Publication Types: Research

Minor salivary gland tumors: A clinicopathological study of 18 cases

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Received: 13/09/2007
Accepted: 16/07/2008

Indexed in:
-Index Medicus / MEDLINE / PubMed
-EMBASE, Excerpta Medica
-SCOPUS
-Indice Médico Español
-IBECS

Pons-Vicente O, Almendros-Marqués N, Berini-Aytés L, Gay-Escoda C. Minor salivary gland tumors: A clinicopathological study of 18 cases. Med Oral Patol Oral Cir Bucal. 2008 Sep1;13(9):E582-8.

http://www.medicinaoral.com/medoralfree01/v13i9/medoralv13i9p582.pdf

Abstract

Introduction: Minor salivary gland tumors (MSGTs) are infrequent, representing 10-15% of all salivary neoplasms. Despite this low frequency, MSGTs conform a heterogeneous group of neoplasms characterized by a broad range of histological types.

Patients and method: We identified cases of MSGT in a retrospective study of the biopsies made in the period 1997-2007 in the Service of Oral Surgery (Dental Clinic of the University of Barcelona, Spain). The data collected comprised patient age and sex, the clinical characteristics and location of the tumor, the duration of the lesion, its size, the treatment provided, and the histopathological findings.

Results: Of the 18 cases of MSGT studied, 12 corresponded to women (66.7%) and 6 to men (33.3%). The great majority (94.4%) were benign tumors. The preferential location was the posterior third of the hard palate (33.2%), followed by the soft palate (16.7%) and the mucosa of the upper lip (16.7%). The histopathological diagnoses of our MSGTs comprised 10 pleomorphic adenomas (55.3%), 2 cystadenomas (11.1%), 1 myoepithelioma (5.6%), 1 sialadenoma papilliferum (5.6%), 1 basal cell adenoma (5.6%), 1 Warthin's tumor (5.6%), 1 canalicular adenoma (5.6%), and 1 low-grade polymorphic adenocarcinoma (5.6%).

Discussion and conclusions: Coinciding with our own results, the literature describes a high recurrence rate for MSGTs (5-30%) when surgical removal is incomplete. Six percent of all benign minor salivary gland tumors are considered to relapse, versus 65% of all malignant lesions. Periodic clinical controls are required, since the possibility of malignant transformation must be taken into account.

Key words: *Oral tumors, minor salivary glands, histopathological diagnosis, local recurrence.*

Introduction

Salivary gland neoplasms represent less than 1% of all tumors, and 3-5% of all head and neck neoplasms. Minor salivary gland tumors (MSGTs) are infrequent, accounting for 10-15% of all salivary neoplasms, and are fundamentally located in the palate (50%), lips (15%), cheek mucosa (12%), tongue (5%) and floor of the mouth (5%), among other regions. Despite their relatively low frequency, MSGTs represent a heterogeneous group of neoplasms, with a broad range of histological types and growth patterns. Because of this great diversity and the lack of uniform criteria, many classifications have been developed, and the establishment of an adequate clinical-histological correlation proves difficult (1,2).

The first classification of salivary glands tumors, developed by the World Health Organization (WHO) in 1972, was posteriorly revised under the supervision of Prof. Seifert in 1991. The second edition of the histological classification of salivary gland tumors included new entities and suppressed the concept of "monomorphic adenoma", in view of the diversity of the tumors that were grouped under this designation - giving rise to 11 independent histopathological entities (3). Due to the great morphological diversity of these tumors and the need to establish a precise diagnosis, a consensus meeting was held in Lyon (France), giving rise to a new classification of salivary gland tumors, published in the year 2005 (4).

The proportion of malignant tumors of the minor salivary glands is very high (50%) – the preferential locations being the floor of the mouth (90%), the retromolar trigone (90%), the tongue (85%) and the lower lip (60%). In contrast, neoplasms of the upper lip are usually benign tumors (75%).

