

Lipomas of the oral cavity: clinical and histopathologic study of 41 cases in a Brazilian population

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Abstract This study evaluated the clinical and histopathologic aspects of 41 cases of oral lipomas diagnosed in a Brazilian population. All records from patients diagnosed with oral lipoma between 1970 and 2008 were reviewed. Histological sections were evaluated by light microscopy. There was a predominance of females (2.4:1), with a peak incidence between the sixth and seventh decade. The buccal mucosa was the most affected site (53.7%), followed by the buccal sulcus (14.6%) and tongue (9.8%). Tumor size ranged from 0.5 to 10 cm and the mean reported duration was 48 months. Histologically, the following variants were identified: lipoma (41.5%), fibrolipoma (34.1%), spindle cell lipoma (9.8%), sialolipoma (9.8%), osteolipoma (2.4%), and chondrolipoma (2.4%). Most tumors were well delimited, irrespective of the variant. Lipomas are rare tumors of the oral cavity. The characterization of new variants, such as sialolipomas, and the identification of histological subtypes in already known variants, such as

low-fat and fat-free spindle cell lipomas, highlight the importance for careful microscopic evaluation of these tumors, which might be combined with immunohistochemistry in some cases.

Keywords Lipoma · Oral cavity · Histopathology · Immunohistochemistry

Introduction

Lipomas are benign tumors consisting of mature adipocytes arranged in lobules that are separated by fibrous connective tissue septa, sometimes associated with other mesenchymal elements. Different histopathological variants have been described [1, 2]. Although lipomas are one of the most common mesenchymal neoplasms [1–3], the head and neck regions are affected in 20% of cases [2] and only 1–4% of these tumors are located in the oral cavity [4, 5].

Clinically, these tumors manifest as asymptomatic, slow-growing, and submucosal nodules [2, 6]. The most affected anatomical sites in the oral cavity include the buccal mucosa, lips, and tongue [1, 2, 6]. The floor of the mouth [3, 6], palate [3, 7], retromolar pad [1, 6], and salivary glands [6] are less frequently involved.

The following histopathological variants of lipomas have been described: fibrolipoma, osteolipoma, chondrolipoma, intramuscular lipoma, angiolipoma, angiomyolipoma, myolipoma, myelolipoma, chondroid lipoma, spindle cell lipoma, pleomorphic lipoma, and sialolipoma [1, 8, 9]. Treatment of lipomas consists of simple surgical removal, irrespective of the histological subtype, with no recurrence being expected [2, 6, 10].

Most lipomas located in the oral cavity are described in the literature in the form of case reports [11–14]. Furthermore,

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the few case series of lipomas of the oral cavity [1–3, 6, 7] have reported divergent results in terms of gender preference and the frequency of histopathological variants of this neoplasm.

Thus, the objective of the present study was to retrospectively analyze the clinical and pathological findings of a case series of lipomas of the oral cavity stored in the files of an Oral Pathology Service.

Materials and methods

All cases of lipoma of the oral cavity kept in the files of the Laboratory of Oral Pathology, Department of Dentistry, Federal University of Rio Grande do Norte (UFRN), and diagnosed between January 1970 and August 2008 were reviewed. The following data were obtained from the biopsy request form: patient age and gender, anatomical location, tumor size, and tumor duration.

For histopathological analysis, all slides containing hematoxylin/eosin-stained 5- μ m thick sections were reassessed. The histopathological variants of lipomas were classified according to the classifications proposed by Gnep [4] and Weiss and Goldblum [9], which include lipoma, fibrolipoma, chondrolipoma, osteolipoma, intermuscular and intramuscular lipoma, angiolipoma, myolipoma, myelolipoma, benign lipoblastoma, chondroid lipoma, spindle cell lipoma, pleomorphic lipoma, and salivary gland lipoma.

