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Pediatric malignant salivary gland tumors: 60 year follow up☆

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ABSTRACT

Objective: To evaluate the presentation, treatments and outcomes in pediatric patients with salivary gland malignancies.
Study design: Retrospective chart review (1950–2012), Prospective phone interview.
Methods: Patients ≤18 years old with a salivary gland malignancy treated at our institution were identified. Patients were also contacted by phone for a follow up survey.
Results: Fifty-six patients were identified. Tumor origin was 88% parotid (n = 49), 5% (n = 3) submandibular and 7% (n = 4) minor salivary glands. Time from onset of symptoms to diagnosis was over one year (mean = 14.4 years). Fifteen out of 52 patients with major gland malignancy had a locoregional recurrence and local recurrences were almost all after initial enucleation. Two of these patients died of disease (overall disease specific survival = 96%). Three out of 4 patients with minor gland malignancy had a local recurrence and two patients with high grade pathology developed metastases and died of their disease (overall survival = 50%). On long term follow up survey in 13 patients (25%), 100% reported normal facial movement and 54% described symptoms of Frey's syndrome, which is higher than other reported series in children. Recurrence was noted up to 45 years after initial treatment.
Conclusions: The majority of malignant pediatric salivary gland tumors are low grade and have excellent survival, especially if found at an early stage. Minor salivary gland malignancies, particularly high grade, have a worse prognosis. Long term mild Frey's syndrome can be expected in approximately half of patients. We advocate a need for long term follow up and increased awareness among providers to diagnose these patients earlier.

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1. Introduction

Salivary gland tumors are uncommon in children and adolescents and represent only 0.5% of pediatric malignancies [1]. In adults, approximately 15–25% of salivary gland tumors are malignant [2] compared to approximately 25–50% in the pediatric population [3–6]. As a whole, salivary gland malignancies are a heterogeneous group of cancers, with differing behaviors based on factors such as location, histologic type, grade and stage.

Due to the rarity of salivary gland malignancies in the pediatric population and lack of large single institution clinical studies, it is challenging to develop a consensus on treatment. The degree of surgery and the role of adjuvant treatment remain unclear. Optimizing a balance between good oncologic outcome and long term morbidity is paramount. Additionally, long term functional and cosmetic outcomes are somewhat unknown in this patient population as the majority of data in existence is via retrospective chart review which may not capture these complications.

The goal of this study is to examine a series of pediatric patients with salivary gland malignancies treated at a single tertiary care referral center and followed for up to 62 years to aid in answering the challenging question of treatment and long term functional outcomes for these children.

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2. Materials and methods

After institutional review board approval, a retrospective chart review was performed (1950–2012) and all patients less than or equal to 18 years of age with a histologically confirmed salivary gland malignancy evaluated or treated at the Mayo Clinic in Rochester, Minnesota were identified. Patients' medical records were reviewed for demographic data, presentation, diagnostic testing, management strategy and clinical outcomes. Tumors were staged based upon the 2008 AJCC TNM staging classification system. Follow up length was calculated from the date of surgery until the last known contact with the patient.

Time from initial surgery to recurrence at the primary site or neck was the outcome. Subjects were censored at time of last follow-up or death. Kaplan-Meier estimates of the survival function were obtained using available case analysis and risk factors were compared using the log-rank test. A Bonferroni correction was used for multiple testing of definitive surgery types.

Patients and or the parents of underage patients were contacted for long term follow up conducted via standardized phone interview conducted by trained personnel of the Mayo Clinic Survey Research Center. The enrolled subjects provided written and oral consent.

3. Results

3.1. Demographics

Fifty six patients age less than or equal to eighteen years were identified. Twenty-four were male and 32 were female. The patients ranged in age from 3 to 18 years old, with a mean of 14.1 years.

3.2. Clinical presentation

All but one patient presented with a salivary gland mass. The majority of patients (91%) had painless masses. No patients presented with facial nerve weakness. Mean time between onset of symptoms and diagnosis was 14.4 months.

4. Major gland

4.1. Tumor characteristics

Of the 56 cases, 49 involved the parotid gland and 3 involved the submandibular gland. Information on histology, grade and stage can be found in Table 1. All patients were clinically N0 with no evidence of distant metastases. Tumor grade was available for 35 patients. All intermediate or high grade lesions were classified as mucoepidermoid carcinoma with the exception of one high grade synovial cell sarcoma. Five patients had adverse pathologic features; 4 tumors with extracapsular spread and 1 with vascular invasion.

4.2. Treatment

A large proportion of patients (55%) underwent some degree of operative management at another institution. Approximately half (14 of 29 cases) of these cases underwent an incomplete procedure and after obtaining final pathologic diagnosis were transferred to our tertiary center for definitive surgical management. The majority of these patients had either an enucleation or superficial parotidectomy and then underwent total parotidectomy after evaluation at our institution. Of the patients that had completion surgery at our institution, residual tumor was found in about half of the surgical specimens (47%). Definitive treatment for primary parotid malignancies was as follows: 22% enucleation of tumor, 10% superficial parotidectomy, 49% total parotidectomy with facial nerve preservation, 16% total parotidectomy with at least partial facial nerve resection and primary chemoradiation in 2% (Table 1). Approximately 40% of parotid tumors underwent a neck dissection. The majority of neck dissections (65%) were limited to area II; 15% included areas II and III. No cervical lymph nodes were involved, but 11% of patients had positive intraparotid lymph nodes. All submandibular gland malignancies were treated with resection of the gland as well as dissection of nodal area IB. No surrounding Ib lymph nodes were positive. One patient with rhabdomyosarcoma underwent primary chemotherapy and radiation due to the large and infiltrative nature of the tumor.

Three patients, all with primary parotid malignancies, received adjuvant radiation after surgery. These were as follows: T3 mucoepidermoid carcinoma with invasion into the masseter muscle, T3 high grade mucoepidermoid carcinoma with positive intraparotid lymph nodes and a T3 adenoid cystic carcinoma. Two patients received chemotherapy and radiation: one with rhabdomyosarcoma and one with T4b mucoepidermoid carcinoma. The average radiation dosage delivered to these patients was 5600 Gy. One patient with lymphoma of the parotid gland received chemotherapy alone after surgery (Table 1).

Table 1
Parotid and submandibular gland tumor characteristics and treatment outcomes.

	n	%
Histology		
Mucoepidermoid carcinoma	27	52
Acinic cell carcinoma	16	31
Adenoid cystic carcinoma	3	6
Rhabdomyosarcoma	2	4
Adenocarcinoma	1	2
Lymphoma	1	2
Polymorphous hemangioendothelioma	1	2
Synovial cell sarcoma	1	2
Tumor grade		
Low	23	66
Intermediate	9	26
High	3	8
T stage		
T1	22	49
T2	13	29
T3	9	20
T4	1	2
Stage		
Stage I	21	48
Stage II	14	32
Stage III	8	18
Stage IV	1	2
Definitive treatment (parotid tumors)		
Enucleation	11	22
Superficial parotidectomy	5	10
Total parotidectomy	32	65
Primary chemoradiation	1	2
Adjuvant radiation	3	6
Adjuvant chemoradiation	2	4
Recurrence		
Local	14	27
Regional (neck)	2	4
Distant metastasis	2	4
Outcomes		
Alive NED	48	85
Dead of disease	4	7
Dead of other cause	4	7

4.3. Outcomes

Fourteen out of 52 patients had a local recurrence, 2 had a cervical recurrence, 2 developed distant metastases and 2 died of their disease. A description of the clinical course for patients with a local recurrence can be found in Appendix 1. Local recurrences

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