While tumors of the salivary glands can appear at any age, the maximum incidence is in the fourth decade of life for benign lesions and in the fifth decade for malignant tumors though different authors consider the peak incidence to correspond to the period between the fifth and seventh decades of life. Classically, these lesions have been reported to be more frequent in women, though the proportion varies according to the histological type of tumor.

The etiopathogenesis of MSGTs remains unclear (1). In this context, it has not been possible to correlate smoking to salivary gland cancer, and exposure to ionizing radiation to date has been the only confirmed risk factor for tumors of the salivary glands (5,6).

The most frequent clinical presentation of benign MSGTs is in the form of a well delimited, smooth and uniform nodular tumor with a normal overlying surface color. The lesion is typically asymptomatic and displaceable, usually single, and without adherence to either superficial or deep layers.

One of the clinical features that allow differentiation between benign and malignant MSGTs is the evolutive course, since the former tend to be insidious and slow-growing, with an average course of 3-6 years, while malignant lesions are fast-growing (typically under one year) and can ulcerate, become overinfected, and cause external or interstitial bleeding giving rise to superficial telangiectasias. The clinical data most suggestive of malignancy are pain, adherence to deep or superficial layers, epidermal involvement and/or ulceration, and the presence of neck adenopathies.

MSGTs have a high recurrence rate (5-30%) when surgical removal is incomplete, and the possibility of malignant transformation must be taken into consideration. Six percent of all benign minor salivary gland tumors are considered to relapse, versus 65% of all malignant lesions. This capacity to relapse is related to the histopathological characteristics of the tumor, and particularly to the initial treatment provided.

The diagnosis of MSGTs is based on the clinical history and physical exploration, supported by complementary techniques such as magnetic resonance imaging (MRI), computed tomography (CT) alone or combined with sialography and fine needle aspiration biopsy (FNAB). The combination of some of these techniques is able to offer a tentative diagnosis that posteriorly must be confirmed by the corresponding intraoperative histopathological study.

The present study describes MSGTs according to patient age and sex, tumor location, clinical and histopathological characteristics, and treatment, based on a series of 18 cases. A review of the literature is also made, and emphasis is placed on the need for periodic controls, due to the important relapse potential and aggressivity of these lesions.

Patients and Method

A retrospective study was made of all the biopsies obtained between January 1997 and May 2007, in the Service of Oral Surgery (Dental Clinic of the University of Barcelona, Spain). During this period of time a total of 1972 biopsies were made, of which 18 corresponded to MSGTs (12 women and 6 men). The diagnosis of MSGT was based on clinical and histopathological criteria, and all the pathology reports were reviewed by the Department of Pathology (Bellvitge University Hospital, Barcelona, Spain) based on the most recent histological classification of salivary gland tumors, published by the WHO in 2005.

All cases identified as MSGTs were treated by residents of the Master of Oral Surgery and Implantology (University of Barcelona Dental School, Spain), with the exception of a single case that was directly referred to Bellvitge University Hospital as a result of histological confirmation of malignancy. This was the only case in our series operated upon by maxillofacial surgeons – treatment consisting of a partial maxillectomy with postoperative radiotherapy, followed by second step reconstruction of the upper maxillary defect using a temporal muscle flap.

From each clinical history we recorded the age and sex of the patient, the clinical characteristics and location of the tumor, the time elapsed to histopathological diagnosis, the size of the tumor, and the definitive histopathological diagnosis. We also evaluated the results of the complementary diagnostic tests, and the possible appearance of local relapses over a mean follow-up period of 1.8 years. The treatment provided in each case, the biopsy technique used, and the definitive histopathological result were documented. In addition, the incidence of MSGTs in our Service of Oral Surgery was determined.

Based on these data, a descriptive statistical analysis was made using the Statistical Package for the Social Sciences, version 12.0 (SPSS v.12.0; SPSS, Chicago, IL, USA).

