Pediatric solid tumor

Pediatric Solid Tumors refer to a diverse group of malignant neoplasms that occur in children and adolescents, originating from solid tissues like muscle, bone, or organs. They differ biologically and clinically from adult tumors, requiring unique diagnostic and therapeutic approaches.

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Types of Pediatric Solid Tumors

1. **Central Nervous System (CNS) Tumors**:
    1. Most common solid tumors in children.
    2. Examples: Medulloblastoma, gliomas, ependymomas.

2. **Neuroblastoma**:
    1. Originates from neural crest cells.
    2. Commonly arises in the adrenal glands or sympathetic ganglia.
    3. Often diagnosed in children <5 years old.

3. **Wilms Tumor (Nephroblastoma)**:
    1. Kidney cancer primarily affecting children <5 years old.
    2. Usually presents as an abdominal mass.

4. **Rhabdomyosarcoma (RMS)**:
    1. Malignant tumor of skeletal muscle.
    2. Subtypes: Embryonal (more common) and alveolar.

5. **Ewing Sarcoma**:
    1. Aggressive tumor of bone or soft tissue.
    2. Common sites: pelvis, femur, ribs.

6. **Osteosarcoma**:
    1. Most common primary bone cancer in children.
    2. Often affects long bones (e.g., femur, tibia).

7. **Hepatoblastoma**:
    1. Rare liver cancer, typically seen in children under 3 years old.

8. **Retinoblastoma**:
    1. Tumor of the retina.
    2. Can be hereditary or sporadic.

9. **Germ Cell Tumors**:

1. Originate from germ cells.
2. Locations: gonads (testes/ovaries) or extragonadal (mediastinum, sacrococcygeal region).

10. **Other Rare Tumors**:

1. Examples: Desmoplastic small round cell tumor, fibrosarcoma, and hepatocellular carcinoma.

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Key Features of Pediatric Solid Tumors

1. **Unique Biology**:

1. Often arise from developmental tissues and have specific genetic abnormalities (e.g., MYCN amplification in neuroblastoma, EWSR1-FLI1 fusion in Ewing sarcoma).

2. **Age of Onset**:

1. Typically occur during infancy, childhood, or adolescence.

3. **Rapid Growth**:

1. Many pediatric tumors are highly proliferative but may also be highly responsive to therapy.

4. **Prognosis**:

1. Generally better than adult cancers due to high sensitivity to chemotherapy and radiation.
2. Prognosis depends on tumor type, stage, and genetic features.

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Diagnostic Approaches

1. **Clinical Presentation**:

1. Symptoms vary by tumor type and location (e.g., abdominal mass in Wilms tumor, bone pain in osteosarcoma).

2. **Imaging**:

1. Ultrasound, MRI, CT scans, and PET scans for tumor localization and staging.

3. **Biopsy and Histopathology**:

1. Essential for definitive diagnosis and subtyping.

4. **Molecular and Genetic Testing**:

1. Identifies key mutations or markers (e.g., ALK mutations in neuroblastoma).

5. **Tumor Markers**:

1. Examples: Alpha-fetoprotein (AFP) in hepatoblastoma, beta-hCG in germ cell tumors.

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Treatment Strategies

1. **Surgery**:
    1. Often the first step for localized tumors (e.g., Wilms tumor, osteosarcoma).
2. **Chemotherapy**:
    1. Multi-agent regimens are standard, particularly for metastatic or systemic disease (e.g., neuroblastoma, RMS).
3. **Radiation Therapy**:
    1. Used sparingly due to long-term side effects.
    2. Indicated in tumors like medulloblastoma or Ewing sarcoma.
4. **Targeted Therapies**:
    1. Involves drugs targeting specific mutations or pathways (e.g., ALK inhibitors for neuroblastoma).
5. **Immunotherapy**:
    1. Emerging treatments, such as GD2-targeted therapy in neuroblastoma.
6. **Stem Cell Transplant**:
    1. High-dose chemotherapy followed by autologous stem cell rescue for high-risk neuroblastoma.

