

Sialolipoma of minor salivary glands

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Abstract

Sialolipoma is a recently described histologic variant of lipoma and is characterized by well-demarcated proliferation of mature adipocytes with secondary entrapment of salivary gland elements. These tumors have been observed in both the major and minor salivary glands, with more than 20 cases being reported in the English literature. In general, the clinical presentation of sialolipomas of the minor salivary glands suggests a diagnostic hypothesis of salivary gland lesions, commonly neoplasms. In the major salivary glands, the clinical features suggest either a salivary gland neoplasm or a lipoma. Surgical excision is the treatment of choice for sialolipomas, with no reports of recurrence or malignant transformation. The present article reports 4 additional cases of sialolipoma, all of them affecting the minor salivary glands, and reviews the literature regarding clinicopathologic aspects, differential diagnosis, and therapeutic management of this recently recognized histologic variant of lipoma.

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Keywords:

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1. Introduction

Lipomas are benign neoplasms of mature adipose tissue that are relatively uncommon in the oral cavity, corresponding to 0.1% to 5.0% of all benign tumors at this anatomical site [1]. Despite their low frequency, several histopathologic variants of lipoma have been identified in the oral cavity, including fibrolipoma, angiolipoma, chondrolipoma, chondroid lipoma, pleomorphic lipoma, and spindle-cell lipoma [2–4].

Sialolipomas, which have been recognized as a distinct entity by Nagao et al [5], are characterized by a well-demarcated proliferation of mature adipocytes with secondary entrapment of salivary gland elements [5,6]. These tumors have been observed in both the major [3,7] and minor salivary glands [4,6,8]. To our knowledge, more than 20

cases of sialolipoma have been reported in the English literature (Pubmed database).

The present article reports 4 additional cases of sialolipoma, all of them affecting the minor salivary glands, and reviews the literature regarding clinicopathologic aspects, differential diagnosis, and therapeutic management of this recently recognized histologic variant of lipoma.

2. Case reports

2.1. Case 1

A 27-year-old woman was referred to our department for evaluation of a painless, firm, pinkish nodule located in the posterior region of the lateral margin of the tongue (Fig. 1). The nodule measured 1.0 × 1.0 cm in diameter and had been noted by the patient 5 years earlier. The patient's medical history was unremarkable. An excisional biopsy was performed based on the initial clinical diagnosis of fibroma. Microscopic analysis revealed proliferation of mature adipocytes and the presence of entrapped salivary gland parenchyma showing atrophic mucous acini and markedly dilated ducts

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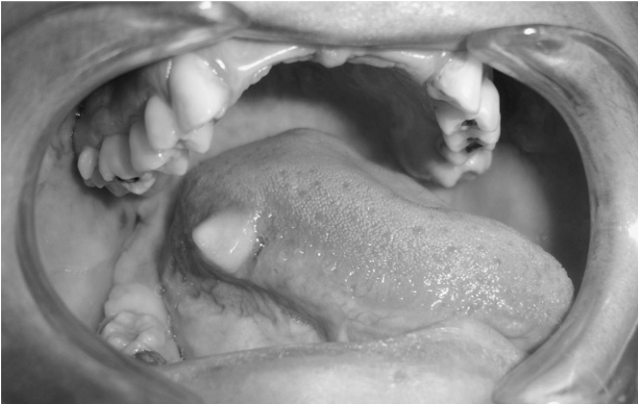


Fig. 1. A firm, pinkish nodule located in the posterior region of the lateral margin of the tongue.

(Fig. 2). The adipose tissue accounted for about 50% of the tumor volume, and the glandular elements presented as sparsely distributed epithelial islands of variable size. Fibrosis, squamous metaplasia of duct cells, and a discrete lymphoplasmacytic inflammatory infiltrate were also observed. A sharp demarcation from the surrounding tissue was noted at the periphery of the tumor. The definitive diagnosis was sialolipoma. The postoperative recovery was uneventful.