In four cases, streptavidin–biotin immunohistochemistry with anti-CD34 monoclonal antibody (Clone QBEnd 10, Dako, Glostrup, Denmark; dilution 1:50, overnight) was used to confirm the diagnosis of spindle cell lipoma. Antigen retrieval was performed in a Pascal chamber (Tris/EDTA, pH 9.0) for 3 min.

The study was approved by the Ethics Committee of UFRN (protocol 033/08).

Results

Forty-six cases of lipoma were identified during the study period. After histopathological reevaluation, five tumors were excluded from the sample because they were cases of herniated adipose tissue or fibrous polyp associated with secondary entrapment of adipose tissue. Thus, the final sample consisted of 41 cases of lipoma, corresponding to 0.4% of all lesions stored in the files of the Laboratory of Oral Pathology, Department of Dentistry, UFRN. Twenty-nine (70.7%) of these cases were diagnosed in women and 12 (29.3%) in men, with a male/female proportion of 2.4:1. The mean patient age was 56.7 years (range 18–75). No information regarding age was available for three (7.3%)

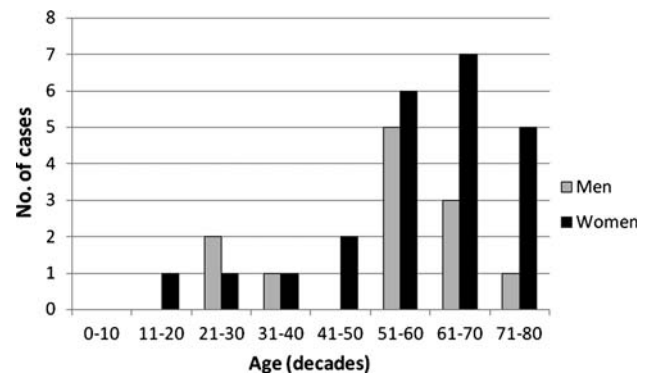


Fig. 1 Age and sex distribution of lipomas of the oral cavity

female patients. The distribution of cases according to age and gender revealed a peak incidence between the sixth and seventh decade of life (Fig. 1).

The most affected anatomical site was the buccal mucosa (53.7%), followed by the buccal sulcus (14.6%), tongue (9.8%), floor of the mouth (7.3%), and retromolar pad (7.3%). Tumor size ranged from 0.5 to 10 cm, with a mean diameter of 2.1 cm. The duration of the tumor ranged from 6 months to 15 years, with a mean duration of 48 months.

Histologically, the following variants were identified: lipoma in 17 (41.5%) cases, fibrolipoma in 14 (34.1%), spindle cell lipoma in 4 (9.8%), sialolipoma in 4 (9.8%), osteolipoma in one case (2.4%), and chondrolipoma in one (2.4%). The distribution of the histological subtypes of lipoma according to anatomical site is shown in Table 1.

The lipomas consisted of typical mature adipocytes which presented a discrete variation in size. The nuclei were flat and pushed to the periphery. These cells were arranged in lobules, intermingled with thin septa of fibrous connective tissue. In two cases involving the jugal mucosa and in one case involving the tongue, focal areas of dissociation of skeletal muscle bundles were observed deep inside the specimen (Fig. 2a). Fibrolipomas presented lobules consisting of mature adipocytes similar to classical lipomas, intermingled with thick septa of fibrous connective tissue (Fig. 2b).