Results

The proportion of MSGTs in our Service of Oral Surgery in relation to the 1972 biopsies performed in the period between January 1997 and May 2007 was 0.9%. Eighteen MSGTs were identified - pleomorphic adenoma (PA) being the most frequent histological type (10 cases; 55.3%) followed by cystadenoma (2 cases; 11.1%). Other histopathological presentations in our series of MSGTs were myoepithelioma (1 case; 5.6%), sialadenoma papilliferum (1 case; 5.6%), basal cell adenoma (1 case; 5.6%), Warthin's tumor (1 case; 5.6%), canalicular adenoma (1 case; 5.6%) and low-grade polymorphic adenocarcinoma (LGPA)(1 case; 5.6%). The histopathological diagnoses established in our series are reported in Table 1.

The percentage of benign tumors was 94.4% (17 cases), and the only malignancy corresponded to LGPA. The benign tumors showed a marked female predilection (58.8%). Of the 18 cases of MSGT studied, 12 were recorded in women (66.7%) and 6 in men (33.3%), yielding a male/female proportion of 1:2 (Table 1). The mean patient age was 51.8 years (range 22-86 years; standard deviation (SD) 18.9).

The preferential location of MSGTs was the posterior

Table 1. Distribution of minor salivary gland tumors according to patient age and sex, histological diagnosis, frequency, location, and duration of the lesions.

Case	Age (years)	Sex	Histological diagnosis	Frequency	Location	Course (months)
1	38	F	Pleomorphic adenoma	55.3 %	Cheek mucosa	12
2	37	M			Hard palate	60
3	82	M			Hard palate	24
4	36	M			Soft palate	72
5	45	F			Soft palate	6
6	50	F			Retrotuberosity zone	4
7	28	F			Hard palate	1
8	51	F			Upper lip mucosa	120
9	38	F			Cheek mucosa	132
10	54	F			Soft palate	240
11	22	F	Basal cell adenoma	5.6 %	Retromolar trigone	2
12	46	F	Sialadenoma papilliferum	5.6 %	Hard palate	156
13	50	F	Low-grade polymorphic adenocarcinoma	5.6 %	Hard palate	8
14	61	F	Myoepithelioma	5.6 %	Upper lip mucosa	24
15	78	M	Cystadenoma	11.1 %	Lower lip mucosa - cheek mucosa	3
16	86	M			Retromolar trigone	18
17	73	F	Warthin's tumor	5.6 %	Hard palate	96
18	57	M	Canalicular adenoma	5.6 %	Upper lip mucosa	4
	Mean 51.8	F/M 2/1			Hard palate: 33.2% Lower lip mucosa: 5.6% Soft palate: 16.7% Cheek mucosa: 11.1% Upper lip mucosa: 16.7% Tuberosity: 5.6% Retromolar trigone: 11.1%	Mean 55

F: female, M: male

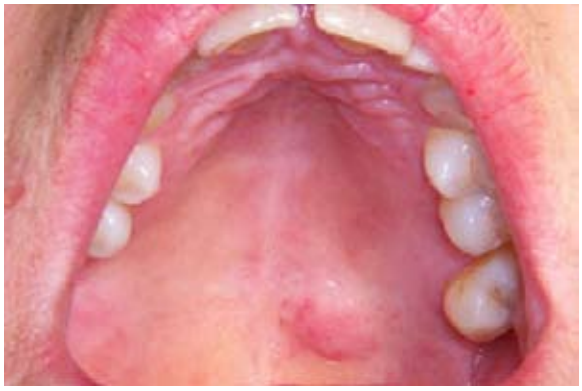

Fig. 1. Clinical view of a pleomorphic adenoma located in the posterior third of the hard palate (case 10).

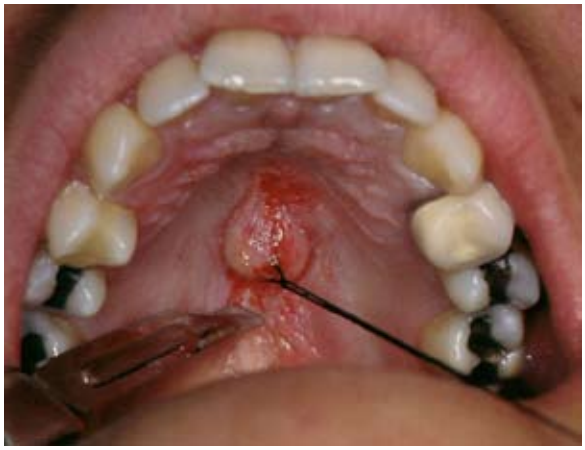

Fig. 2. Clinical view of surgical resection – biopsy of a palatal tumor using the cold scalpel (case 7).

