Journal of Cranio-Maxillo-Facial Surgery 45 (2017) 585–588

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Diagnostic and therapeutic modalities for 287 malignant and benign salivary tumors: A cohort study

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ARTICLE INFO

Article history:
Paper received 23 July 2016
Accepted 11 January 2017
Available online 25 January 2017

Keywords:
Salivary glands
Tumors
Benign
Malignant
Diagnosis
Etiology

ABSTRACT

Background: Salivary gland tumors (SGT's), 3–10% of head/neck tumors, exhibit a striking range of morphological diversity. This minimally symptomatic disease can be challenging to diagnose, and therapeutic policy is still controversial.
Methods: We compared benign and malignant cohorts according to diagnostic modality utilized and therapeutic modality administered over 20 years in a single medical center.
Results: Of 287 cases, 216 had benign tumors and 71 had malignant tumors. Treatment was surgery-based in 99% of cases, often accompanied by radiotherapy and/or chemotherapy. Rates of imaging and biopsy for diagnosis were significantly higher in malignant than benign tumors. Fine-needle aspiration (FNA) was used in 90.3% of benign tumors. Of 71 malignant tumors, 69 underwent surgery to fully remove the malignant tumor. Adjuvant therapy included 22 neck dissections (30%), 28 radiotherapy (39.4%), 12 chemotherapy (16.9%) and 10 combined radio-chemotherapy (14.1%). Partial parotidectomy, submandibular sialoadenectomy and local excision were used in 78.1%, 8.3% and 6.9% of benign cases. Total parotidectomy, sub-total maxillectomy and wide excision were used in 16.9%, 12.7% and 22.6% of malignant cases.
Discussion: Diagnostic and therapeutic modalities for treatment of salivary tumor at our hospital are presented and discussed with respect to others. A paradigm of therapy administered in our institute is presented.

1. Introduction

In 2005 the World Health Organization introduced a comprehensive classification of salivary gland tumors (Barnes et al., 2005), showing a striking range of morphological diversity among different tumor types and sometimes within an individual tumor mass. Salivary gland tumors (SGT's), most of which are benign, make up 3–10% of all head and neck tumors (Ellis and Auclair, 1995). Malignant SGT's demonstrate an unpredictable clinical course marked by frequent locoregional failure and distant metastasis, often occurring years after diagnosis (Bell et al., 2005).

Choice of therapeutic procedure for SGT's is based on clinical evaluation and diagnostic tests: ultrasonography (US), fine-needle aspiration cytology (FNA), endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), biopsy, CT and MRI. All available treatment algorithms emphasize the role of radical surgery in obtaining good outcome for malignant tumors (Bensadoun et al., 2005). For malignant disease, adjuvant post-operative radiotherapy (RT) is recommended in cases of advanced tumor stage, high-grade tumor, perineural or lymphovascular invasion, close or positive resection margins, extra-parotid extension or lymph node involvement (Thomson et al., 2016). RT is known to improve locoregional control after surgical resections; however, the absolute indications for postoperative radiotherapy in salivary cancer remain controversial due to side effects (Surakanti and Agulnik, 2008). Chemotherapy has become a major part of the definitive and postoperative treatment setting, though there is little evidence

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http://dx.doi.org/10.1016/j.jcms.2017.01.017
1010-5182/

that it can improve outcome in salivary cancer. Tanvetyanon et al. (2009) showed that use of chemo-radiation (CRT) is associated with significantly better local control with no difference in the overall survival compared to patients receiving radiotherapy alone (Tanvetyanon et al., 2009).

The purpose of this study was to analyze diagnostic and therapeutic modalities used in our medical center for the various tumor types and the different anatomical sites of occurrence.

2. Methods and materials

2.1. Study design and patients

Although this retrospective study relied solely upon data from patient files and there was no interaction between investigators and patients, approval was obtained from the Helsinki Committee for Ethics. During the 20-year period from 1996 to 2015 a total of 287 patients received definitive treatment for primary salivary gland tumors, 216 benign and 71 malignant, at Rambam Medical Center in Haifa, Israel. Treatment was based on surgery in 284/287 (99%) of cases, occasionally combined with radiotherapy, chemotherapy or both. Definitive diagnosis was based on pathological tissue analysis of harvested tumor tissue in these cases, and on fine needle aspiration in the remaining three patients, two with inoperable malignant tumors (treated with chemotherapy) and one with benign tumor who refused treatment.

Taking medical and demographic data from medical files, we grouped the patients in both the benign and malignant tumor groups according to tumor type. We then compared diagnostic modality utilized and therapeutic modality administered in these two cohorts of patients.