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Challenges in Pediatric Solid Tumors

1. **Late Diagnosis**:
    1. Many tumors are asymptomatic until advanced stages.
2. **Treatment Toxicity**:
    1. Long-term side effects of chemotherapy and radiation include growth disturbances, organ dysfunction, and secondary cancers.
3. **Relapse**:
    1. Recurrent disease is often more resistant to treatment.
4. **Psychosocial Impact**:
    1. Diagnosis and treatment can significantly affect a child’s quality of life and development.
5. **Rare Tumors**:
    1. Limited research and treatment options for rare pediatric solid tumors.

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Advances in Pediatric Oncology

1. **Precision Medicine**:
    1. Use of molecular profiling to guide therapy (e.g., identifying actionable mutations).
2. **Liquid Biopsies**:
    1. Detect circulating tumor DNA (ctDNA) for monitoring and prognosis.
3. **Proton Therapy**:
    1. Offers more precise radiation delivery, reducing damage to healthy tissues.
4. **CAR-T Cell Therapy**:
    1. Showing promise in certain solid tumors.
5. **Clinical Trials**:
    1. Emphasis on novel agents and combination therapies to improve outcomes.

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Prognosis Prognosis varies widely by tumor type: - Favorable for localized Wilms tumor and low-risk neuroblastoma (>90% survival). - Poorer for metastatic or high-risk tumors like relapsed Ewing sarcoma or high-risk neuroblastoma.

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Conclusion Pediatric solid tumors are a diverse group of cancers with unique biological features. Advances in diagnostic techniques, multimodal therapy, and emerging precision medicine approaches are improving outcomes. However, challenges like late diagnosis, treatment toxicity, and tumor relapse necessitate ongoing research and innovation in pediatric oncology.

A review of the current state of liquid biopsy research for the most common non-central nervous system pediatric solid tumors. These include neuroblastoma, renal tumors, germ cell tumors, osteosarcoma, Ewing sarcoma, rhabdomyosarcoma other soft tissue sarcomas, and liver tumors. Within this selection, we discuss the most important or recent studies involving liquid biopsy-based biomarkers, anticipated clinical applications, and the current challenges for success. Furthermore, we provide an overview of liquid biopsy-based biomarker publication output for each tumor type based on a comprehensive literature search between 1989 and 2023. Per the study identified, we list the relevant liquid biopsy-based biomarkers, matrices (e.g., peripheral blood, bone marrow, or cerebrospinal fluid), analytes (e.g., circulating cell-free and tumor DNA, microRNAs, and circulating tumor cells), methods (e.g., digital droplet PCR and next-generation sequencing), the involved pediatric patient cohort, and proposed applications. As such, we identified 344 unique publications. Taken together, while the liquid biopsy field in pediatric oncology is still behind adult oncology, potentially relevant publications have increased over the last decade. Importantly, steps towards clinical implementation are rapidly gaining ground, notably through the validation of liquid biopsy-based biomarkers in pediatric clinical trials [1)].

Gong et al. retrospectively analyzed the basic clinical characteristics of the patients, including age, cancer type, and sex distribution, and further analyzed the somatic and germline mutations of cancer-related genes in a Chinese pediatric cohort. In addition, we investigated the clinical significance of genomic mutations on therapeutic, prognostic, diagnostic, and preventive actions.

The study enrolled 318 pediatric patients, including 234 patients with CNS tumors and 84 patients with non-CNS tumors. Somatic mutation analysis showed that there were significant differences in mutation types between CNS tumors and non-CNS tumors. P/LP germline variants were identified in 8.49% of patients. In total, 42.8% of patients prompted diagnostic, 37.7% of patients prompted prognostic, 58.2% of patients prompted therapeutic, and 8.5% of patients prompted tumor-predisposing and preventive, and we found that genomic findings might improve clinical management.

The study is the first large-scale study to analyze the landscape of genetic mutations in pediatric patients with solid tumors in China. Genomic findings in CNS and non-CNS solid pediatric tumors provide evidence for the clinical classification and individualized treatment of pediatric tumors, and they will facilitate the improvement of clinical management. Data presented in this study should serve as a reference to guide the future design of clinical trials [2)]

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2)
Gong J, Dong L, Wang C, Luo N, Han T, Li M, Sun T, Ding R, Han B, Li G. Molecular genomic landscape of pediatric solid tumors in Chinese patients: implications for clinical significance. J Cancer Res Clin Oncol. 2023 May 4. doi: 10.1007/s00432-023-04756-5. Epub ahead of print. PMID: 37140698.