Pediatric Tonsil Cancer: A National and Institutional Perspective

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Objective To evaluate childhood and adolescent tonsil cancer incidence and to identify the clinical characteristics indicative of those patients who would benefit from urgent operative intervention.

Study design The Surveillance, Epidemiology and End Results 18 database, inclusive of national cancer statistics from 1973 to 2013, provided quantitative tonsil cancer incidence data. An institutional retrospective chart review of pediatric patients diagnosed with tonsil malignancy from January 2013 to January 2017 identified supplementary qualitative clinical presentation information.

Results The Surveillance, Epidemiology and End Results 18 database included 138 pediatric patients with tonsil cancer with an age-adjusted incidence rate of 0.021/100 000 patients per year. The majority of cases were unilateral (79.7%), and there was both a male and Caucasian predominance. Non-Hodgkin lymphoma (84.1%) was the most common malignancy, of which Burkitt lymphoma (31.1%), diffuse large B-cell lymphoma (26.8%), and follicular lymphoma (10.1%) were the most common subtypes. Five tonsillar malignancy patients were identified upon institutional chart review. The majority likewise had non-Hodgkin lymphoma and all shared a history of rapid tonsillar enlargement over ≤12 weeks. Significant tonsillar asymmetry was present in 4 patients. Four patients additionally exhibited prominent cervical lymphadenopathy.

Conclusions Pediatric tonsil cancer is rare, with non-Hodgkin lymphoma accounting for the majority of pediatric tonsillar malignancies. A high index of suspicion is appropriate in children who present with relatively rapid tonsil enlargement, tonsillar asymmetry characterized by a difference in tonsillar size of ≥2 degrees on the Brodsky scale, or concurrent prominent cervical lymphadenopathy. *(J Pediatr 2018;■■:■■-■■).*

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Approximately 530 000 children undergo tonsillectomy in the US on an annual basis.[1] The principal indications are obstruction (approximately 75%) and infection (approximately 25%).[2,3] A much smaller subset of pediatric patients undergo tonsillectomy for a variety of other reasons, such as dysphagia, failure to thrive, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, and periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome. The most concerning of the alternative indications for surgery is tonsillar asymmetry with suspicion of malignancy.[4]

Although patients diagnosed with tonsillar malignancy typically exhibit asymmetrical tonsils, the majority of tonsillar asymmetry is innocuous. Multiple studies have shown that the clinical observation of tonsillar asymmetry, alternatively termed unilateral tonsillar enlargement (UTE), does not often reflect true asymmetric size when the tonsils are physically compared after excision.[5-7] This discrepancy is largely attributed to differences in tonsil position relative to the depth of the tonsillar fossa.[7] In view of the limited accuracy of the oropharyngeal examination in detecting truly asymmetric tonsils, the performance of tonsillectomy for UTE in the pediatric age group is controversial.[4-9]

Given the anesthesia exposure and complication risks of tonsillectomy, yet the significant concern of missing a tonsillar malignancy, we sought to examine pediatric tonsillar cancer from both a national and institutional perspective. The Surveillance, Epidemiology and End Results (SEER) database provided the national perspective, and an institutional approach was used to identify additional clinical presentation factors to help define which patients with UTE should undergo excision for pathologic examination purposes.

Methods

The SEER 18 database (SEER*Stat software, version 18.0, National Cancer Institute; Bethesda, MD) was used to examine pediatric tonsil malignancy from a

DLBCL	Diffuse large B-cell lymphoma
SEER	Surveillance, Epidemiology and End Results (database)
UTE	Unilateral tonsillar enlargement

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national perspective. SEER data collection was initiated in 1973. The first database, SEER 9, included 9 registries covering Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah. SEER subsequently expanded its geographic range to enhance coverage of cancer incidence in minority populations to represent more accurately the general population. In 1992, SEER 13 was created with the addition of registries from Los Angeles, San Jose-Monterrey, and rural Georgia, as well as the Alaska native tumor registry.

The most recent SEER 18 registry, established in 2001, includes additional data from the populations of greater California, greater Georgia, Kentucky, Louisiana, and New Jersey. The SEER 18 database reports data collected from 28% of the US population, offering the most current and accurate cancer incidence and national prevalence data from 1973 through 2014.[10,11]

The SEER 18 database was assessed for patients with malignancies diagnosed between 0 and 19 years of age. Using the "Primary Site-Labeled" search option, patients with malignancies of the "tonsillar fossa, tonsillar pillar, overlapping lesion of the tonsil, tonsil, lateral wall of the oropharynx, or overlapping lesion of the oropharynx," diagnosed between 1973 and 2013 were included. Patients were excluded if they were >19 years of age or if the specific oropharyngeal site of their tumor was not specified.

