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ORIGINAL PAPER

Spindle Cell Lipoma of the Tongue: A Clinicopathologic Study of 8 Cases and Review of the Literature

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Abstract Spindle cell lipoma is a histologically distinct variant of lipoma characteristically arising in the subcutis of the posterior neck, upper back, or shoulder. Spindle cell lipomas infrequently occur within the oral cavity and, in particular, rarely involve the tongue. The clinical and pathologic features of eight cases of spindle cell lipoma affecting the tongue were analyzed. The study group included five men and three women ranging in age from 35 to 80 years (mean 57.4 years). Most lesions presented as either a painless or slowly growing lingual mass. The tumors were well circumscribed and characterized microscopically by a mixture of mature adipocytes, cytologically bland spindle cells, and interspersed bundles of thick collagen fibers in variable proportions. Myxoid stroma was a prominent feature in three lesions. The spindle cells were positive with CD34, while negative with S-100 protein, desmin, and smooth muscle actin. Treatment consisted of local excision in all cases. There have been no recurrences to date, with clinical follow up information available for all patients (range 11–118 months; mean 50.8 months). Lingual examples of spindle cell lipoma should be distinguished from other fat containing spindle cell neoplasms that can arise at this anatomic site.

Keywords Spindle cell lipoma · Tongue · Lingual · Pleomorphic adenoma

Introduction

Benign lipomatous neoplasms are uncommon, but well documented tumors affecting the oral cavity. Histologically, the majority is represented by ordinary lipomas and fibrolipomas [1–8]. In contrast, spindle cell lipomas are rarely encountered in the oral region. The frequency of spindle cell lipomas among reported series of intraoral lipomatous tumors originating from single institutions varies from 0 to 9.8 % [2–4, 6–8]. Unlike ordinary lipomas, which are readily recognized, spindle cell lipomas can be morphologically diverse and potentially confused with other lipomatous and non-lipomatous spindle cell neoplasms. While most ordinary lipomas of the oral cavity involve the buccal mucosa, tongue or lip [1–8], lingual examples of spindle cell lipoma remain rare. The reported literature pertaining to spindle cell lipoma of the tongue is relatively sparse and comprised predominantly of single case reports and limited descriptions of small numbers of cases among larger series of lipomas of the oral cavity [3, 5, 9–21]. In this study, we analyzed eight new cases of lingual spindle cell lipoma in order to further characterize the clinicopathologic features of this uncommon type of intraoral lipomatous tumor.

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Table 1 Immunohistochemical panel

Antigen/antibody	Company	Dilution	Results
CD34 (QBEnd/10)	Ventana	Neat	7/7 (strong, diffuse cytoplasmic positive)
S-100 protein	Dako	1:2,000	0/7 (negative in spindle cells; positive in adipocytes)
Desmin	Dako	1:400	0/6 (negative)
Smooth muscle actin (asm-1)	Leica	1:200	0/6 (negative)

Materials and Methods

Eight cases of spindle cell lipoma involving the tongue were identified from the files of the Departments of Pathology within Southern California Permanente Medical Group and Johns Hopkins Medical Institutions between 1997 and 2014. Hematoxylin and eosin stained slides from all cases were reviewed. Clinical data, treatment, and follow-up information were obtained from the medical records.

Immunophenotypic analysis was performed in all cases with available suitable material by a standardized Envision™ method employing 4 μm-thick, formalin fixed, paraffin embedded sections. Table 1 documents the commercially available immunohistochemical antibody panel used. Epitope retrieval was performed, as required by the manufacturer guidelines. Standard positive controls were used throughout, with serum used as the negative control. The antibody reactions were graded as absent to weak (0 to 1+), moderate (2+ to 3+) and strong (4+) staining, and the fraction of positive cells was determined by separating them into four groups: <10, 11–50, 51–90, and >90 %.

This clinical investigation was conducted in accordance and compliance with all statutes, directives, and guidelines of an Internal Review Board authorization (#5968) performed under the direction of Southern California Permanente Medical Group and the Code of Federal Regulations, Title 45, Part 46.

Results

Clinical Features

The clinical data are summarized in Table 2. The study population was comprised of 5 men and 3 women with ages at presentation ranging from 35 to 80 years (mean 57.4 years; median 61.5 years). Six patients presented with a painless nodule, two of which were associated with a gradual increase in size. Only one patient reported associated pain. One tumor was discovered incidentally in a patient undergoing evaluation for a squamous cell carcinoma of the retromolar trigone. The duration of symptoms ranged from 1 week to "years" (mean 8.4 months). The tumors affected the left (n = 5) or right (n = 3) tongue, without any midline lesions.