2.2. Statistical evaluation

For the categorical variables, numbers and percentages were calculated. The distributions for categorical variables between the two study groups were compared and analyzed by Chi square test (a parametric test) or Fisher–Irwin exact test (a non-parametric test for small numbers).

For continuous variables ranges, medians, means and standard deviations were calculated. Test for normality was done by Shapiro–Wilks. The results of continuous variables between the two study groups were compared and analyzed by 2 sample T-test for differences in means (a parametric test) or by Wilcoxon rank-sum test (a non-parametric test). All statistical tests were analyzed to a significance level of 0.05.

3. Results

3.1. Types of salivary gland tumors

Of 216 benign tumors, 138 (64%) were pleomorphic adenomas (PA), and other benign tumor prevalence rates were: Whartin's tumor (23%), recurrent PA (5.1%), oncocytoma (2.8%), myoepithelioma (1.9%), cystadenoma (1.4%) and basal cell adenoma (0.9%). There were 12 different types of malignant tumors: mucoepidermoid carcinoma was most prevalent (22/71, 31%) followed by adenoidcystic carcinoma (16.9%), squamous cell carcinoma (SCC) (11.3%), polymorphous adenocarcinoma (9.9%) and acinic cell carcinoma (9.9%), pleomorphic adenoma with squamous metaplasia (5.6%), adenocarcinoma (4.2%), carcinoma ex pleomorphic carcinoma (4.2%), myoepithelial carcinoma (2.8%), low-grade cyst adenocarcinoma (1.4%), epithelial-myoepithelial carcinoma (1.4%) and basal cell adenocarcinoma (1.4%).

3.2. Diagnostic modalities

Four diagnostic modalities – CT, PET-CT, MRI and biopsy – were utilized at a significantly higher rate in malignant tumor patients than in benign tumor patients (Table 1). These modalities were used in 78.1 %, 39.4%, 42.3% and 43.7% of malignant tumor patients, respectively, higher by 1.4, 20.7, 3.8, and 9.1 than in benign tumors ($P < 0.0001$). In contrast, FNA was used in 90.3% of benign tumor patients, 1.52 times more often than in the malignant tumor group (59.2% of cases) ($P < 0.0001$). Two diagnostic modalities – EUA-FNA and US, were used at a similar rate in both the benign and malignant tumor groups (Table 1).

3.3. Therapeutic modalities

3.3.1. Salivary gland surgery

Nine different surgical procedures were performed in 278 patients according to the salivary gland and specific subcompartment involved, and size and type of tumor. While local excision included only limited volume of surrounding healthy tissue around the tumor mass, wide excision included much wider margins (of up to 1 cm). For example, in the case of parotid gland, excision included the mass and an accessory lobe of the parotid gland. However, local excision included extracapsular excision as indicated.

Each of the following six procedures were performed in at least 10 patients: partial parotidectomy, total parotidectomy, submandibular sialoadenectomy, wide excision, local excision and subtotal maxillectomy (for minor malignant SGTs). Subtotal maxillectomies were performed in three cases, two malignant and one benign (a relatively large >2 cm in size myoepithelioma on minor salivary gland in the hard palate), sublingual sialoadenectomy in two malignancies and partial glossectomy in one. Three surgical procedures were the “therapy of choice” for benign tumors: partial parotidectomy (including partial superficial parotidectomy), submandibular sialoadenectomy and local excision, used in 78.1%, 8.3% and 6.9% of cases, respectively, at significantly higher rates by 2.5 ($P < 0.0001$), 1.9 ($P < 0.0001$) and 2.4 (NS), respectively, than in malignant tumors. In contrast, three surgical procedures were the “therapy of choice” for malignant tumors: total parotidectomy, subtotal maxillectomy and wide excision, used in 16.9%, 12.7% and 22.6% of malignant tumors, respectively, significantly higher by 3.6 ($P < 0.0001$), 25.4 ($P < 0.0001$) and 45.2 (NS) respectively, than in benign tumor patients (Table 2). Occasionally and whenever possible the facial nerve was spared if it was not involved within the malignant tumor.

3.3.2. Adjuvant therapy

Almost all malignant tumor patients, 69/71, underwent definitive salivary gland surgery. Neck dissections were performed in 22 cases (30%), modified (i.e. modified radical) in 16 and radical in 6 (Table 3). Of the 69 operated patients, 28 had radiotherapy (39.4%), 12 chemotherapy (16.9%) and 10 had combined radiochemotherapy (14.1%). Two benign tumor patients who suffered from recurrent pleomorphic adenomas received radiotherapy as well. Apart from these, no other benign tumor patient received adjuvant therapy (Table 3).

4. Discussion

4.1. Comparisons with other studies

The distribution of benign and malignant tumors in the current study is quite similar to previous reports, and therefore we consider our study group to be adequate and representative (de Oliveira