International Journal of Pediatric Otorhinolaryngology 112 (2018) 109–112

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

A review of pediatric middle ear tumors and analysis of the demographics, management, and survival of pediatric rhabdomyosarcomas of the middle ear

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ARTICLE INFO

Keywords:
Pediatric middle ear tumors
Rhabdomyosarcoma
Treatment of pediatric middle ear rhabdomyosarcoma

ABSTRACT

Objective: To examine the types of pediatric middle ear tumors and review the demographics, management, and survival of pediatric patients with rhabdomyosarcoma (RMS) of the middle ear.
Methods: Pediatric patients in the Surveillance, Epidemiology, and End Results (SEER) database were included from 1973 to 2014 based on a diagnosis of middle ear tumors using the ICD O-3 code: C30.1: Middle ear primary site. Patients were included from ages 0–18 years.
Results: Forty pediatric middle ear tumor cases were identified. Twenty patients were female (50%). Twenty-seven (67.5%) cases were rhabdomyosarcomas (RMS). Pediatric RMS patients tended to be diagnosed in early childhood (mean age 5.30 years, standard deviation 2.9, range 1.00–13.00, 59.3% of patients were ages 5 or below). Most pediatric RMS patients received chemotherapy and radiation therapy as part of the treatment regimen (88.8%). Finally, the 5-year overall and disease-specific survival rates were 59% and 63% respectively.
Conclusions: Pediatric middle ear tumors are rare. Females and male pediatric patients are both at risk for middle ear tumors. RMS is the most common malignant middle ear tumor affecting pediatric patients. Despite the use of multimodality therapies, survival rates for pediatric patients with RMS of the middle ear are low. Physicians may consider including middle ear tumors on the differential diagnosis for pediatric patients with symptoms presenting similarly to non-resolving otitis media.

1. Introduction

Tumors of the middle ear are extremely rare [1,2]. They can be categorized into several histological types including rhabdomyosarcoma, Langerhans cell histiocytosis, adenocarcinoma, squamous cell carcinoma, carcinoid tumors, peripheral neuroectodermal tumors, and malignant lymphoma. Middle ear tumors may present initially as hearing loss or recurrent otitis media progressing to facial nerve palsy [2,3]. The non-specific nature of these symptoms result in many patients presenting with late stage cancer.

The most common histological type of malignant middle ear tumor is rhabdomyosarcoma (RMS), an aggressive and highly malignant soft tissue tumor originating from undifferentiated skeletal muscle. Often congenital in nature, RMS is predominately a childhood cancer with over 50% of cases identified in children younger than 10 years old [4]. While accounting for half of all pediatric soft tissue sarcomas, RMS is a very rare tumor overall with an estimated incidence of 4.3 cases per million in the United States [5]. These tumors often arise in the head and neck and can be divided into 3 subtypes: orbital, parameningeal (ear, mastoid, nasal cavity, nasal sinuses, infratemporal fossa, pterygopalatine fossa), and nonorbital nonparameningeal (all other head and neck sites) as well as 2 main histological subgroups: embryonal and alveolar. RMS in the parameningeal region, such as the middle ear, is associated with poor prognosis [6].

In 1972, the Intergroup Rhabdomyosarcoma Study Group (IRSG), now part of the Children's Oncology Group, was formed to identify prognostic factors, develop therapies and improve outcomes for RMS patients; however, their last publication regarding middle ear RMS was published in 2001. Since then, there have been no recent studies with an adequate sample size to provide an in depth examination of current demographics, treatment modalities, and survival for middle ear RMS and other tumors. This study aims to provide an up to date review on

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https://doi.org/10.1016/j.ijporl.2018.06.017
Received 9 January 2018; Received in revised form 9 May 2018; Accepted 8 June 2018
Available online 12 June 2018
0165-5876/

pediatric malignant middle ear tumors, particularly RMS, using patient population data extracted from the Surveillance, Epidemiology and End Results (SEER) registry.

2. Methods

Case-based data was obtained using the National Cancer Institute's SEER database. The SEER 18 Registry Research Data with Custom Treatment Data (cases from 1973 to 2014, released April 2017, based on the November 2016 submission) was utilized [7]. This study was exempt from review by the Office of Research Integrity of the Medical University of South Carolina and was not considered human subjects research by the Boston Medical Center Institutional Review Board. Cases were included based using the ICD O-3 code of C30.1: Middle ear primary site. Patients were included from ages 00–18 years based on the documented age at diagnosis.

All data analyses were performed with SPSS 24.0 (IBM Corporation, Armonk, NY), SigmaPlot 12.5 (Systat Software, San Jose, CA), and MedCalc software 16.8 (MedCalc Software bvba, Ostend, Belgium). All continuous variables were tested for normal distribution as determined by the Kolmogorov-Smirnov test. Categorical variables were summarized by frequency, percentage, and/or range. Continuous variables were summarized by median (interquartile range) or mean (standard deviation) where appropriate. 2-year and 5-year survival was calculated using Kaplan-Meier estimates of survival. A p value of < 0.05 was considered to indicate a statistically significant difference for all statistical tests.