2.2. Case 2

A 73-year-old woman presented with a painless mass located on the left side of the floor of her mouth. The mass was well demarcated, was covered with a nonulcerated mucosa of normal color, and measured 4.0×1.0 cm in diameter. Her medical history was noncontributory. An excisional biopsy was performed based on the initial clinical diagnosis of ranula. Histopathologic examination revealed proliferation of mature adipocytes with entrapped mucous

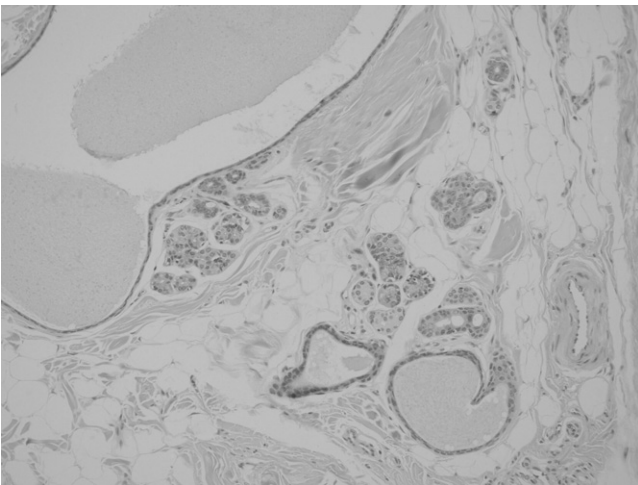


Fig. 2. Microscopic analysis revealed proliferation of mature adipocytes and the presence of entrapped salivary gland parenchyma showing atrophic mucous acini and markedly dilated ducts (400 \times).

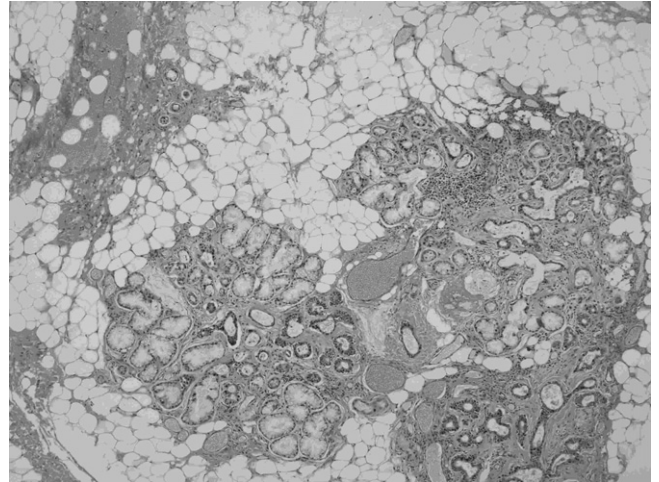


Fig. 3. The glandular parenchyma exhibited fibrosis, acinar atrophy, dilated ducts with foci of squamous metaplasia and oncocytic change, and a moderate lymphoplasmacytic inflammatory infiltrate (100 \times).

acini and ducts of the minor salivary glands. The glandular parenchyma exhibited fibrosis, acinar atrophy, dilated ducts with foci of squamous metaplasia and oncocytic change, and a moderate lymphoplasmacytic inflammatory infiltrate (Fig. 3). The adipose tissue accounted for most of the tumor volume (65%), and the glandular component presented as epithelial islands of variable size distributed throughout the tumor (Fig. 4). A thin fibrous capsule was observed at the periphery of the tumor. The definitive diagnosis was sialolipoma. The postoperative course was uneventful.

2.3. Case 3

A 65-year-old female patient sought a general dentist for evaluation of a painless nodule located in the buccal