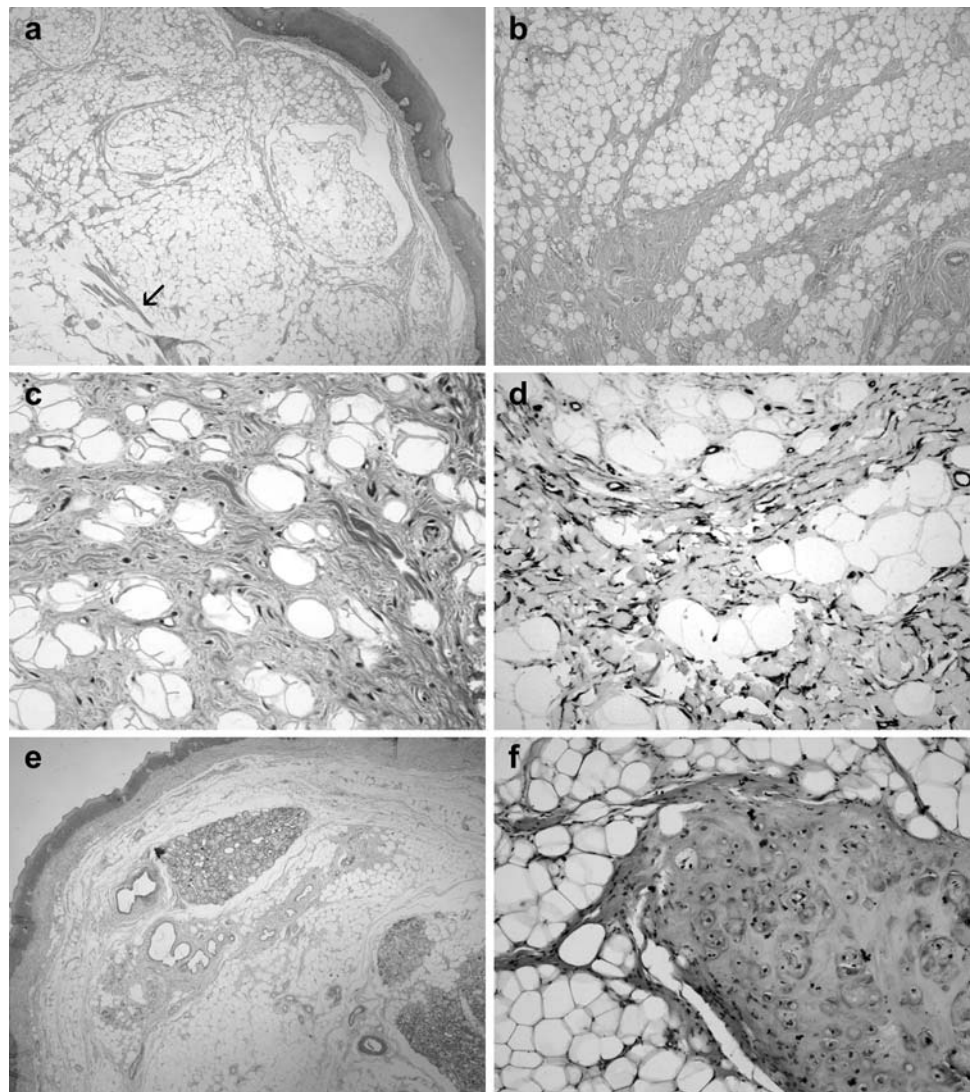
Spindle cell lipomas were characterized by a combination of typical mature adipocytes and spindle-shaped cells. The latter cells were either associated with short and thick collagen fiber bundles or embedded in a myxoid matrix (Fig. 2c). The spindle-shaped cells presented a single elongated nucleus and bipolar cytoplasmic processes. No lipoblastic activity was observed. In all four cases, the spindle-shaped cells showed diffuse immunopositivity for anti-CD34 antibody (Fig. 2d).

Sialolipomas were characterized by the proliferation of typical mature adipocytes that permeated the acini and ducts of the minor salivary glands (Fig. 2e). Areas of variable degrees of acinar atrophy and ductal ectasia were

Table 1 Distribution of cases of oral lipoma according to anatomic location

	Lipoma	Fibrolipoma	Spindle cell lipoma	Sialolipoma	Osteolipoma	Chondrolipoma	Total
Buccal mucosa	10	9	2	1	–	–	22 (53.7%)
Buccal sulcus	1	3	1	–	1	–	6 (14.6%)
Tongue	1	1	–	1	–	1	4 (9.8%)
Floor of mouth	2	–	–	1	–	–	3 (7.3%)
Retromolar pad	1	1	1	–	–	–	3 (7.3%)
Palate	1	–	–	–	–	–	1 (2.4%)
Lip	1	–	–	–	–	–	1 (2.4%)
Unknown	–	–	–	1	–	–	1 (2.4%)
Total	17 (41.5%)	14 (34.1%)	4 (9.8%)	4 (9.8%)	1 (2.4%)	1 (2.4%)	41 (100.0%)