3. Results

3.1. All middle ear tumors

Forty pediatric patients were diagnosed with a middle ear tumor based on the pre-determined search criteria. The mean age of the total cohort was 6.30 years (standard deviation 4.2, range 1.00–18.00) (Table 1). Twenty (50.0%) patients were female and 20 (50.0%) patients were male. Thirty-two (80.0%) patients were Caucasian, 5 (12.5%) were African American, and 3 (7.5%) were Asian/Pacific Islander. 67.5% of patients had a histological type of rhabdomyosarcoma, while Langerhans cell histiocytosis was found in 10.0% of patients.

Table 1
Patient demographics and oncologic characteristics of all middle ear tumors.

Characteristic	Total
Cases (%)	40 (100)
Mean Age (SD, Range)	6.30 (4.2, 1.00–18.00)
Sex No. (%)	
Female	20 (50.0)
Male	20 (50.0)
Race No. (%)	
Asian	3 (7.5)
Black	5 (12.5)
White	32 (80.0)
Histological Type No. (%)	
8140/3: Adenocarcinoma, NOS	1 (2.5)
8200/3: Adenoid cystic carcinoma	1 (2.5)
8240/3: Carcinoid tumor, NOS	1 (2.5)
8260/3: Papillary adenocarcinoma, NOS	3 (7.5)
8900/3: Rhabdomyosarcoma, NOS	2 (5.0)
8910/3: Embryonal rhabdomyosarcoma, NOS	24 (60.0)
8912/3: Spindle cell rhabdomyosarcoma	1 (2.5)
9364/3: Peripheral neuroectodermal tumor	2 (5.0)
9590/3: Malignant lymphoma, NOS	1 (2.5)
9751/3: Langerhans cell histiocytosis	3 (7.5)
9754/3: Langerhans cell histiocytosis, disseminated	1 (2.5)

Asian: Asian and Pacific Islanders, NOS: Not Otherwise Specified, SD: Standard Deviation.

Table 2
Patient demographics, oncologic characteristics, and treatment of middle ear rhabdomyosarcoma.

Characteristic	Total
Cases (%)	27 (100)
Mean Age (SD, Range)	5.30 (2.9, 1.00–13.00)
Sex No. (%)	
Female	15 (55.6)
Male	12 (44.4)
Race No. (%)	
Asian	2 (7.4)
Black	3 (11.1)
White	22 (81.5)
Histological Type No. (%)	
8900/3: Rhabdomyosarcoma, NOS	2 (7.4)
8910/3: Embryonal rhabdomyosarcoma, NOS	24 (88.9)
8912/3: Spindle cell rhabdomyosarcoma	1 (3.7)
Extent of Disease No. (%)	
Localized	3 (11.1)
Regional	10 (37.0)
Distant	5 (18.5)
Not Available	9 (33.3)
Surgery, Radiation, and/or Chemotherapy No. (%)	
None*¶	1 (3.7)
Radiation and Chemotherapy	8 (29.6)
Surgery, Radiation, and Chemotherapy	9 (33.3)
Radiation, Chemotherapy, and Unknown Surgery Status	5 (18.5)
Radioisotope Therapy and Chemotherapy	2 (7.4)
Chemotherapy Only*	2 (7.4)

Asian: Asian and Pacific Islanders, NOS: Not Otherwise Specified, SD: Standard Deviation, *"None/Unknown" radiation status; ¶ "None/Unknown" chemotherapy status.

3.2. Rhabdomyosarcoma of the middle ear

Twenty-seven pediatric patients were diagnosed with a middle ear rhabdomyosarcoma. All documented cases occurred from 1973 to 2013. The mean age of the total cohort was 5.30 years (standard deviation 2.9, range 1.00–13.00) (Table 2). Fifteen (55.6%) patients were female and 12 (44.4%) patients were male. Twenty-two (81.5%) patients were Caucasian, 3 (11.1%) were African American, and 2 (7.4%) were Asian/Pacific Islander. 88.9% of patients had a histological type of "8910/3: Embryonal rhabdomyosarcoma, NOS". Regarding extent of disease, 3 (11.1%) patients had localized disease, 10 (37.0%) had regional disease, and 5 (18.5%) had distant disease. Table 2 also describes the type of surgery, radiation, and chemotherapy regimens received by pediatric patients diagnosed with a middle ear rhabdomyosarcoma tumor. 1 (3.7%) patient did not receive any treatment (no surgery, chemotherapy, or radiation), 8 (29.6%) patients received both radiation and chemotherapy, and 9 (33.3%) patients underwent radiation, chemotherapy, and surgical management (Table 2).

3.3. Survival

Ten (37.0%) overall deaths were noted within this study with 9 (33.3%) being disease-specific. All 9 disease-specific deaths occurred within three years from the time of diagnosis. As shown in Table 3, the 2-year overall survival for the total cohort was 76%, and the 2-year disease-specific survival for the total cohort was 76% (all deaths within 2 years were disease-specific). The 5-year overall survival for the total cohort was 59%, and the 5-year disease-specific survival for the total cohort was 63%. Fig. 1 depicts the disease-specific survival of all pediatric patients diagnosed with a middle ear rhabdomyosarcoma in this study.

4. Discussion

Pediatric middle ear tumors continue to be rare within the United