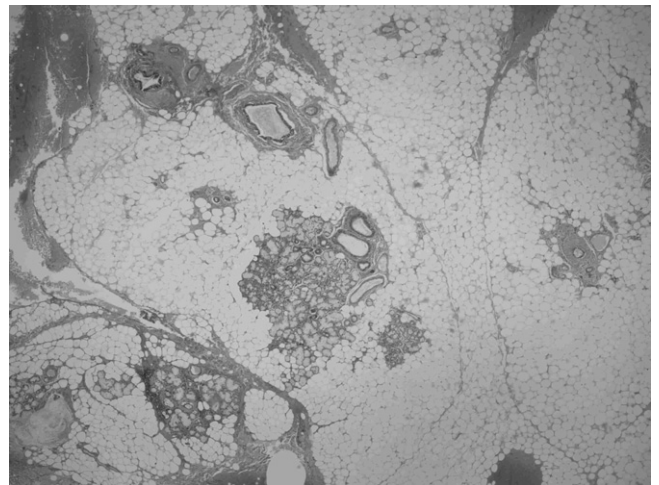


Fig. 4. The adipose tissue accounted for most of the tumor volume (65%), and the glandular component presented as epithelial islands of variable size distributed throughout the tumor (100 \times).

mucosa. The lesion was well demarcated, measured 2.0 cm in maximum diameter, and had been noted by the patient 2 years earlier. The overlying mucosa was intact and of normal color. An excisional biopsy was performed based on the clinical presentation of a fibroma. Microscopic examination revealed a well-circumscribed tumor consisting of mature adipose tissue and the presence of entrapped salivary gland parenchyma showing fibrosis, acinar atrophy, and dilated ducts with foci of oncocyctic change. The glandular component presented as sparsely distributed epithelial islands, and the adipose tissue accounted for most of the tumor volume (60%). A discrete lymphoplasmacytic inflammatory infiltrate was superimposed on the glandular parenchyma. There was a sharp demarcation of the tumor from the surrounding connective tissue (Fig. 5). The definitive diagnosis was sialolipoma.

2.4. Case 4

A 68-year-old woman was seen for evaluation of a symptomatic, well-demarcated, firm, pinkish swelling located in the retromolar pad. The lesion measured 0.9 cm in maximum diameter. An excisional biopsy was performed based on the initial clinical diagnosis of fibroma. Microscopic analysis of the specimen revealed proliferation of mature adipocytes enclosing the salivary gland parenchyma. The glandular component presented acinar atrophy and ductal dilatation associated with a discrete lymphoplasmacytic inflammatory infiltrate. The adipose tissue accounted for 50% of the tumor volume, and the glandular component presented as sparsely distributed epithelial islands of variable size. A thin fibrous capsule was observed at the periphery of the tumor. The final diagnosis was sialolipoma. The patient showed no clinical signs of recurrence 14 months after surgical excision.

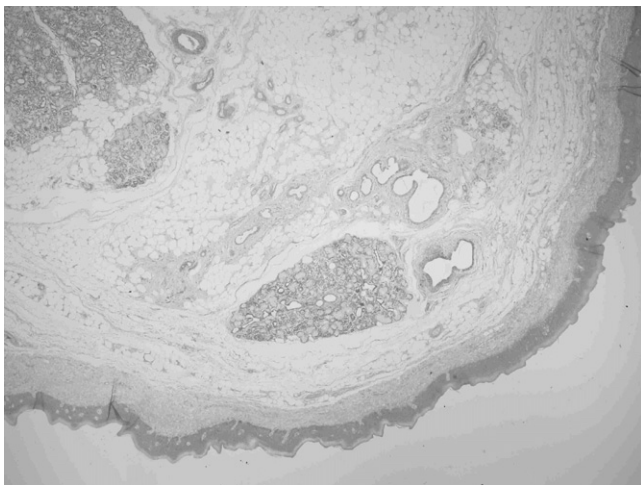


Fig. 5. There was a sharp demarcation of the tumor from the surrounding connective tissue (40 \times).

3. Discussion

Sialolipoma is a histologic variant of lipoma and is characterized by well-demarcated proliferation of mature adipocytes with secondary involvement of salivary gland parenchyma [5,6]. These tumors share similar clinical features with conventional lipomas, such as a wide range in patient age and the presence of a slow-growing and asymptomatic mass [5].

Analysis of the 4 present cases, in addition to 26 other cases published in the literature (Table 1), shows a wide range in patient age for sialolipomas, which can affect from newborns [3] to the elderly [5,6,12] (mean age, 50.7 years). Although previous studies have reported a male preference [5,6], a review of the cases published so far revealed a slightly higher frequency of sialolipomas among females (53.6%).