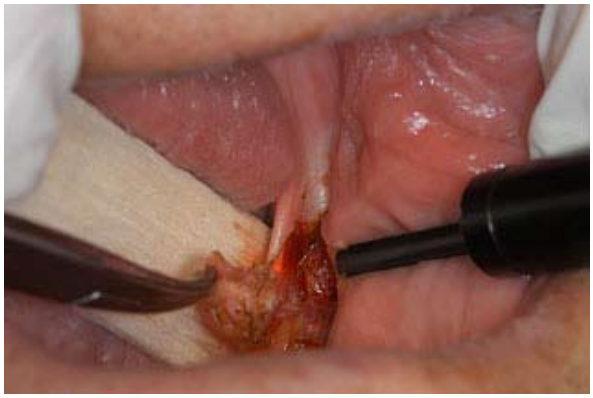

Fig. 3. Clinical view of surgical resection – biopsy of a tumor in the retromolar trigone using the CO2 laser (case 16).

third of the hard palate (33.2%)(Figure 1), followed by the soft palate (16.7%) and the upper lip mucosa (16.7%). Other locations were the cheek mucosa and the region of the retromolar trigone, with a frequency of 11.1% in both cases. Lastly, one case was documented in the lower lip mucosa (5.6%), and another in the tuberosity of the upper maxilla (5.6%). Of note are the facts that 49.9% of the MSGTs in our series were located in the palate, and that 94.1% of the palatal MSGTs were benign. The distribution of the 18 MSGTs by patient age and sex, histological diagnosis, location and duration of the lesion is shown in Table 1.

The most frequent clinical presentation of MSGT of our sample was in the form of a soft (9 cases) or slightly indurated lesion (9 cases) located in the hard or soft palate (49.9% of the total). Most of the tumors (72.2%) were asymptomatic, while 16.7% generated pain in response to palpation. Among the patients with symptoms (27.8%), swallowing discomfort was particularly common (80%).

In our review, only one MSGT presented perineural invasion, without evidence of bone or vascular infiltration. At the time of clinical diagnosis, three cases presented superficial ulceration (16.7%), while one showed telangiectasias of the adjacent oral mucosa (5.6%).

The mean tumor size was 1.0 x 1.3 cm, with two lesions reaching 2 cm in size. The mean time elapsed to the diagnosis of benign MSGT was 55 months. The single malignant lesion developed rapidly in 8 months before the histopathological diagnosis was established. The follow-up period ranged from 2-48 months (Table 2).

Complementary diagnostic tests were made in 44.6% of the cases, fundamentally in the form of CT (3 cases), followed by CT associated to preoperative biopsy (3 cases). In one case (12.5%) CT was requested and FNAB was performed, while in another case an MRI scan was requested (Table 2).

Surgical removal of the tumor with safety margins and posterior histopathological study was the treatment of first choice in 16 cases (88.9%). Two cases (11.1%) were subjected to an incisional biopsy, and in one them the histological study confirmed the presence of malignancy.

As to the surgical techniques used for the treatment of MSGTs, 77.8% of the tumors in our sample were resected using the cold scalpel, while in the remaining four cases (22.2%) the CO2 laser was used at a power setting of 6W. Figures 2 and 3 show the different techniques used for resection-biopsy of the MSGTs in our series.

The postoperative controls revealed on case of local recurrence (5.8%) among the overall benign lesions. The rest of MSGTs showed no evidence of recurrence over a mean follow-up period of 22 months (Table 2).

Discussion

Tumors originating in the minor salivary glands are infrequent, and represent less than 20% of all salivary

Table 2. Distribution of minor salivary gland tumors according to clinical symptoms, the need for complementary tests, treatment and technique, follow-up and relapse.

