tbody>
</table>
Common Pediatric Malignancies

- Neutropenic ulcers of oral mucosa
- Gingival hypertrophy and inflammation
- Numb chin syndrome.

The prognosis of acute lymphocytic leukemia is generally good; and the cure rate is 85% in children. The treatment consists of multiple chemotherapeutic drugs; and those who cannot be treated with this mode are then treated with hematopoietic stem cell transplantation (HSCT).

**Acute Myeloid Leukemia**

Acute myeloid leukemia (AML) is characterized by arrest in maturation of myeloid cells leading to increase in number

### Table 1: Classification of childhood cancer

<table>
<thead>
<tr>
<th>1. Leukemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Lymphoid leukemia excluding ALL</td>
</tr>
<tr>
<td>(b) Acute leukemia excluding AML</td>
</tr>
<tr>
<td>(c) Chronic myeloid leukemia</td>
</tr>
<tr>
<td>(d) Other specified leukemias</td>
</tr>
<tr>
<td>(e) Unspecified leukemias</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Lymphomas and reticuloendothelial neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Hodgkin’s disease</td>
</tr>
<tr>
<td>(b) Non-Hodgkin’s lymphomas</td>
</tr>
<tr>
<td>(c) Burkitt’s lymphoma</td>
</tr>
<tr>
<td>(d) Miscellaneous lymphoreticular neoplasms</td>
</tr>
<tr>
<td>(e) Unspecified lymphomas</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. CNS and miscellaneous intracranial and intraspinal neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Ependymoma</td>
</tr>
<tr>
<td>(b) Astrocytoma</td>
</tr>
<tr>
<td>(c) Primitive neuroectodermal tumors</td>
</tr>
<tr>
<td>(d) Other gliomas</td>
</tr>
<tr>
<td>(e) Miscellaneous intracranial and intraspinal neoplasms</td>
</tr>
<tr>
<td>(f) Unspecified intracranial and intraspinal neoplasms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Sympathetic nervous system tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Neuroblastoma and ganglioneuroblastoma</td>
</tr>
<tr>
<td>(b) Other sympathetic nervous system tumors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Retinoblastoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Renal tumors</td>
</tr>
<tr>
<td>(a) Wilms’ tumor, rhabdoid and clear cell sarcoma</td>
</tr>
<tr>
<td>(b) Renal carcinoma</td>
</tr>
<tr>
<td>(c) Unspecified malignant renal tumors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. Hepatic tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Hepatoblastoma</td>
</tr>
<tr>
<td>(b) Hepatic carcinoma</td>
</tr>
<tr>
<td>(c) Unspecified malignant hepatic tumors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8. Malignant bone tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) osteosarcoma</td>
</tr>
<tr>
<td>(b) Chondrosarcoma</td>
</tr>
<tr>
<td>(c) Ewing’s sarcoma</td>
</tr>
<tr>
<td>(d) Other specified malignant bone tumors</td>
</tr>
<tr>
<td>(e) Unspecified malignant bone tumors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9. Soft-tissue sarcomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Rhabdomyosarcoma and embryonal sarcoma</td>
</tr>
<tr>
<td>(b) Fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms</td>
</tr>
<tr>
<td>(c) Kaposi’s sarcoma</td>
</tr>
<tr>
<td>(d) Other specified soft tissue sarcomas</td>
</tr>
<tr>
<td>(e) Unspecified soft-tissue sarcomas</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>10. Germ-cell, trophoblastic and other gonadal neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Intracranial and intraspinal germ-cell tumors</td>
</tr>
<tr>
<td>(b) Other and unspecified nongonadal germ-cell tumors</td>
</tr>
<tr>
<td>(c) Gonadal germ-cell tumors</td>
</tr>
<tr>
<td>(d) Gonadal carcinomas</td>
</tr>
<tr>
<td>(e) Other and unspecified malignant gonadal tumors</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>11. Carcinomas and other malignant epithelial neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Adrenocortical carcinoma</td>
</tr>
<tr>
<td>(b) Thyroid carcinoma</td>
</tr>
<tr>
<td>(c) Nasopharyngeal carcinoma</td>
</tr>
<tr>
<td>(d) Malignant melanoma</td>
</tr>
<tr>
<td>(e) Skin carcinoma</td>
</tr>
<tr>
<td>(f) Other and unspecified carcinomas</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>12. Other and unspecified malignant neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Other specified malignant tumors</td>
</tr>
<tr>
<td>(b) Other unspecified malignant tumors</td>
</tr>
</tbody>
</table>
of myeloblasts in the bone marrow, hemopoietic insufficiency (with or without leukocytosis) and infiltration of bone marrow and other tissues by blast cells.

