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Pediatric sinonasal malignancies: A population-based analysis

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ABSTRACT

Introduction: Pediatric Sinonasal Malignancies (PedsSNM) are rare and usually associated with a poor prognosis. We aim to investigate the epidemiology, tumor characteristics, and survival of PedsSNM using a population-based database to augment the scant literature on this topic.
Methods: The Surveillance, Epidemiology, and End Results database was queried for patients ≤18 years diagnosed with PedsSNM between the years of 1973 and 2013. Data on incidence, tumor characteristics, and survival were analyzed.
Results: In total, 210 patients with PedsSNM were identified. Demographically, 54.3% were female, 72.6% were white, and the mean age was 10.7 years. Overall incidence was 0.036 per 100,000 individuals between the years of 2000 and 2013. The nasal cavity was the most frequent primary site (37.1%) and rhabdomyosarcoma was the most frequent malignancy (50.5%). Five-, 10-, and 20-year disease-specific survival (DSS) rates were 60.2%, 46.1%, and 20.6%, respectively. Grade IV tumors made up the largest group (37.3%), and such tumors exhibited the worst 5-, 10-, and 20-year survival ($P < 0.05$). Distant disease predicted the worst 5-, 10-, and 20-year survival, followed by regional, then localized disease ($P < 0.01$). Patients treated with surgery alone had a higher 20-year survival ($P = 0.0425$). No significant differences in survival were observed between race, gender, primary site, or histology.
Conclusions: PedsSNM frequently presented as Grade IV tumors. The nasal cavity was the most common primary site and rhabdomyosarcoma was the most frequent histology. Patients receiving surgery alone had the highest survival; however, this may be a reflection of smaller, less aggressive tumors preferentially being treated with surgery alone.

1. Introduction

While less than 5% of head and neck malignancies arise from the nasal cavity and paransasal sinuses, pediatric sinonasal malignancies (PedsSNM) are even rarer [1,2]. The presenting symptoms of nasal obstruction, facial swelling, ophthalmic complaints, rhinorrhea, epistaxis, rhinosinusitis, and chronic upper respiratory tract infections are nonspecific and can be easily mistaken for more common conditions [1–4]. Diagnosis is often delayed by weeks to years and results in advanced disease stage at presentation [2–5]. PedsSNM have been shown to have distinct epidemiological, clinicopathologic, histological, and survival differences compared to adult sinonasal malignancies, emphasizing the value of examining these malignancies in pediatric patients

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alone [1,2]. Given the rarity of PedsSNM, we used the US National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database to identify a large, nationally representative cohort, with long-term surveillance. SEER is a multicenter, population-based record that has collected information on malignancies since 1973, and is exempt from institutional biases. Until recently, case reports, systematic reviews, and single-institution studies largely accounted for the scant literature on PedsSNM [4]. Shapiro et al. conducted the first database analysis of PedsSNM and provided some valuable information about their demographic and clinicopathologic characteristics. Their series was limited to 63 cases, and they could not provide any survival analyses due to their small sample size [3]. Gerth et al. have thus far been the only ones to provide survival analyses using SEER. Our study examines 210 PedsSNM patients, provides updated analyses of any previously reported survival trends, and compares our findings to that of the literature. Furthermore, we investigate the role of other potential prognostic indicators of survival not previously explored, such as histological grade at diagnosis.

2. Materials and methods

The SEER 18 database was queried in order to obtain frequency, survival, and incidence data for all pediatric sinonasal tumors of the head and neck between the years 1973 through 2013. Sinonasal lymphoma cases were excluded from our analysis to facilitate staging and survival analyses. The SEER database is maintained by the National Cancer Institute (Bethesda, Maryland) and provided all the analyzed information including patient demographics, tumor characteristics, and incidence and survival rates. The SEER 18 database is an amalgamation of data collected from 18 registries from Connecticut, New Jersey, Georgia, Louisiana, Kentucky, New Mexico, Utah, California, Hawaii, Alaska, Oklahoma, Arizona, Michigan, Washington, and Iowa. Some of the registries are statewide registries, as in the case of New Jersey and Connecticut state registries. Others cover a particular metropolitan area, as in the case of the Los Angeles and San Franscico-Oakland registries. Overall, the database captures 28% of the population in the US. The data are void of any private identifiable health records, thus this study has been exempt from Institutional Review Board (IRB) approval as per the standing policy of the IRB of Rutgers New Jersey Medical School, Newark, New Jersey.