Case	Symptoms	Complementary tests	Treatment	Technique	Follow-up (months)	Relapse
1	No	No	RSM	CO_2 laser	18	No
2	No	CT	RSM	Cold scalpel	48	No
3	No	CT and preoperative biopsy	RSM	Cold scalpel	36	No
4	Swallowing discomfort	CT and FNAB	RSM	Cold scalpel	24	No
5	No	No	RSM	Cold scalpel	18	No
6	Swallowing discomfort, pain on palpation	No	RSM	Cold scalpel	24	No
7	No	No	RSM	Cold scalpel	15	No
8	No	No	RSM	Cold scalpel	48	No
9	No	No	RSM	CO_2 laser	36	No
10	No	No	RSM	Cold scalpel	12	No
11	No	CT	RSM	Cold scalpel	24	No
12	Swallowing discomfort	No	RSM	Cold scalpel	36	No
13	Swallowing discomfort, pain on palpation	CT and preoperative biopsy	Incisional biopsy. Partial maxillectomy and RT	Cold scalpel	24	No
14	No	CT and preoperative biopsy	RSM	Cold scalpel	10	No
15	Pain on palpation	No	Incisional biopsy. RSM	Cold scalpel	12	No
16	No	MRI	RSM	CO_2 laser	8	No
17	No	CT	RSM	Cold scalpel and CO_2 laser	3	1 month
18	No	No	RSM	Cold scalpel	2	No
					Mean 22	

CT: computed tomography; RSM: surgical resection with safety margins; MRI: magnetic resonance imaging; RT: radiotherapy; FNAB: fine needle aspiration biopsy.

neoplasms. Racial and geographic variations in their frequency and distribution have been reported (7-9). Most studies of salivary neoplasms include both the major and the minor salivary glands, and few articles focus only on MSGTs. In addition, there is great variability regarding the different diagnostic criteria applied to salivary glands tumors in the different classifications of the WHO (3). In our study, all cases were histologically re-evaluated based on the more recent salivary gland tumor classification of 2005. However, most of the studies reviewed in the literature are based on earlier classifications; as a result, comparisons must be established with caution (4).

In our series the incidence of MSGTs was very low (0.9%) in relation to the total biopsies performed during the study period (1997-2007). This is explained by the fact that the patients were received in our Service of Oral Surgery from the primary care setting, which usually refers tumor patients to hospital centers.

MSGTs can be located anywhere in the upper aerodigestive tract, though the most frequently affected location

is the oral cavity, and particularly the palate – where the concentration of minor salivary glands is greater. Such lesions also can be found in the cheek mucosa, in the region of the retromolar trigone, the lips, the oropharynx, or in the nasal cavities and paranasal sinuses (5,8,10). In the series published by Waldron et al. (11), the palate was the most commonly affected location (42.5%), followed by the upper lip (18.5%), oral mucosa (15%), retromolar trigone (5.4%), floor of the mouth (4.9%) and lower lip (3.3%), among other zones. In contrast, other authors report a higher presence of MSGTs in the palatal region, representing 65-80% of the total (1-3,5,7). In our review, the preferential location of MSGTs was the posterior third of the hard palate (33.2%), followed by the soft palate (16.7%), the upper lip mucosa (16.7%), cheek mucosa (11.1%), and retromolar trigone (11.1%). A single case was located in the lower lip mucosa (5.6%), with another case in the tuberosity of the upper maxilla (5.6%). Thus, 49.9% of the MSGTs were located in the palate, and 94.1% of the total palatal MSGTs were benign.

The proportion of malignant minor salivary gland tumors is close to 50%, though agreement is lacking as regards the incidence of malignancy in the different studies published in the literature to date (1,2,4,7-10,12-14). In contraposition to the most important MSGT series found in the literature, we recorded only one case of malignancy (5.6%). This again may be due to the fact that the patients were referred to our Service from the primary care setting, not from specific institutions such as cancer reference centers – where the incidence of salivary neoplasms is biased in favor of malignant lesions. Consequently, our findings are in line with those of earlier publications (2,7,11,12,14-17) showing a predominance of benign tumors versus malignant lesions, with a percentage incidence of 51.3-72.1%. In contrast, other studies have reported a variable proportion of malignancy of between 62.8-88.2% (9,18-20).