With respect to salivary gland type, 15 (50%) of the 30 cases reviewed in our study involved the minor salivary glands; and 15 (50%) affected the major salivary glands. Regarding major salivary gland sialolipomas, 13 (86.7%) cases were observed in the parotid gland [3,5,7,10,11]; and only 2 (13.3%) affected the submandibular gland [12]. With respect to minor salivary gland sialolipomas, we found no preference for a specific site, with cases involving the soft palate, hard palate, tongue, buccal mucosa, floor of the mouth, buccal sulcus, retromolar pad, and lower lip [1,5,6,8,9,15].

Clinically, sialolipomas present as a slowly growing, asymptomatic swelling [4,6,8,9,12]. Tumors located in the major salivary glands usually measure 1.0 to 7.0 cm in diameter (Table 1) (mean, 3.7 cm). In the minor salivary glands, tumor size usually ranges from 0.9 to 4.0 cm in maximum diameter (mean, 1.7 cm). The reported duration is quite variable, ranging from 2 months to 11 years (Table 1).

In most cases, the initial clinical diagnosis of sialolipomas located in the minor salivary glands is benign salivary gland neoplasms such as pleomorphic adenoma or low-grade mucoepidermoid carcinoma [5,6,8]. Although in 3 of our cases the clinical diagnosis suggested was fibroma, one lesion located in the floor of the mouth was clinically diagnosed as ranula. Similarly, Lin et al [9] reported a case of sialolipoma involving the floor of the mouth that raised a clinical diagnostic hypothesis of ranula. In the major salivary glands, the clinical features suggest either salivary gland neoplasm [10] or lipoma [5,7].

Computed tomography and magnetic resonance imaging (MRI) might be useful for the diagnosis of sialolipomas, which appear as a well-circumscribed tumor presenting a low-intensity computed tomographic signal and high MRI intensity [5]. Accordingly, Sakai et al [8] reported a case of sialolipoma located in the palate that showed hyperintensity on T1-weighted images and isointensity on T2-weighted images, features resembling those of subcutaneous fat. However, in the case reported by Hornigold et al [3], despite the identification of a fibrous capsule upon histologic examination, MRI failed to detect a well-defined

Table 1
Clinical characteristics, treatment, and follow-up of 30 published cases of sialolipoma