Pathologic Features

On gross examination, the tumors were nodular, with homogeneous, tan to yellow, lobulated cut surfaces. The tumors ranged from 0.2 to 2.5 cm in maximum dimension (mean 1.1 cm).

Microscopically, all lesions were well circumscribed with pushing borders, and often surrounded by a thin, collagenous pseudocapsule (Fig. 1). Infiltration into adjacent skeletal muscle was not identified. The tumors were composed of a mixture of adipocytes and spindle cells in varying proportions (Fig. 2). The lipomatous component was represented by mature adipocytes with slight variation in size. Nuclei were small and peripherally located. Two tumors exhibited areas of atrophy with smaller adipocytes mimicking lipoblasts (Fig. 3). The nuclei of these cells, however, were not enlarged and lacked hyperchromasia or scalloping. True lipoblasts were not observed. The lesional spindle cells were randomly oriented and had short, ovoid nuclei with inconspicuous nucleoli and scant cytoplasm. The spindle cells were frequently associated with thick bundles of eosinophilic collagen fibers. The spindle cells lacked atypical features and no pleomorphic or enlarged multinucleated cells were observed. Most tumors were comprised of relatively equal quantities of adipocytes and spindle cells. One tumor was composed predominantly of mature adipose tissue and resembled an ordinary lipoma but also exhibited scattered interstitial spindle cells between lobules of adipocytes (Fig. 4). A prominent myxoid stroma was present in three cases (Fig. 5). Two of these myxoid predominant lesions exhibited foci comprised of small, multivacuolated adipocytes, imparting a chondroid lipoma-like appearance (Fig. 6). Neither the lipomatous nor the spindle cell elements of the tumors showed evidence of necrosis or mitotic activity.

By immunohistochemical analysis, the lesional spindle cells were strongly immunoreactive for CD34 in all tumors evaluated (7/7). The adipocytic component of the tumors was positive for S-100 protein, however, the spindle cells were nonreactive (0/7). The spindle cells were likewise negative for desmin (0/6) and smooth muscle actin (0/6).

Treatment and Follow-up

All of the tumors were treated by local surgical excision only without additional treatment. Clinical follow up was

Table 2 Clinicopathologic features of eight cases of spindle cell lipoma of the tongue

Case no.	Age (in years)	Sex	Clinical presentation	Symptom duration	Laterality	Size (cm)	Treatment	Follow-up (in months)
1	62	Male	Incidental finding	NA	Left	1.0	Local excision	ANED (115)
2	62	Male	Painless nodule	6 months	Right	0.4	Local excision	ANED (33)
3	61	Female	Slow growing nodule	"years"	Left	2.5	Local excision	ANED (29)
4	80	Male	Painless nodule	2 months	Left	1.3	Local excision	ANED (13)
5	65	Female	Slow growing nodule	2 months	Right	0.2	Local excision	ANED (118)
6	35	Male	Painful lump	1 week	Left	1.7	Local excision	ANED (67)
7	47	Female	Painless nodule	2 weeks	Right	NA	Local excision	ANED (20)
8	47	Male	Painless nodule	12 months	Left	0.5	Local excision	ANED (11)

NA not available, *ANED* alive with no evidence of disease

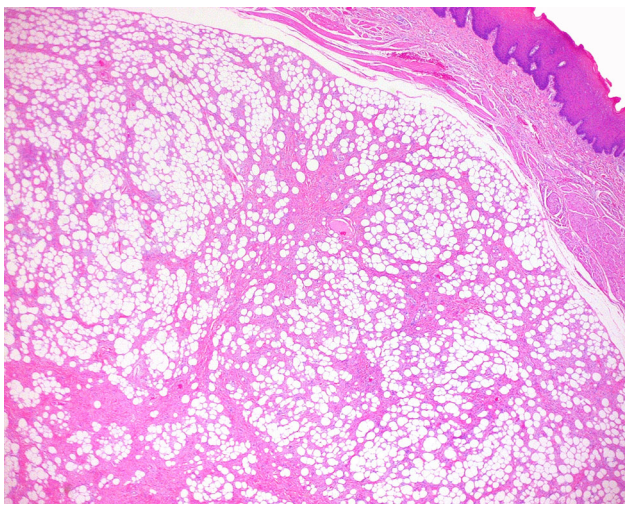

Fig. 1 Spindle cell lipomas involving the tongue are microscopically well circumscribed submucosal nodules