According to different authors, MSGTs can appear at any age, though most such lesions appear between the fifth and seventh decades of life (49.8% of our sample), and mainly affect women (7). Of our 18 MSGTs, 12 corresponded to women (66.7%) and 6 to men (33.3%) – in coincidence with other publications (7,8,11).

The most common benign histological type was pleomorphic adenoma (PA)(55.3%), in coincidence with different studies (1,2,5,7-11,13,15,21) that report a variable incidence of between 40-72% of all salivary gland tumors. The exception is the low incidence (19%) of PA lesions reported by Spiro (21). Likewise, PA has been reported to present a predilection for the hard palate and the posterior third of the soft palate, followed by the cheek and lip mucosas – in coincidence with our own results. Some authors consider pleomorphic adenomas to correspond to low-grade malignancies, based on the following characteristics: poorly defined limits, multifocal presentation, aggressivity, the capacity to relapse, and potential malignization over the long term (11). Pleomorphic adenoma relapse, which is almost always due to incomplete surgical resection of the lesion, manifests especially in the form of multiple foci, and is estimated to occur in 5-30% of cases.

Cystadenoma was the second most frequent benign tumor in our series (11.1%), though the incidence reported in the literature is lower (between 2-4.7% of all salivary neoplasms)(11,22). In the most important series, 65% of all cystadenomas are located in the major salivary glands, while 35% are found in the minor salivary glands (22-25).

Warthin's tumor is the second most common benign salivary gland tumor after PA, representing 10-15% of all salivary gland tumors. Although it may be regarded as exclusively a parotid gland tumor, some cases have been reported in the submaxillary gland, and even in the minor salivary glands at lip and palatal level. This coincides with our only such documented lesion (5.6%), located in the posterior third of the hard palate.

Regarding malignant tumors of the minor salivary glands, only one such lesion was found in our study (5.6%), corresponding to low-grade polymorphic adenocarcinoma (LGPA). This tumor is characterized by its cytological uniformity, morphological diversity and low metastasizing potential (1,2,11). In concordance with the case in our series, Kovalic et al. (26) advocate combined therapy in the form of surgical removal with safety margins, associated to radiotherapy (RT), for carcinomas of the palatal minor salivary glands. However, some authors consider that RT may induce malignization of possible remnant tumor cells (27).

Salivary gland tumor growth is usually slow, with an estimated evolutive course of between 3-6 years. This agrees with our own observed average of 4.6 years.

As regards the use of complementary studies, computed tomography (CT) was the most widely requested technique (38,9%), either alone or in combination with other diagnostic procedures such as preoperative biopsies or fine needle aspiration biopsy (FNAB). A cytological study based on FNAB of salivary gland lesions reported histopathological correlation in 40% of the benign neoplasms and in 80% of the malignant lesions (28), while Chan et al. (29) reported a diagnostic accuracy of 77%. In one case of our series, FNAB reported the presence of PA, which was posteriorly confirmed by histopathological study of the tumor (Table 2). Cerulli et al. (30), on comparing the diagnostic precision of FNAB cytology and preoperative biopsy with the histopathological study of the resection piece, found FNAB to offer an accuracy of 91.6%, while correlation of the preoperative biopsy to the final histopathological report was 100%.

The treatment of choice for benign MSGTs is surgical removal with safety margins, followed by histopathological study to establish the final diagnosis. In our series, postoperative follow-up identified one case of local relapse

one month after surgical resection. This case corresponded to Warthin's tumor (5.8% of the total benign MSGTs), in coincidence with earlier publications describing a variable recurrence rate of 5-30%. Periodic controls are therefore advised in patients with MSGTs, due to the important relapse potential and aggressivity of these lesions.

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