To generalize the data gathered from the SEER registry to the US pediatric population, incidence data were age adjusted and normalized to the 2000 US standard population census. A ratio of the number of pediatric tonsil cancer cases to the total number of patients aged 0-19 years in the SEER database was calculated for each year. The data were then weighted based on the proportion of patients in the SEER database compared with the 2000 US standard population. These annual incidence rates were averaged to obtain the final age adjusted incidence rate.

In parallel, a comprehensive chart review of all patients diagnosed with tonsillar asymmetry and/or tonsillar malignancies at our institution between January 2013 and January 2017 was also performed. Data collected included demographics, clinical presentation, examination findings, laboratory studies, imaging results, and histopathology. Tonsil size was standardized using the Brodsky scale.[12] In this classification system, tonsils are referenced relative to the oropharyngeal midline and graded on a 1-4 scale according to the fraction of the airway space the tonsil obstructs.[12] A tonsil size of 1+ corresponds with ≤25% oropharyngeal airway obstruction, 2+ means 50% of the airway space is obstructed, grade 3+ represents ≤75% obstruction, and grade 4+ tonsils completely obstruct the airway (**Figure**; available at www.jpeds.com). We defined "significant" tonsil asymmetry as tonsils that differed in size by ≥2 grades on the Brodsky scale. Volumetric data were calculated using the formula for ellipsoid volume ($V = 4/3\pi abc$) for patients who underwent bilateral tonsillectomy. A paired *t* test was used to compare tonsil volume between specimens taken from the same patient. Prominent cervical lymphadenopathy was defined as having ≥1 enlarged lymph node ≥1 cm within one of the cervical chains. Patients who underwent tonsillectomy because of concern regarding post-transplant lymphoproliferative disorder were excluded from this review.

The Boston Children's Hospital Institutional Review Board approved this retrospective study prior to data acquisition. Institutional Review Board guidelines were followed.

Results

SEER Data

Pediatric patients with a tonsillar malignancy (N = 138) were identified using the SEER 18 database.[11] The overall age adjusted incidence rate was 0.021/100 000 per year. There were 25 children <5 years of age, of which only 2 were <12 months of age. The majority of patients were in the 5- to 19-year-old age categories, with nearly equal distributions between 5-9, 10-14, and 15-19 years of age. Patients were primarily Caucasian (n = 112; 81.2%). There were more than twice as many males (n = 94; 68.1%) as females.

Non-Hodgkin lymphoma was the most common malignancy, constituting 87.0% of cases (n = 120) (**Table I**). Burkitt lymphoma was the most common subtype (n = 43; 31.1%), followed by diffuse large B-cell lymphoma (DLBCL; n = 37 [26.8%]) and follicular lymphoma (n = 14; 10.1%). Rhabdomyosarcoma (n = 5; 3.62%), synovial sarcoma (n = 2; 1.44%), and plasmacytoma (n = 3; 2.2%) were comparatively rare SEER cohort diagnoses.

Among the 110 patients whose malignancies were unilateral, the incidence of malignancy was nearly equal between the right (n = 49; 35.5%) and left (n = 61; 44.2%) tonsils. In 16.0% of patients (n = 22), the primary malignancy was bilateral. Laterality was not specified for 6 cases.

Institutional Data

Data regarding the institutional tonsil malignancy cases are summarized in **Table II**. These data are consistent with the SEER findings in that 3 of the 5 children in our institutional cohort had Burkitt lymphoma; the other 2 children notably had acute lymphoblastic leukemia. Similar to the SEER cohort, 4 of the 5 children were male, all were Caucasian, and all were between the ages of 3 and 10 years. In 4 of the 5 children, their diagnosis was ascertained by tonsillectomy; tonsillectomy was deferred in 1 child because flow cytometry of a peripheral blood sample had already confirmed the diagnosis.

Of the 5 cases of tonsillar malignancy in the institutional cohort, 2 presented with obstructive sleep-disordered breathing manifestations. One of the 2 children who presented with obstructive symptoms also exhibited unilateral tonsillar asymmetry. Of the 4 patients who presented with unilateral tonsillar hypertrophy, 3 underwent bilateral tonsillectomy. The median tonsil volume was 20.3 cm^3 (range, 12.4-36.8 cm^3) in the affected tonsil compared with 2.7 cm^3 (range, 1.2-3.2 cm^3) in the contralateral tonsil. Prominent cervical lymphadenopathy was present in 4 of the 5 children on initial examination. Symptom duration before presentation ranged from 3 to 12 weeks. There was preoperative concern for malignancy in all of these patients.

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