Fig. 2 **a** Lipoma showing lobules of mature adipocytes and focal area of dissociation of skeletal muscle bundles (*arrow*) (H&E, 40 \times). **b** Fibrolipoma revealing lobules of adipocytes interspersed by thick bands of dense connective tissue (H&E, 100 \times). **c** Spindle cell lipoma showing mature adipocytes, uniform spindle cells, myxoid matrix, and short bundles of collagen (H&E, 200 \times). **d** Spindle cells uniformly positive for CD34 (H&E, 200 \times). **e** Sialolipoma showing islands of salivary gland parenchyma with atrophic acini and dilated ducts, enclosed in a mature adipose tissue (H&E, 40 \times). **f** Chondrolipoma disclosing island of mature cartilage inside a proliferation of mature fat cells (H&E, 200 \times)



observed in the gland parenchyma which was permeated by a mononuclear inflammatory infiltrate. Areas of fibrosis were observed in some cases, in addition to occasional ducts exhibiting squamous metaplasia and oncocytic differentiation. Islands of gland parenchyma of variable sizes

were distributed either randomly among proliferating adipocytes or along the periphery of the tumor.

Here, in one studied case, islands of cartilaginous tissue were identified amid proliferating typical mature adipocytes, a finding characterizing chondrolipoma (Fig. 2f).

Table 2 Distribution of cases of oral lipoma reported in the literature according to histopathologic variant

	Seldin et al. (1967)		Epivatianos et al. (2000)		Said-Al-Naief et al. (2001)		Fregnani et al. (2003)		Furlong et al. (2004)		Trandafir et al. (2007)		Present study	
	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%	Cases	%
Lipoma	24	92.3	9	69.2	83	56.8	21	45.6	48	50.5	14	73.7	18	41.5
Fibrolipoma	2	7.7	2	15.4	50	34.2	18	39.1	1	1.1	4	21.0	14	34.1
Spindle cell lipoma	–	–	–	–	2	1.4	1	2.2	42	44.2	–	–	4	9.8
Sialolipoma	–	–	–	–	–	–	2	4.4	–	–	–	–	4	9.8
Chondrolipoma	–	–	–	–	–	–	–	–	2	2.1	–	–	1	2.4
Osteolipoma	–	–	–	–	–	–	–	–	–	–	–	–	1	2.4
Chondroid lipoma	–	–	–	–	–	–	–	–	2	2.1	–	–	–	–
Intramuscular lipoma	–	–	2	15.4	–	–	4	8.7	–	–	–	–	–	–
Angiolipoma	–	–	–	–	3	2.1	–	–	–	–	–	–	–	–
Myxoid lipoma	–	–	–	–	8	5.5	–	–	–	–	1	5.3	–	–
Total	26	100.0	13	100.0	146	100.0	46	100.0	95	100.0	19	100.0	41	100.0

These cartilage islands were continuous with septa of fibrous connective tissue and contained lacunae filled with chondrocytes. No myxoid areas, lipoblasts, atypias, hyperchromasia, or mitotic figures were detected. On the other hand, osteolipoma was characterized by the deposition of lamellar bone tissue surrounded by a small band of fibrous connective tissue amid proliferating mature adipocytes arranged in lobules.

Most tumors studied were well delimited, irrespective of the histopathological variant. The presence of a thin capsule of fibrous connective tissue was a variable finding.

Discussion

Lipomas of the oral cavity are infrequent [4, 5] and account for only 0.5% of all tumors diagnosed at oral pathology services [6]. Coherently, in the present study, lipomas corresponded to 0.4% of all tumors diagnosed at the Laboratory of Oral Pathology, Department of Dentistry of UFRN.

