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Malignancies in Children: A Comprehensive Review for Pediatricians

Dr. Venugopal Reddy. I

Medical Director and Pediatrician, Ovum Woman and Child Speciality Hospital, Banaglore, India.

Abstract

Childhood malignancies, including acute lymphoblastic leukemia (ALL), lymphomas, and other solid tumors, constitute a significant cause of morbidity and mortality worldwide. Early recognition, timely diagnosis, and multidisciplinary management are crucial for improving outcomes. This comprehensive review integrates epidemiology, clinical features, diagnostic strategies, recent advances, treatment modalities, and supportive care considerations pertinent to pediatric malignancies. Special focus is given to ALL and lymphomas as the most common pediatric cancers, with additional discussion on other malignancies. The article is designed to guide pediatricians in early detection, evidence-based evaluation, and coordinated care to optimize patient outcomes, especially in high-burden clinical settings.

Keywords: Pediatric malignancies, Childhood cancer, Acute lymphoblastic leukemia (ALL), Pediatric lymphoma, Hodgkin lymphoma, Non-Hodgkin lymphoma, Pediatric oncology, Cancer diagnosis in children.

Introduction

Pediatric malignancies, while relatively rare compared to adult cancers, present formidable clinical challenges due to their aggressive nature, subtle early symptoms, and potential for rapid progression. Leukemias and lymphomas make up a large proportion of childhood cancers, with acute lymphoblastic leukemia (ALL) accounting for approximately 25–30% of cases worldwide, and lymphomas comprising 10–15%. Early clinical signs often overlap with common benign conditions, necessitating a high index of suspicion and structured diagnostic approach.

The role of pediatricians is pivotal in recognizing early manifestations, initiating appropriate investigations, and coordinating multidisciplinary management. This review provides an up-to-date, evidence-based framework focusing on ALL and lymphomas, highlights diagnostic algorithms, recent molecular and therapeutic advances, and discusses other pediatric malignancies to enhance clinical practice and foster informed dialogue among pediatric care providers.

Epidemiology

- The global incidence of childhood cancer is approximately 140 per million children annually.
- Leukemias are the most common cancers in children, with ALL representing 75–80% of acute leukemia cases.
- Lymphomas (both Hodgkin and non-Hodgkin) contribute significantly, with non-Hodgkin lymphoma (NHL) more common in younger children.
- Geographic, ethnic, and environmental factors influence cancer incidence and subtype distribution.

- Increasing urbanization and improved diagnostic capabilities have led to higher reported cases in regions such as India, including Bangalore.

Specific Malignancies in Children

Acute Lymphoblastic Leukemia (ALL)

Overview

ALL is a clonal malignancy of lymphoid progenitor cells involving the bone marrow and blood. Median age of presentation in children is 2–5 years. It is curable in over 85% of cases with current treatment protocols.

Clinical Features

- Symptoms related to bone marrow failure: pallor, bruising, bleeding, recurrent infections
- Bone pain and limping
- Generalized lymphadenopathy and hepatosplenomegaly
- Fever without clear infectious focus, unexplained weight loss
- CNS involvement in some cases (headache, vomiting, cranial nerve palsies)

Diagnosis

- Complete blood count (CBC) and peripheral smear revealing blasts
- Bone marrow aspiration and biopsy for definitive diagnosis and immunophenotyping
- Flow cytometry to determine lineage (B-cell vs. T-cell)
- Cytogenetic and molecular studies (e.g., Philadelphia chromosome t(9;22), MLL rearrangement) for prognostication and risk stratification
- Cerebrospinal fluid (CSF) analysis via lumbar puncture for CNS disease staging
- Imaging (Chest X-ray) to evaluate for mediastinal mass, particularly in T-cell ALL

Treatment

- Multi-phase chemotherapy protocols: induction, consolidation, and maintenance
- CNS prophylaxis using intrathecal chemotherapy ± cranial irradiation (case-dependent)
- Hematopoietic stem cell transplantation (HSCT) in high-risk or relapsed disease
- Supportive care addressing infection prevention, transfusion support, and management of therapy toxicity

Prognosis

- Cure rates exceed 85% in developed settings; somewhat lower in resource-limited regions
- Prognosis linked to age at diagnosis, initial white blood cell count, cytogenetic abnormalities, and minimal residual disease (MRD) status

Lymphomas

Types

- Hodgkin lymphoma (HL): Characterized by Reed-Sternberg cells; often presents in adolescents with painless cervical lymphadenopathy
- Non-Hodgkin lymphoma (NHL): A heterogeneous group including Burkitt lymphoma, lymphoblastic lymphoma, diffuse large B-cell lymphoma, with variable clinical presentations