Gender distribution shows that the incidence of AML in first years of life incidence rate is equal for both boys and girls. Later on there is a slight male predominance. Childhood AML has also been found associated with certain genetic disorders, for example children with Down syndrome have a 10 to 20-fold increased likelihood of developing acute leukemia. Other inherited diseases associated with AML include Klinefelter’s syndrome, Fanconi anemia and neurofibromatosis.

Chronic Myeloid Leukemia
Chronic myeloid leukemia (CML) is characterized by reduction of red blood cells and raised WBC count and lack of platelets leading to thrombocytopenia that results in easy bruising and bleeding. Other oral findings secondary to leukemia include ulceration due to an impaired immune defense; oral candidiasis, herpetic ulcers, gingival enlargement and periodontal bone loss secondary to immune alteration and infiltration by leukemic cells may be presenting features.

SOFT TISSUE TUMORS

Soft tissue has been defined as nonepithelial extraskeletal tissue of the body, exclusive the reticuloendothelial system, and glia and supporting tissue of various parenchymal organs; are histologically classified, as benign or malignant. A number of aggressive malignant tumors occur, such as sarcomas. Although the etiology of sarcomas remain obscure, a possible genetic origin is proposed, as there is an association with the alternative lengthening of telomeres (ALT) mechanism an about half of the osteosarcomas, soft tissue sarcomas and glioblastomas. From a clinical point of view, at least three separate clinical groups of malignant soft tissue sarcomas are encountered in childhood; congenital fibrosarcoma, rhabdomyosarcoma (RMS) and nonrhabdomyosarcoma soft tissue carcinoma.

Fibrosarcoma
This is the commonest in the <1 year age group, occurs in the extremities, is benign and rarely metastasizes.

Rhabdomyosarcoma
This is a malignant tumor of striated muscle, which usually displays early local invasiveness and may later metastasize via lymphatic and hematogenous pathways. It is derived from mesenchymal cells that differentiate along rhabdomyoblastic lines, it is the most common tumor encountered in childhood, occurring even in the perinatal period. Most common sites include the head and neck, leg and feet and thigh. The incidence of rhabdomyosarcoma in childhood and adolescence is 60%, and is higher in the first decade of life with 83%.

Histopathologically, rhabdomyosarcoma is of 3 types:
- Embryonal RMS—most common, prevalence of 53 to 64% of all rhabdomyosarcomas in childhood; occurs in orbit, head and neck, abdomen and genitourinary tract; and has two favorable subtypes:
  - The spindle cell embryonal variant seen in paratesticular RMS
  - Some head and neck tumors and sarcoma botryoides of the genitourinary tract.
- Alveolar RMS—prevalence of 21% of all rhabdomyosarcomas in children and occurs mostly on the trunks or extremities; has 2 subtypes, the undifferentiated sarcomas and the pleomorphic (adult) type.
- Pleomorphic RMS—frequency of 1% and is virtually unknown in childhood, mostly presents in adults.

Clinically, the primary tumor is usually located in the orbit, head and neck superficial and in parameninges. Clinical symptoms will depend on the location of the tumor and usually present with a painless, enlarging mass that can obstruct a sinus, grow into the nasal cavity, cause proptosis, or simulate chronic otitis media and clinical symptoms include nasal discharge or obstruction of the airways, otorrhea, and rapid proptosis. The deeper the tumor is situated, the signs and symptoms arise due to compression of nerves, blocked vessels or both. The parameningeal localization is the most frequent and has a poor prognosis; usually located in pterygoid infratemporal fossa, nasopharyngeal cavity, paranasal sinuses and middle ear and mastoid, and these constitute 92% of cases.

Staging in rhabdomyosarcoma: The current staging system used is the IRSG system (Intergroup Rhabdomyosarcoma Study Group)—refer Table 2.

The size of the primary tumor is a prognostic factor; tumor less than or equal to 5 cm are classified in the subgroup A, and tumors larger than 5 cm are classified in subgroup B. Rhabdomyosarcoma is a systemic disease, with high probability of spread to lymph nodes, bone and bone marrow, and peritoneal spaces; the patients are classified on the basis of low, moderate or high-risk treatment failure. The low-risk patients have tumors mainly of embryonal variety, located in favorable anatomic locations in oropharynx, scalp, parotid, neck, larynx, cheeks, eyelids and hypopharynx and also in genitourinary system; the survival rate is over 90% when treated with vincristine and dactinomycin with or without radiotherapy. The intermediate-risk patients are mainly of embryonal variety, survival rate around...
50 to 75% and they require complementary therapy along with radiotherapy. The high-risk patients have only 25% chance of survival.

