Pediatric Head and Neck Malignancies

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KEYWORDS

• Pediatric malignancies • Pediatric tumors • Pediatric head and neck malignancies
• Pediatric head and neck tumors • Pediatric sarcomas • Pediatric carcinoma

KEY POINTS

- Pediatric head and neck malignancies are rare, and therefore there is a lack of high-level evidence to guide treatment.
- Pediatric head and neck malignancies are often treated with multimodality treatment. One must be cognizant of the potential side effects on young growing patients.
- In surgical diseases, obtaining clear surgical margins seems to be the single most important prognostic factor in improving survival.

Head and neck (H&N) malignancies are rare in pediatric patients, and represent 12% of all pediatric malignancies.[1] The incidence of these H&N tumors is 1.49 cases per 1,000,000 person-years. Despite that, pediatric malignancies account for the second largest cause death in children, after accidental trauma.

Among the most common pediatric H&N malignancies are lymphomas (27%), neural tumors including primitive neurectodermal tumors (PNET; 23%), thyroid malignancies (21%), soft tissue sarcomas (12%), nasopharyngeal carcinoma, skeletal malignancies, and salivary gland malignancies.[2]

Although an exhaustive review of all pediatric H&N malignancies is beyond the scope of this article, the most common and relevant malignancies that affect children are discussed, with the exception of salivary gland malignancies, which are discussed elsewhere in this issue.

LYMPHOMA

Hematogenous malignancies are the most common cancers in children. Of these, acute lymphocytic leukemia is the most common, accounting for about one-third of pediatric malignancies. Lymphomas rank as the most common pediatric cancer.[2] They are divided into Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). There have been significant advances in the treatment of these diseases in the last 30 years and survival has more than doubled, with cure rates for lymphomas approaching 90%.[3]

Hodgkin lymphoma has a bimodal distribution with a peak in adolescence and adulthood. Approximately 1000 new cases present in the pediatric age group annually in the United States. The incidence is 50 per million, and only 5% of tumors occur in children younger than age 10. The pediatric disease has a male preponderance (2:1 male/female ratio) and has been associated with the Epstein-Barr virus.[4] Most of these patients (about 80%) present with asymptomatic cervical adenopathy, without "B" symptoms (fever, night sweats, weight loss), which can be associated with Hodgkin lymphoma and NHL and have prognostic significance (staging).[5] This disease can be broadly divided into two categories: the more common "classical" Hodgkin lymphoma, comprising 90% of cases, and the "lymphocyte-predominant" type of

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Hodgkin lymphoma. Classical Hodgkin disease is further classified into the following subtypes, in the order of prevalence: nodular sclerosing Hodgkin lymphoma (65%), mixed cellularity Hodgkin lymphoma (22%), and lymphocyte depleted Hodgkin (rare in children).[6] The Ann Arbor staging system is used to stage these tumors according to whether disease is localized, and whether it involves organs on both sides of the diaphragm. Staging work-up should include a computed tomography of the neck, chest, and abdomen. Blood tests that are indicated include a complete blood count with differential, erythrocyte sedimentation rate, renal and hepatic function tests, and alkaline phosphatase. A histopathologic hallmark of this disease is the Reed-Sternberg cells.[4] Treatment is nonsurgical, and is based on risk stratification, and also depends on the stage of the disease. Lymph node biopsy is often needed for diagnosis because fine-needle aspiration (FNA) biopsy often has a low diagnostic yield. Early and low-risk localized disease has been traditionally treated with radiation with acceptable cure rates. Advanced and high-risk disease is treated with a combination of multiagent chemotherapy and radiotherapy.[6] Recent trends in the treatment of Hodgkin disease have shifted toward multimodality therapy to limit the toxicities associated with chemotherapy and radiation therapy.

NHL has a male preponderance with a 2:1 to 3:1 male/female ratio, and it is more common in white persons. Systematic reviews have shown an overall increase in annual incidence of this disease since the mid-1970s with 600 new cases occurring annually in the United States.[7] Unlike the bimodal distribution in Hodgkin disease, NHL has an increasing incidence with age, with only 25% of cases occurring in children younger than age 10.[7] Adult NHL tends to be typically a nodal disease; in contrast, pediatric lymphoma has a propensity for involving extranodal sites. Most cases present in the mediastinum or abdomen, but about 10% of cases present primarily in the H&N. The most commonly involved sites in the H&N include cervical lymph nodes, salivary glands, larynx, sinuses, orbit, and Waldeyer ring.[8] This disease tends to be grow rapidly, and early diagnosis is critical for prompt appropriate treatment. The histopathology of these diseases is widely varied and generally categorized into low, intermediate, and high grade depending on how aggressive the tumor behaves. Most tumors in children are high-grade lesions.[9] The most common NHLs in children are mature B-cell lymphomas, which includes Burkitt lymphoma and diffuse large B-cell lymphomas, followed by lymphoblastic and anaplastic large cell lymphomas.[3]

Diagnosis is established via incisional biopsy and histopathologic analysis of the involved tissue. As in Hodgkin disease, FNA tends to be of limited value. A cervical lymph node excision is the preferred method for diagnosis in cases of cervical adenopathy.[10] Biopsy tissue should be sent fresh (not fixed) for histopathology to facilitate flow cytometry, immunohistochemical staining, and other specialized stains and testing. Surgery is reserved for a diagnostic role, with the mainstay of treatment being multiagent chemotherapy. A CHOP-based regimen (cyclophosphamide, hydroxydaunomycin, vincristine, and prednisone) is most commonly used in these cases. Prognosis depends on the stage, and with recent advances in chemotherapy regimens achieving survival of more than 80% is typical.[3]

RHABDOMYOSARCOMA

Whereas in the adult patient rhabdomyosarcoma accounts for a minority of the pathology of H&N cancers, this malignancy is one of the most common tumors of childhood. It affects about 250 children per year in the United States.[11] It is the third most common soft tissue malignant neoplasm after Wilms tumor and neuroblastoma, accounting for 13% of all pediatric cancers. The H&N is the most common site of rhabdomyoscarcoma, accounting for 35% to 40% of these tumors.

These tumors are bimodal in distribution, and often present in patients younger than 5 years of age and between 10 and 18 years of age.[12] An asymptomatic mass is the most common presenting finding. Within the H&N, the eye is a very common subsite for rhabdomyoscarcoma, followed by the oral cavity (**Fig. 1**) and the pharynx.

Histologically, rhabdomyosarcoma is one of the "small round blue cell" tumors, presenting with sheets of small cells with large prominent nuclei. Rhabdomyosarcoma is divided according to histopathology into three distinct categories: (1) embryonal, (2) alveolar, and (3) pleomorphic. The embryonal type is most common at birth, and the alveolar form peaks in childhood and adolescence.[13] Embryonal is the most common type accounting for 75% of H&N cases, with the botryoid subtype demonstrating a more favorable prognosis.[14] Alveolar rhabdomyosarcoma has a worse prognosis. The 5-year survival rate for the embryonal type is 97% in nonorbital, nonparameningeal cases, whereas the alveolar type has a survival rate of 67%.[15]

Management of these tumors is often multimodal, with chemotherapy playing a key role. The Intergroup Rhabdomyosarcoma Study (IRS I-IV) has established a staging and grouping