Case	Author	Age	Sex	Location	Duration	Size	Treatment	Follow-up
1	Nagao et al [5]	20	M	Parotid	4 mo	3.5 cm	Superficial parotidectomy	91 mo
2	Nagao et al [5]	45	F	Parotid	10 y	6 cm	Superficial parotidectomy	85 mo
3	Nagao et al [5]	67	M	Parotid	2 mo	1.7 cm	Superficial parotidectomy	37 mo
4	Nagao et al [5]	66	F	Parotid	5 mo	6 cm	Superficial parotidectomy	35 mo
5	Nagao et al [5]	42	M	Parotid	10 y	6 cm	Superficial parotidectomy	20 mo
6	Nagao et al [5]	66	M	Soft palate	72 mo	2.2 cm	Surgical excision	11 mo
7	Nagao et al [5]	75	M	Hard palate	3 y	1 cm	Surgical excision	NA
8	Hornigold et al [3]	0	F	Parotid	2.5 mo	3 cm	Superficial parotidectomy	2 y
9	Lin et al [9]	67	F	Floor of mouth	1 y	3 cm	Surgical excision	2 y
10	Michaelidis et al [7]	44	M	Parotid	18 mo	3.5 cm	Total parotidectomy	2 y
11	Sakai et al [8]	60	F	Hard palate	10 y	1.8 cm	Surgical excision	No evidence of disease
12	Walts and Perzik [10]	48	M	Parotid	NA	3.5 cm	Superficial parotidectomy	No evidence of disease
13	Walts and Perzik [10]	65	M	Parotid	2 mo	2.6 cm	Superficial parotidectomy	No evidence of disease
14	Baker et al [11]	44	M	Parotid	2 mo	1 cm	Superficial parotidectomy	30 mo
15	Fregnani et al [1]	NA	NA	Tongue	NA	NA	Surgical excision	No evidence of disease
16	Fregnani et al [1]	NA	NA	Buccal sulcus	NA	NA	Surgical excision	No evidence of disease
17	Ramer et al [6]	84	F	Buccal mucosa	NA	1 cm	Surgical excision	11 mo
18	Ramer et al [6]	43	F	Soft palate	NA	2 cm	Surgical excision	NA
19	Parente et al [12]	77	F	Submandibular	months	3 × 2 × 1.8 cm	Surgical excision	22 mo
20	Ponniah et al [4]	60	M	Floor of mouth	NA	2 cm	NA	2 y
21	Kadivar et al [13]	3	F	Parotid	8 mo	3 cm	Surgical excision	NA
22	Bansal et al [14]	11	M	Parotid	11 y	7 × 7 cm	Surgical excision	1 y
23	de Freitas et al [15]	38	M	Lower lip	NA	1 cm	Surgical excision	NA
24	Okada et al [16]	66	F	Hard palate	10 y	1.2 × 1 × 1 cm	Surgical excision	NA
25	Jang et al [17]	62	F	Submandibular	3 y	5 cm	Surgical excision	17 mo
26	Dogan et al [18]	33	M	Parotid	1 y	2 × 2 cm	Surgical excision	No evidence of disease
27	Present study	27	F	Tongue	5 y	1 cm	Surgical excision	1.5 mo
28	Present study	73	F	Floor of mouth	NA	4 cm	Surgical excision	NA
29	Present study	65	F	Buccal mucosa	2 y	2 cm	Surgical excision	NA
30	Present study	68	F	Retromolar pad	NA	0.9 cm	Surgical excision	14 mo

NA indicates not available.

margin of the tumor. In fact, according to these authors, MRI suggested that the tumor apparently had extended into the subcutaneous fat.

Histologically, sialolipomas are well-circumscribed lesions characterized by proliferation of mature adipocytes with secondary involvement of salivary gland parenchyma [3-6]. In an immunohistochemical and ultrastructural study of sialolipoma cases, Nagao et al [5] observed that the glandular components within the tumor consisted of regularly organized epithelial and myoepithelial elements and possessed normal specific cellular phenotypes and no proliferative activity, features seen in normal salivary gland tissue. Thus, the glandular components of sialolipomas probably become entrapped during lipomatous proliferation rather than representing true neoplastic elements [5].

Slight differences in the proportion of adipose and glandular components are observed according to the type of salivary gland affected [5,6]. In the major salivary glands, adipose tissue accounts for 75% to 90% of the neoplasm [3,5,12]. In the case of tumors located in the minor salivary glands, lipomatous tissue accounts for 50% to 80% of their volume [4-6]. Coherently, in the present cases, adipose tissue accounted for 50% to 65% of the tumor volume.

The glandular component consists of epithelial islands sparsely distributed throughout the tumor [5-7]. Occasionally, these epithelial islands are found at the periphery of the tumor [5,8,9]. In addition, in some cases of sialolipoma located in the palate, the epithelial components were found to be clustered [5]. In the present cases, the glandular component consisted of epithelial islands of variable size, sparsely distributed throughout the tumor.

One of the histologic criteria for the diagnosis of sialolipoma is the identification of a fibrous capsule around the tumor [4-8], a finding observed in 2 of the 4 cases reported here. According to Ponniah et al [4], with few exceptions, almost all parts of the oral cavity contain salivary glands although at variable amounts. Thus, any intraoral lipoma that occurs at these sites might be intermingled with adjacent salivary gland elements [4]. However, to diagnosis a sialolipoma in the context of minor salivary glands, the amount of adipose tissue and glandular elements should be in equal proportions limited peripherally by a fibrous capsule [4].