**Nonrhabdomyosarcoma Soft Tissue Tumors**

Nonrhabdomyosarcoma soft tissue tumors are a heterogeneous group of mesenchymal cell tumors and the distribution varies with age; myofibromas and fibrosarcoma are more common in infants, whereas the synovial sarcoma and malignant peripheral nerve sheath tumor is more common in older children and adolescents. Approximately 20% of soft tissue tumors that occur in the children under 20 years are presented in the first year of age, and of these just over half presented in the first 3 months of life. 85% of soft tissue tumors present in the first year of life are classified as benign or borderline lesions and the remaining 15% being malignant. Some of the benign lesions include infantile hemangioendothelioma, lymphangiomas, myofibromas, fibrous histiocytoma and congenital fibrosarcoma; while embryonal rhabdomyosarcoma and primitive neuroectodermal tumor comprise the malignant lesions.

The anatomical location of primary tumor in descending order of frequency is head and neck, trunk and extremities. The most frequent primary site was in limbs—66% (in fibrosarcoma), head, neck and trunk—70% (in myofibromas) and 77% in limbs and tendons (in synovial sarcoma).13 The most common clinical presentation is a painless mass, although the involved adjacent structures can cause pain and other symptoms. The treatment and prognosis depend upon the extent of disease and the histological variety. Radiation therapy is usually successful where the location and size of the tumor is less than 5 cm.

**NEUROBLASTOMA**

Neuroblastoma is the most common solid tumor in children under 1 year of age, the overall incidence is 58/1,000,000 infants per year14 and 16% of infant neuroblastomas are diagnosed in the first month following birth, and 41% present during the first 3 months of life.15 Perinatal neuroblastomas arise from the cells of the neuroblastic nodules in the fetal adrenal gland. However, it is important to distinguish these clinically apparent masses from the minute collections of neuroblastoma cells that are seen at autopsy in newborns, because these aggregates share many of the morphologic features of neuroblastoma tumors, including the presence of mitotic figures and infiltration of the adrenal cortex, they have been termed ‘neuroblastoma in situ’.16 The distinguishing features are the small size of these nodules, frequent association with intra-adrenal cysts and absence in infants over 3 months of age.

The first symptoms are often vague, such as loss of appetite, tiredness and pain in the bones. If the tumor occurs in the abdomen, then there will be difficulty in passing urine followed by constipation. If the tumor affects the chest area, there will be dyspnea and if the tumor is present in the neck, there will be dyspnea followed by choking. Occasionally, there are deposits of neuroblastoma in the skin that appear as small, blue-colored lumps.

A newer staging system is currently being developed by the International Neuroblastoma Risk Group (INRG) which is widely followed:

- **Stage L1:** The tumor is localized and has not spread into important areas (vital structures) nearby. It can be removed by surgery.
- **Stage L2:** The tumor is localized but has ‘image-defined risk factors’ and can not be safely removed by surgery.
- **Stage M:** The tumor has spread to other parts of the body.
- **Stage MS:** The tumor has spread to the skin, liver and/or the bone marrow in children younger than 18 months old.

The treatment of neuroblastoma depends on the age of the child, the size and position of the tumor, the tumor biology (including the MYCN status) and whether the neuroblastoma has spread.

**LYMPHOMA**

The most common presentation of lymphoma in children with AIDS is fever and weight loss.
HIV-associated non-Hodgkin’s lymphoma is more advanced at presentation with extranodal manifestations, including hepatomegaly, jaundice, abdominal distension, CNS symptoms, pancytopenia and bone pain. Malignancy needs to be carefully considered in HIV-infected children who exhibit any combination of the above symptoms. The clinical presentation tends to be atypical and more aggressive with an increase in bone marrow involvement. The oral findings in Hodgkin’s lymphoma are xerostomia; radiation induced caries, osteoradionecrosis and reduced immune response, and in addition the following are also noted; inflammatory gingival overgrowth, premature root resorption of deciduous teeth and alveolar bone loss in conjunction with regression of gingival overgrowth.17

CONCLUSION

The spectrum of malignancies that occur in children is distinctive when compared to those that occur in older adults. The embryonal cancers that predominate among young children (e.g. neuroblastoma, retinoblastoma) are very uncommon among older age groups. While some types of acute leukemias and CNS cancers are shared with both the older adult and the young childhood populations, the 15 to 19 years old group experiences high rates of a set of tumors including germ cell tumors, Hodgkin’s disease, and the bone cancers that are relatively characteristic of the adolescent/young adult age group.

REFERENCES


ABOUT THE AUTHORS

Deepak Viswanath (Corresponding Author)
Professor and Head, Department of Pedodontics and Preventive Dentistry, Krishnadevaraya College of Dental Sciences, Bengaluru Karnataka, India, Phone: 9480226226, e-mail: pedodons@gmail.com

DN Umashankar
Reader, Department of Oral and Maxillofacial Surgery, Krishnadevaraya College of Dental Sciences, Bengaluru, Karnataka, India

R Mahesh Kumar
Reader, Department of Oral and Maxillofacial Surgery, Krishnadevaraya College of Dental Sciences, Bengaluru, Karnataka, India