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Original Research

Intra-oral minor salivary gland tumors: A pathological study of 131 cases in the Japanese population

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ABSTRACT

Objective: Intra-oral minor salivary gland tumors are relatively rare. This study aimed to clarify the frequency and distribution of intra-oral minor salivary gland tumors in Japanese patients.

Methods: We retrospectively analyzed the histopathological records of 131 patients with minor salivary gland tumors that were surgically treated between 1967 and 2017 at a single institution.

Results: Of the 131 minor salivary gland tumors, 61 (47%) were benign and 70 (53%) were malignant. The male:female ratio was 1:1.8 for benign cases and 1:1 for malignant cases. Most of the tumors occurred in the palate, followed by the floor of the mouth. The most frequent minor salivary gland tumor was pleomorphic adenoma among benign tumors and adenoid cystic carcinoma among malignant tumors. The rarest minor salivary gland tumors were Warthin tumors and basal cell adenocarcinoma, accounting for only 0.8% of all cases.

Conclusions: The present study determined the incidence rates of these rare tumors.

1. Introduction

Intra-oral minor salivary gland tumors (IMSGTs) are rare tumors comprising approximately < 1% of all head and neck tumors and < 25% of all salivary gland tumors (SGTs) [1,2]. Despite the low incidence, IMSGTs represent a heterogeneous group of tumors with differences in clinical and histopathological appearances. The incidence of IMSGTs is lower than that of major SGTs; however, IMSGTs are more commonly malignant compared to major SGTs [3].

The frequencies and distribution of major SGTs and IMSGTs have not been clearly determined in previous studies because many studies included both major SGTs and IMSGTs. Therefore, studies focusing on IMSGTs only are limited. Moreover, previous studies in Japan have not documented the frequency and distribution pattern of IMSGTs well. In particular, the frequencies of rare IMSGTs such as basal cell adenocarcinoma (BCAC) and Warthin tumor (WT) are not clear [1,2].

Therefore, this study aimed to evaluate the frequency and distribution pattern of IMSGTs in our institution and to compare the data with other studies from different geographic locations and racial populations.

2. Methods

This retrospective observational study was performed using the data from the histopathological reporting registry and archived samples at the Department of Oral and Maxillofacial Surgery, Yokohama City University Graduate School of Medicine. The data were systematically searched for all cases of IMSGTs during a 50-year period (1967–2017).

IMSGTs were classified according to the criteria of the World Health Organization (WHO) working group on the histological classification of salivary gland tumors published in 2005. All cases were reassessed histologically according to the WHO 2005 classification. Clinical information regarding patient age, sex, and tumor location was also obtained from biopsy submission forms.

The categorical data (the age of patients and sex distribution considering both benign and malignant tumors) were statistically analyzed using the t-test. A p-value of < 0.05 was considered statistically significant.

3. Results

During the 50-year period, a total of 131 cases of IMSGTs were

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Table 1
Patient's characteristics.

Characteristics	Values	P value
No. of patients	131	
Types of tumor		
Benign	61	NS
Malignant	70	
Median age (years) (range)		
Benign	46.7 (8-74)	NS
Malignant	57.5 (20-89)	
Sex		
Benign (M: F)	22: 39	NS
Malignant (M: F)	34: 36	

M, male; F, female.

Note: Values represent number of patients, except as otherwise stated.

observed. A total of 61 (47%) patients had benign tumors and 70 patients (53%) had malignant tumors. The median age of patients with benign tumors and malignant tumors was 46.7 years (range, 8–74 years) and 57.5 years (range, 20–89 years), respectively. There was no significant difference in the age of patients with benign and malignant tumors ($p = NS$, respectively). Among patients with benign and malignant tumors, the male:female ratio was 1:1.8 and 1:1, respectively (Table 1) ($P = NS$).

Data on anatomical distribution, histopathological types, and localization of IMSGTs are shown in Table 2. Most of the tumors occurred in the palate (53.4%) followed by the floor of the mouth (13.7%), buccal mucosa (12.2%), tongue (7.6%), alveolar mucosa (6.9%) and lip mucosa (6.1%). Pleomorphic adenoma (PA) was the most frequent benign tumor, accounting for 41.2% of all tumors (54 of 131) followed by basal cell adenoma (BCA), warthin tumor (WT) and myoepithelioma (MEO). As regards to malignant tumor, adenoid cystic carcinoma (ACC) was the most frequent tumor accounting for 25.2% of all tumors (33 of 131) followed by mucoepidermoid carcinoma (MC), adenocarcinoma not otherwise specified (ACNOS), acinic cell carcinoma (AC), clear cell carcinoma, not otherwise specified (CCNOS), carcinoma ex pleomorphic adenoma (CEPA) and basal cell adenocarcinoma (BCAC).