2.1. Patient and tumor characteristics

International Classification of Disease for Oncology, 3rd Edition (ICD-O-3) topography codes corresponding to all sinonasal tumors were initially used to query case data from the SEER 18 database (C30.0, C31.0, C31.1, C31.2, C31.3, C31.8, C31.9). This dataset was further confined to only include patient cases who were under 18 years of age. The resultant data were then stratified by age groups, gender, race, histology, and primary site. Tumor properties were further analyzed by grade, extension of disease, and treatment modalities. All unknown values were included in the reported results; however, they have been omitted from distribution calculations.

2.2. Statistical analysis

Pediatric sinonasal tumors diagnosed between 2000 and 2013 were reported for incidence trends as reported per 100,000 when adjusted to the standard 2000 US population (Census P25-1130). Calculated annual percent change (APC) was observed with 1-year end points. Weight least squares were utilized for APC significance testing.

SEER*Stat 8.3.2 (National Cancer Institute, Bethesda, MD) was used to extract all patient data, which were subsequently organized on Microsoft Excel 2016 spreadsheets (Microsoft Corporation, Redmond, WA). Survival analysis for 5-, 10-, and 20-years was then accomplished using the binary scheme utilized in Kaplan-Meier analysis. All untraced patients were excluded from analyses, while traced patients were assigned ones and zeros based on their disease-specific survival (DSS) by the end of each time period, respectively. Demographic frequency distributions did however include all patient cases. Chi-square tests were used to compare categorical variables. JMP Statistical Discovery 12.2 (SAS Institute, Cary, NC) was then utilized to calculate log-rank analysis and Kaplan-Meier curves for all resultant data. Significance levels were set to $\propto = 0.05$ for all tests.

3. Results

3.1. Patient and tumor characteristics

A total of 210 PedsSNM patients, 18 years old or younger, were identified from the SEER database (Table 1). The mean age at diagnosis was 10.7 years with a standard deviation of 5.64 years. By gender, 45.7% were male and 54.3% were female. By race, 72.6% were white, 21.2% were black, 5.3% were Asian/Pacific Islander, and 1.0% were American Indian/Alaskan Native. This distribution represents prevalence only.

By primary site, the nasal cavity was the most commonly involved subsite (37.1%), followed by the maxillary sinus (27.6%), and ethmoid sinus (17.1%). By histology, rhabdomyosarcoma was the most common type (50.5%), followed by olfactory neuroblastoma (17.6%), sarcoma not otherwise specified (NOS) (11.4%), and squamous cell carcinoma (2.9%). The remaining distribution of primary site and histologies is available in Table 2.

Anatomic site distribution varied significantly by histology (Table 3) ($p < 0.0001$). Most olfactory neuroblastomas were in the nasal cavity (73.0%). Sarcoma NOS was more commonly seen in the maxillary sinus (41.7%), and rhabdomyosarcomas were distributed almost evenly throughout the different sinonasal sites.

The most common histology varied by age ($p = 0.025$). In the 0–3 year age group, rhabdomyosarcoma (76.0%) was by far the most common histology. However, in the 12–15 year age group, olfactory neuroblastoma (40.9%) was almost as common as rhabdomyosarcoma (45.5%).

The distribution of tumor grade among cases demonstrated a propensity for grade IV disease (37.3%), followed by grade II (25.3%), grade III (22.7%), and grade I (14.7%) (Table 4).

Table 1
Demographics of pediatric sinonasal malignancies.

	N	%
Mean age of diagnosis (± SD)	10.7 ± 5.64	–
Total	210	100.0%
Age groups (years)		
0–3	35	16.7%
4–7	27	12.9%
8–11	36	17.1%
12–15	58	27.6%
16–18	54	25.7%
Gender		
Female	114	54.3%
Male	96	45.7%
Race		
White	151	72.6%
Black	44	21.2%
Asian or Pacific Islander	11	5.3%
American Indian/Alaska Native	2	1.0%
Unknown	2	–