Clinical Presentation

- Painless lymphadenopathy (cervical, axillary, inguinal regions)
- “B symptoms”: fever, night sweats, weight loss

- Mediastinal masses causing cough, dyspnea, superior vena cava syndrome
- Extranodal involvement: abdominal masses, CNS symptoms, skin lesions

Diagnosis

- Excisional biopsy of lymph node or affected tissue for histopathology, immunohistochemistry, and flow cytometry
- Imaging: contrast-enhanced CT, PET-CT for staging and treatment response assessment
- Bone marrow biopsy to evaluate marrow infiltration
- Laboratory assessments including serum LDH as tumor burden marker

Treatment

- Chemotherapy regimens vary according to histological subtype and stage (e.g., ABVD for HL, intensive chemotherapy for Burkitt lymphoma)
- Radiotherapy generally reserved for bulky disease or residual lesions
- Emerging immunotherapies (e.g., monoclonal antibodies, checkpoint inhibitors) showing efficacy in relapsed/refractory disease

Prognosis

- Early-stage Hodgkin lymphoma: >90% cure rate
- NHL prognosis depends on subtype and stage; Burkitt lymphoma responds well to intensive short-course chemotherapy

Other Pediatric Malignancies

- Neuroblastoma: Common extracranial solid tumor of infancy, arising from sympathetic nervous tissue. Presents with abdominal mass, bone pain.
- Wilms Tumor: Pediatric renal tumor typically in toddlers, presenting as abdominal swelling.
- Brain Tumors: Including medulloblastoma, astrocytoma, presenting neurological deficits.
- Acute Myeloid Leukemia (AML): Less common than ALL but often more aggressive.
- Rhabdomyosarcoma: Soft tissue sarcoma of head, neck, or genitourinary tract.

Diagnostic Algorithm for Suspected Pediatric Malignancies

Step	Action	Rationale
1	Comprehensive history and physical examination	Identify warning signs (persistent fever, lymphadenopathy, organomegaly)
2	Complete blood count with peripheral blood smear	Detect cytopenias, blasts
3	Biochemical panels including LDH, uric acid	Assess tumor burden and organ function
4	Imaging: Chest X-ray, abdominal ultrasound, CT/MRI	Identify masses, mediastinal involvement, staging

Step	Action	Rationale
5	Bone marrow aspiration and biopsy	Confirm diagnosis of leukemia/lymphoma
6	Excisional lymph node biopsy	Confirm lymphoma histology and subtype
7	Immunophenotyping and genetic/cytogenetic analysis	Classification and risk stratification
8	Lumbar puncture for CSF analysis	Detect CNS involvement
9	Multidisciplinary tumor board review	Formulate individualized treatment plan

Recent Advances and Clinical Updates

- Molecular Diagnostics and Risk Stratification: Advances in cytogenetics and molecular biology have refined prognostic predictions and personalized therapy approaches (Pui et al., Lancet Oncol, 2018).
- Minimal Residual Disease (MRD): MRD monitoring is now standard in ALL, guiding treatment intensification (Campana et al., Blood 2014).
- Targeted Therapies and Immunotherapy:
- CAR-T cell therapy for relapsed/refractory B-cell ALL demonstrates durable remissions (Maude et al., N Engl J Med, 2018).
- Monoclonal antibodies (e.g., rituximab) improve outcomes in certain lymphomas.
- Supportive Care Improvements: Enhanced antimicrobial prophylaxis, improved blood product management, and nutritional support reduce treatment-related mortality.
- Epidemiology: Studies from India report rising detection of lymphoma and ALL reflecting enhanced diagnostic capacity and awareness (Indian J Pediatr, 2025).

Supportive Care and Long-Term Management

- Management of chemotherapy-induced cytopenias, infections, mucositis.
- Psychosocial support for children and families.
- Surveillance for late effects: secondary malignancies, cardiotoxicity, growth impairment.
- Rehabilitation and educational support for survivors.

Conclusion

Pediatric malignancies, particularly ALL and lymphomas, demand early recognition and structured clinical workflows to optimize diagnosis and care. Pediatricians must maintain a high index of suspicion for symptoms such as persistent fever, lymphadenopathy, and unexplained cytopenias. Integration of advanced diagnostics, contemporary treatment protocols, and multidisciplinary collaboration significantly improve survival and quality of life. Continuous education, regional epidemiology awareness, and adoption of emerging therapies are vital to advancing pediatric oncologic care.

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