Commonly, the glandular component presents variable degrees of acinar atrophy and ductal dilatation [3-6]. Other histologic features include lymphocytic infiltration, fibrosis, myxoid change in adipose tissue, and squamous and oncocytic metaplasia in ductal cells [3,5,7,9]. Except for

myxoid change in adipose tissue, all of these features were observed in the present cases.

There are reports of sialolipomas encircling small nerve bundles, particularly sialolipomas affecting the major salivary glands [5,7]. According to Michaelidis et al [7], this finding may suggest either a more aggressive mode of growth of these tumors than that attributed to ordinary lipomas or, alternatively, a multicentric proliferation of adipose tissue, ultimately entrapping interstitial normal structures. The latter hypothesis was based on the demonstration of fatty degeneration of the gland by fine-needle aspiration and biopsy.

Fregnani et al [1] reported increased expression of proliferating cell nuclear antigen in sialolipomas when compared with common lipomas, a finding suggesting faster growth of the former. However, in that study, neither sialolipomas nor conventional lipomas showed recurrence during the follow-up period. In view of the small number of cases reported so far, definitive conclusions regarding the biological behavior of sialolipomas cannot be drawn safely.

The microscopic differential diagnosis of sialolipoma should include lesions containing extensive adipose tissue, such as lipomatous pleomorphic adenoma, lipomatosis, and lipoadenoma [5,6,8,12,19,20]. Although adipose tissue can account for up to 90% of the tumor mass in lipomatous pleomorphic adenoma, the adenomatous tissue in these lesions shows typical features of pleomorphic adenoma, including ducts and sheets or strands of (dark-staining) epithelial cells [21].

Lipomatosis is a nonmalignant overgrowth of adipose tissue throughout the salivary gland parenchyma, resulting in the diffuse enlargement of the latter [5,20]. Although the exact pathophysiology of this condition is still unclear, lipomatosis has been associated with diabetes mellitus, liver cirrhosis, chronic alcoholism, malnutrition, and hormonal disturbances [5,20]. The presence of a fibrous capsule distinguishes sialolipomas from lipomatosis [4–8].

Well-circumscribed tumors with distinct adipose and glandular components, called *adenolipomas* or *lipoadenomas*, have been described in the breast [22], thyroid [23], and skin [24]. Although these terms imply that both glandular and adipose elements are neoplastic, this is not necessarily the case with lipoadenomas and adenolipomas found at various anatomical sites [25]. These lesions consist of an admixture of mature fat cells and branching narrow epithelial tubules lined with columnar cells and supported by basal cells without myoepithelial differentiation [25]. The lack of normal acinar structures in lipoadenomas [25,26] permits their differentiation from sialolipomas [5,8,9].

Some cases of sclerosing polycystic adenosis, a recently described entity, may present a prominent lipomatous stroma [27]. According to Ramer et al [6], sclerosing polycystic adenosis should be included in the differential diagnosis of sialolipomas, particularly when sampling adequacy is less than optimal. In contrast to sclerosing polycystic adenosis,

no proliferation of ductal or acinar cells is observed in sialolipomas [6]. In addition, none of the reported cases of sialolipoma showed cellular atypia in the glandular component, a finding observed in some cases of sclerosing polycystic adenosis [27].

Regarding the therapeutic management of sialolipomas, most of the tumors located in the parotid gland have been treated by superficial parotidectomy [3,5,10]. Simple surgical excision has been used in cases of minor salivary gland sialolipomas [5,6,8,9], similarly to the cases presented here. Despite the lack of follow-up data in some cases (Table 1), no recurrence or malignant transformation has been reported so far.

In conclusion, sialolipoma is a rare histologic variant of lipoma, commonly observed in adults. When involving the minor salivary glands, these tumors show no preference for any site in the oral cavity and clinically suggest a salivary gland neoplasm. Although the diagnostic criteria and microscopic features of sialolipomas have been relatively well established, permitting the differential diagnosis with other important lesions and/or conditions, many aspects regarding the histopathogenesis of these tumors are still unclear. Thus, further studies regarding this newly recognized histologic variant of lipoma should be performed, particularly using molecular biology techniques.

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