4. Discussion

We compared our data with other studies from different geographic locations and racial populations based on WHO 2005 classification. The results of the present study were similar to those of previous studies performed in Asian, African, and European countries in that the ratio of malignant tumors among IMSGTs is high [4–8]. In contrast, studies

performed in American countries reported a predominance of benign tumors [9]. The data in studies from the same geographic locations and racial population often vary even though the studies were performed in the same countries. For example, Kusama et al. [1] and Toida et al. [2] reported that benign tumors were more prevalent in Japan; both these studies were performed at a dental school or a general hospital [1,2]. In contrast, the present study was performed in a university hospital. Various patients including cancer patients are referred to our hospital from nearby hospitals. Hence, it can be presumed that the relative incidence of benign versus malignant IMSGTs is based on the characteristics of each institution, and geographic variations seem to exist [6]. It was supposed that further accumulation of cases was needed to discuss the racial and regional characteristics in Japanese population.

Although there was no statistical significance, it has been said IMSGTs are more common in women than in men; similarly, malignant tumors also have the same tendency for female predominance [5,6,10–12]. Moreover, malignant tumors tend to occur in older individuals compared to benign tumors [3–11]. Studies from Japan, including the present study, have shown similar results [1,2].

The palate (both the hard and soft palates) is the most common site for IMSGTs, of which 40–57% of cases are observed in the palatal mucosa. Other anatomic sites of involvement include the lips, buccal mucosa, tongue, floor of the mouth, and retromolar area [1–7,13–22]. In the present study, the hard palate was the most common site for IMSGTs, and the incidence rate was similar to that observed in previous studies.

As observed in our study, PA has also been reported to be the most common histopathological type of IMSGTs, representing 33.2–58.0% of all benign and malignant tumors. Isacsonet et al. [23] reported that PA accounted for 70.0% of all tumors. Schulenburg [24] showed that intraoral PA was 3–4 times more prevalent in black patients than in white patients. The second most common benign IMSGT type in the present study was basal cell adenoma, similar to that observed in previous studies [25,26].

The histopathological type of malignant IMSGTs is an important prognostic factor. We reviewed previous studies on the incidence of IMSGTs based on WHO 2005 classification. In the present available four databases, namely PubMed, Embase, Scopus, and the Cochrane library, were searched for articles on IMSGTs until 31 December 2015. Previous studies from the USA, Brazil, Venezuela, Australia, and China revealed that mucoepidermoid carcinoma was the most common malignant IMSGTs [3,5,27–30]. However, studies from the UK, the Netherlands, Japan, China, and South Africa revealed that adenoid cystic carcinoma was the most common malignant IMSGTs [2,12,23,31,32]. The results of our study and previous studies showed that adenoid cystic carcinoma

Table 2
Histopathological types and localizations of intraoral minor salivary gland tumors.

Histopathological types	Hard palate	Soft palate	Floor of the mouth	Buccal mucosa	Tongue	Alveolar mucosa	Lip mucosa	Total (%)
Benign								
PA	29	11	2	6	1	0	5	54 (41.2%)
BCA	2	1	0	2	0	0	0	5 (3.8%)
WT	0	0	0	1	0	0	0	1 (0.8%)
MEO	0	1	0	0	0	0	0	1 (0.8%)
Malignant								
ACC	8	1	11	4	3	5	1	33 (25.2%)
MC	7	2	3	2	1	4	0	19 (14.5%)
ACNOS	1	0	1	0	5	0	0	7 (5.3%)
AC	2	1	1	1	0	0	0	5 (3.8%)
CCNOS	1	0	0	0	0	0	2	3 (2.3%)
CEPA	2	0	0	0	0	0	0	2 (1.5%)
BCAC	0	1	0	0	0	0	0	1 (0.8%)
Total (%)	52 (39.7%)	18 (13.7%)	18 (13.7%)	16 (12.2%)	10 (7.6%)	9 (6.9%)	8 (6.1%)	131 (100%)

PA, pleomorphic adenoma; BCA, basal cell adenoma; WT, warthin tumor; MEO, myoepithelioma; ACC, adenoid cystic carcinoma; MC, mucoepidermoid carcinoma; ACNOS, adenocarcinoma, not otherwise specified; AC, acinic cell carcinoma; CCNOS, clear cell carcinoma, not otherwise specified; CEPA, carcinoma ex pleomorphic adenoma; BCAC, basal cell adenocarcinoma.