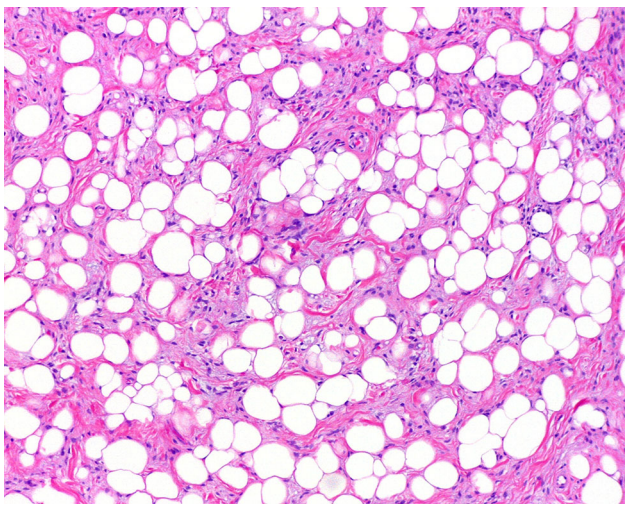

Fig. 2 Typical microscopic appearance of lingual spindle cell lipoma characterized by mature adipocytes, cytologically uniform spindle cells, and dense collagen fibers

available for all patients with a mean duration of 50.8 months (range 11–118 months). None of the patients developed local recurrence and all are alive with no evidence of disease at last follow-up.

Discussion

Spindle cell lipoma, a histologic variant of lipoma first described by Enzinger and Harvey [22], most commonly arises in the subcutaneous tissues of the posterior neck, back, and shoulders. Spindle cell lipomas are infrequently encountered in the oral region, with lingual examples of this entity in particular being distinctly rare. To our knowledge, only 24 cases of spindle cell lipoma involving the tongue have been reported in the English literature [3, 5, 9–21]. The clinical and pathologic features of lingual spindle cell lipoma based on findings from the present series combined with previously published data are summarized in Table 3. Patients with spindle cell lipoma of the tongue are typically older adults (mean 58.2 years) with a male predilection

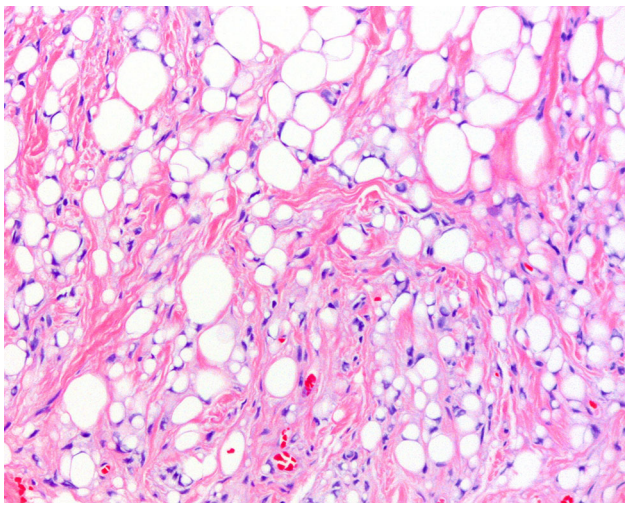

Fig. 3 Areas of atrophy occurring in spindle cell lipomas have a pseudolipoblastic appearance, however the cells lack nuclear hyperchromasia and atypia of true lipoblasts

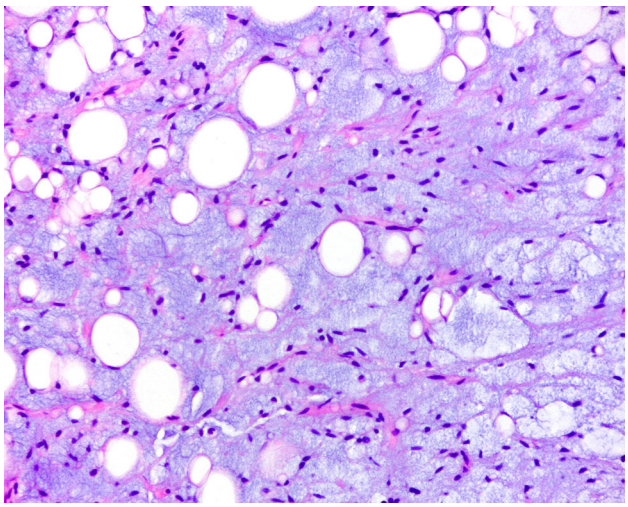

Fig. 5 Spindle cell lipoma of the tongue exhibiting an abundant myxoid matrix. The lesion lacks the plexiform capillary network of myxoid liposarcoma