Lipomas of the oral cavity are diagnosed more frequently in adult patients at a mean age of 50.2–62 years [2, 3, 6, 7]. These data agree with the present study in which lipomas showed a peak incidence between the sixth and seventh decade of life, with a mean age at diagnosis of 56.7 years. In contrast to the male predominance of lipomas involving other regions of the body [9], in the case of lipomas of the oral cavity, studies have demonstrated a relatively similar gender distribution [1], or a slightly higher frequency among women [6, 7, 15]. In the present study, a higher frequency of cases was observed among women, with the female/male proportion (2.4:1) being slightly higher than that reported in the literature [6, 7, 15].

Lipomas of the oral cavity are slow-growing tumors, commonly presenting a mean diameter of 2.0 cm at diagnosis [3, 6, 14]. However, cases of tumors measuring 8.0 and 11.0 cm in diameter have been reported [3, 16]. In this study, although the mean diameter of the tumors was similar to that reported in the literature [3, 6], in one case located in the buccal mucosa, the tumor presented a diameter of 10 cm.

The mean duration of oral lipomas ranges from 3.2 to 6.3 years [3, 6], with the presence of the tumor for more than 50 years having been reported in some cases [17]. According to Furlong et al. [3], oral lipomas might be symptomatic in earlier stages than lipomas located in other regions of the body, a fact that would explain the shorter mean duration observed by these authors. In contrast, Bandéca et al. [2] and Epivatianos et al. [7] emphasized that lipomas of the oral cavity are commonly asymptomatic.

The buccal mucosa is the site most commonly affected by oral lipomas, corresponding to 30.5–45.7% of cases [1, 3, 6, 15]. In the present study, the percentage of cases identified at this site (53.7%) was higher than that reported in the literature [1, 3, 6, 15]. Said-Al-Naief et al. [1] and Furlong et al. [3] identified the lip as the second most common location of oral lipomas, whereas in the present study, only one case (2.4%) of lipoma affecting the lip was observed. Fregnani et al. [6] identified the lip and tongue as the second most affected site of oral lipomas, corresponding to 13% of cases. In the present study, the buccal sulcus and tongue were the second and third most frequently affected sites of lipomas, corresponding to 14.6 and 9.8% of cases, respectively.

With respect to histopathological findings, lipomas and fibrolipomas are the histological variants most frequently

described in the oral cavity [1, 6, 7, 10] (Table 2). Some studies have demonstrated a similar incidence of lipomas and fibrolipomas [18–20], whereas others, like the present investigation, observed a higher proportion of lipomas [1, 5, 7, 10, 15, 21]. According to Fregnani et al. [6], the variations in the frequency of lipomas and fibrolipomas may reflect true geographic and racial differences or are mere divergences in diagnostic criteria. As observed in the present study, five cases previously diagnosed as lipoma were excluded from the sample because they were cases of herniated adipose tissue or fibrous polyp with secondary entrapment of adipose tissue. According to Gnepp [4] and Weiss and Goldblum [9], lipomas and fibrolipomas are well-delimited and discrete-encapsulated tumors, findings that help with the differential diagnosis of herniated adipose tissue and fibrous polyps with secondary entrapment of adipose tissue, respectively.

De Visscher [5] and Hatziotis [21] reported that, in the oral cavity, lipomas are more common among men, whereas fibrolipomas more frequently affect women. However, Fregnani et al. [6] were unable to identify this relationship. The authors observed a male/female proportion of 1:1.5 for lipomas and of 1:1 for fibrolipomas. According to these authors, there is no convincing explanation for this relationship between histological subtype and gender preference. In the present investigation, although the male/female ratio (1:1.4) of lipomas was similar to that reported in other studies [6, 7], 11 (78.6%) of the 14 cases of fibrolipoma were diagnosed in women and only 3 (21.4%) cases were identified among men, corresponding to a male/female proportion of 1:3.6. These findings might represent a particularity of the present sample. Whether there is a true female predominance of fibrolipomas still needs to be determined.