Table 3
Frequency of intraoral minor salivary gland tumors in the past studies.

Country (Reference)	Year	Total case number	Benign (%)				Malignant (%)						
			PA	BCA	WT	MEO	ACC	MC	ACNOS	AC	CCNOS	CEPA	BCAC
USA (9)	2007	380	39.2	1.6	0	1.3	6.3	21.8	2.1	1.6	0.1	0.5	0
Brazil (8)	2006	546	33.2	0	0	0.2	6.4	22.9	3.8	3.8	0.2	0.4	0
Brazil (34)	2015	170	44	1	0	1	11	14	4	0	0	2	2
Croatia (7)	2012	212	39.6	0	0	0.5	29.2	8.5	0	4.2	3.8	5.7	0
Sri Lanka (13)	2009	713	36.8	0.8	0	1.4	16.7	25.5	1.4	2.5	0	2.9	0
India (14)	2008	150	58.0	1.3	0	0	16.7	6.7	6.6	0.7	0	2.0	0.7
Africa (4)	1991	70	48.6	0	0	0	12.9	8.6	4.3	0	0	7.1	0
China (12)	2007	737	37.3	0.5	0.1	6.6	19.4	12.4	5.6	0.9	0	3.0	0
Japan (2)	2005	82	65.9	0	0	0	12.2	9.8	0	2.4	0	2.4	1.2
Japan (Present study)	2018	131	41.2	3.8	0.8	0.8	25.2	14.5	5.3	3.8	2.3	1.5	0.8

PA, pleomorphic adenoma; BCA, basal cell adenoma; WT, warthin tumor; MEO, myoepithelioma; ACC, adenoid cystic carcinoma; MC, mucoepidermoid carcinoma; ACNOS, adenocarcinoma, not otherwise specified; AC, acinic cell carcinoma; CCNOS, clear cell carcinoma, not otherwise specified; CEPA, carcinoma ex pleomorphic adenoma; BCAC, basal cell adenocarcinoma.

accounted for 6.3–29.2% of all IMSGTs cases [8,9,33,34]. Most studies confirmed that mucoepidermoid carcinoma was the most common malignant IMSGTs, representing 6.7–25.5% of all benign and malignant tumors, followed by adenoid cystic carcinoma that accounted for 6.3–29.2% of cases [4,7–9,12–14]. The data obtained in the present study were similar to those in the previous studies. The frequency of both benign and malignant IMSGTs in previous studies is shown in Table 3 [2,4,7–9,12–14,34]. WT arising from minor salivary gland are rarely reported except for a report in China (Table 3). BCAC is reported in a studies of Brazil, India and Japan however the frequency is very low (Table 3).

The present study also included one case each of BCAC and WT among IMSGTs (Table 2). Because WT and BCAC of the minor salivary gland are extremely rare tumors, there are only a few well-documented reviews of these rare tumors arising from the minor salivary gland. Therefore, we reviewed the case reports and series of these rare tumors as reported in the English literature.

BCAC in the minor salivary gland is exceedingly rare. Recent studies have reported only 25 cases in total, 10 of which arose from the palate [16]. Cuthbertson et al. [17] reported 72 cases of intraoral minor salivary gland BCAC in their review article. The mean age at the time of presentation was 56 years (range, 24–90 years), and there was no sex predilection. The most common location was the palate, followed by the buccal mucosa, nasal cavity, floor of the mouth, and upper lip. Regarding the case of BCAC in our study, the tumor location was the soft palate, and the patient was 60 years old.

According to previous studies, WT is a common salivary gland tumor that occurs in the sixth decade of life. A high incidence of WT was also observed in patients from Europe and from parts of the USA [5–9,12]. This entity was rare in African populations and in black people, perhaps owing to the younger age of patients with salivary gland tumors [4]. The data showed a male predominance associated with smoking and a tendency for tumor diversification [5,7,6–9].

5. Conclusions

The findings of the present study and the review of the literature showed that the Japanese population might be characterized by a higher incidence of IMSGTs compared to the populations in other reviewed studies; moreover, there was a predominance of malignant IMSGTs over benign ones. The data in the present study provide information about the frequency of rare IMSGTs such as WT and BCAC. Therefore, the results of this study may be useful to determine the frequency and distribution of such rare IMSGTs in the Japanese population. We recognize the limitations of the present study because of there might be some bias among the institutions according to racial and regional characteristics of IMSGTs. It was supposed that further

accumulation of cases was needed to discuss the racial and regional characteristics in Japanese population in the future.

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