Although representing a well-defined variant, it has been speculated whether intramuscular lipomas of the oral cavity indeed exist or only correspond to a lipoma with secondary entrapment of muscle fibers [6]. In contrast to intramuscular lipomas involving other regions of the body, tumors located in the oral cavity submitted to complete excision rarely show recurrence [6, 7]. Thus, recurrence of intramuscular lipomas of the oral cavity has been associated with incomplete excision of the tumor [16, 22]. In the present study, foci of muscle bundle entrapment were observed in three cases of lipoma, two located in the buccal mucosa and one in the tongue. In view of the lower recurrence rates of intramuscular lipomas of the oral cavity [6, 7] and their frequent location in areas that permit close proximity between proliferating adipocytes and striated muscle tissue [2, 6], these tumors may represent simple lipomas with secondary entrapment of muscle tissue.

Chondrolipomas and osteolipomas are histological variants rarely observed in the oral cavity [12, 14, 23, 24].

Chondrolipomas are characterized by the proliferation of mature adipocytes associated with the deposition of mature cartilaginous tissue [23–25]. Cases of chondrolipoma of the oral cavity have been observed among patients ranging in age from 2 to 72 years [26, 27], and most of the tumors are found in the tongue [3, 24, 25], as observed in the present study, and in the lower lip [23, 26, 28]. Osteolipomas, in turn, are characterized by lamellar bone trabeculae scattered among proliferating mature adipocytes [14, 23]. Most cases of osteolipoma of the oral cavity are diagnosed after the fifth decade of life [12, 14, 23]. The most affected sites in the oral cavity are the buccal sulcus [23] as observed in the present study, alveolar mucosa [14], tongue [29], and buccal mucosa [12]. Different theories have been proposed to explain the formation of bone and cartilaginous tissues in lipomas. One theory suggests that cartilaginous bone and adipose components originate from undifferentiated pluripotent mesenchymal cells [3, 9, 28]. In addition, bone and cartilaginous components may represent a metaplastic process of a preexisting lipoma [9, 12, 24, 25]. The origin of chondrolipomas and osteolipomas from pluripotent cells seems attractive [30]. In vitro studies and experiments using animal models have shown a multidirectional differentiation capacity of stem cells derived from mature adipose tissue [31, 32]. This characteristic permits the development of bone, cartilage, muscle, blood vessels, and fibrous connective tissue from the same precursor cell [31].

Sialolipomas, first described by Nagao et al. [8], are characterized by well-delimited proliferation of mature adipocytes amid salivary gland parenchyma which presents variable degrees of acinar atrophy and ductal ectasia [8, 33]. These tumors have been identified in both major salivary glands, particularly the parotid gland [8, 34, 35], and minor salivary glands [6, 33, 36, 37]. In the latter, no preference for an anatomical site has been described, with reports of cases involving the hard palate [8, 36], soft palate [8, 33], floor of the mouth [11], buccal mucosa [33], tongue [6], and buccal sulcus [6]. Most sialolipomas are identified in adult patients [8, 11, 33, 36]. Although previous studies have reported a male predominance [8, 33], all sialolipoma cases of the present study were diagnosed in women.

In contrast to sialolipomas of the major salivary glands in which the adipose component accounts for 75% [34] to 90% [8] of the tumor, sialolipomas of the minor salivary glands show a percentage of adipose tissue that ranges from 50 to 80% [8, 33, 37]. In minor salivary gland tumors, the glandular component is generally arranged in clusters among proliferating adipocytes [8, 11]. An inflammatory infiltrate of variable intensity and oncocytic foci have also been described [8, 33]. Similar findings were observed in the present study. One important aspect for the diagnosis of minor salivary gland sialolipomas is the identification of the relatively similar proportion of adipose tissue and

salivary gland parenchyma, as well as the presence of a peripheral fibrous capsule [8, 37]. According to Nagao et al. [8], the presence of this capsule permits the distinction of sialolipomas from lipomatosis, a non-tumor deposition of adipose tissue in gland parenchyma which results in the diffuse enlargement of the latter [38].

Spindle cell lipoma, first described by Enzinger and Harvey [39], is an uncommon variant and is generally identified in subcutaneous tissue in the posterior region of the back and neck of adult men [9]. Histologically, these lipomas are characterized by the proliferation of mature adipocytes and CD34-positive spindle-shaped cells, the latter embedded either among short collagen fiber bundles or in a myxoid matrix [40, 41]. One characteristic is that the spindle-shaped cells are immunopositive for CD34 and negative for S-100 protein, smooth muscle alpha-actin, desmin, and factor VIII [13, 40, 42]. The proportion of adipocytes and spindle-shaped cells is variable [1, 40, 43]. Some tumors mainly consist of mature adipocytes, a moderate amount of myxoid matrix and few spindle-shaped cells, whereas other cases demonstrate numerous spindle-shaped cells, thick collagen bundles and a small number of mature adipocytes [43, 44]. In addition, the spindle cell component may only be focal, a fact resulting in the incorrect diagnosis of the tumor as classical lipoma [13, 41]. The cases studied here presented a relatively similar proportion of adipocytes and spindle-shaped cells. In addition, the quantity of myxoid matrix ranged from moderate to scarce, with most cases showing a predominance of areas containing thick and short collagen bundles.

In contrast to other retrospective studies [1, 6], Furlong et al. [3] described spindle cell lipoma as the second most frequent histological variant (44.2%) in the oral cavity, with most cases involving the lip. In the study of Fregnani et al. [6], although the authors identified only one case of spindle cell lipoma, the tumor was also located in the lip. However, no case of spindle cell lipoma in the lip was identified in the present investigation or in the study of Said-Al-Naief et al. [1]. It should be noted that the study of Furlong et al. [3] was conducted at a referral center to which cases of diagnostic difficulty are referred. According to Billings and Folpe [43], despite the relatively direct diagnosis of most cases of spindle cell lipoma, several histological variants such as low-fat and fat-free spindle cell lipomas may pose diagnostic difficulties. However, whether the high proportion of spindle cell lipomas identified in the study of Furlong et al. [3], particularly in the region of the lip corresponds to the true frequency of these tumors, which continues to be a matter of discussion. One important aspect reported in the study of Furlong et al. [3] was the reclassification of 11 cases of spindle cell lipomas previously diagnosed as myxoid lipomas. Billings et al. [40] pointed out that prior to the first report of spindle cell lipoma of the oral

cavity [45], cases of this variant may have been described in the literature under the designation of fibrolipoma or myxoid lipoma. These observations emphasize the importance of immunohistochemical analysis using anti-CD34 antibody [13, 40] in cases of lipomas that present myxoid areas associated with a spindle cell component.

Lipomas of the oral cavity are treated by conservative local excision and recurrence is rare [2, 6, 15, 16]. No important differences in prognosis are observed between the major histopathological variants of lipomas [9]. One important exception are intramuscular lipomas. In these cases, incomplete surgical excision may result in high recurrence rates [16, 22].

In conclusion, lipomas of the oral cavity are rare tumors that usually do not show recurrence after conservative surgical excision, irrespective of the histopathological variant. Although lipomas and fibrolipomas correspond to the largest proportion of diagnosed cases, the characterization of new histopathological variants, such as sialolipomas, and the identification of histological subtypes in already known variants, such as low-fat and fat-free spindle cell lipomas, highlight the importance for careful histopathological evaluation of these tumors, which might be combined with immunohistochemistry in some cases. In view of the low frequency of lipomas of the oral cavity, co-operative multi-center studies are an important tool to clarify divergences in the literature regarding these tumors.

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