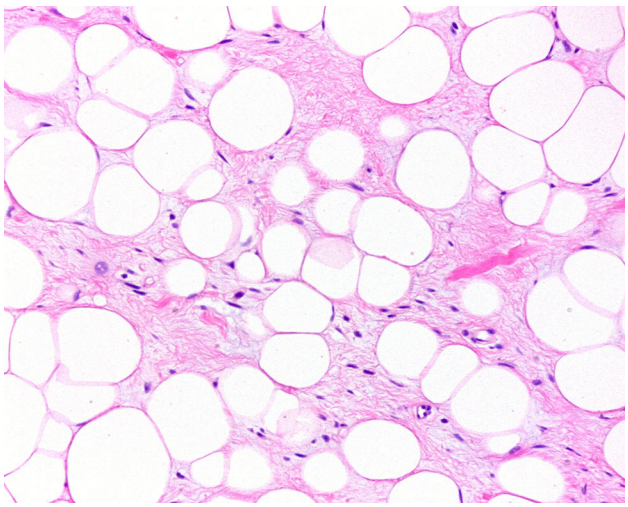

Fig. 4 Adipocyte rich example of lingual spindle cell lipoma with prominent lipomatous component and relatively few spindle cells

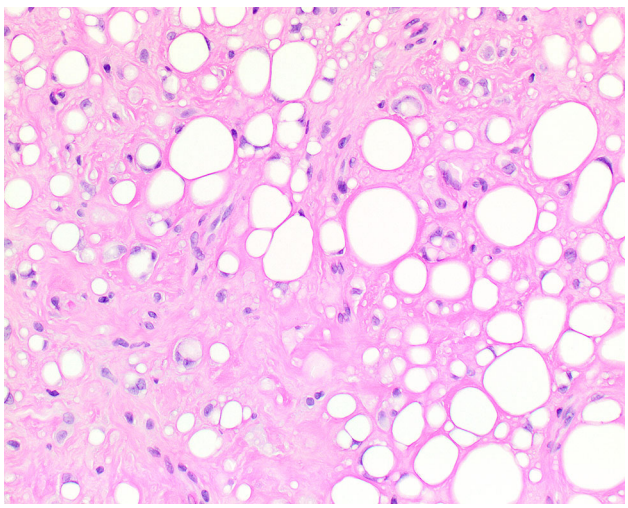

Fig. 6 Example of lingual spindle cell lipoma with an area comprised of small multivacuolated adipocytes within a myxoid background resembling chondroid lipoma

(male:female, 1.9:1). The majority present clinically as a painless mass or swelling, often with a history of slow growth over an extended time period. They are most often solitary, though two patients with bilateral spindle cell lipomas of the tongue have been reported [13, 19]. Lingual spindle cell lipomas are benign neoplasms managed adequately by local excision. The present series along with prior reports with known follow up information have shown no instances of tumor recurrence or aggressive biologic behavior [3, 11, 14, 16, 18, 19, 21].

On gross examination, spindle cell lipomas are well circumscribed neoplasms with a firmer consistency than ordinary lipomas. The cut surface may vary from yellow to grey-white, the latter representing the spindle cell component of the tumor. Spindle cell lipomas arising in the tongue exhibit microscopic features identical to those occurring in other soft tissue sites [22]. The tumor is characteristically composed of a mixture of mature adipocytes and cytologically bland spindle cells. The two components may be present in variable proportions with either element predominating in a given tumor. The spindle cells are typically associated with bundles of brightly eosinophilic collagen with a wiry or ropey appearance. A

Table 3 Summary of current series combined with previously reported cases of spindle cell lipoma of the tongue

Characteristics[a]	Value
Total number of patients	32
Gender	
Male	17
Female	9
Age (in years)	
Range	31–78
Mean	58.2
Median	62.0
Symptom duration (in months)	
Range	0.25–144
Mean	17.4
Median	3.0
Clinical presentation	
Painless mass/ nodule/swelling	16
Slowly enlarging mass	3
Painful nodule	2
Dysarthria/ dysphagia	1
Incidental finding	1
Size (cm)	
Range	0.2–3.5
Mean	1.4
Median	1.1
Laterality	
Right	4
Left	10
Midline	3
Bilateral	2
Patients with follow up	18
Alive, no evidence of disease	18
Follow up (months)	
Range	10–118
Mean	34.6
Median	22.0

[a] Data parameters listed were not stated in all reported cases

myxoid stromal matrix is not uncommon and can be a prominent feature.

Spindle cell lipoma and pleomorphic lipoma, based on shared clinicopathologic and genetic features, are considered a single entity, the latter differing only by the presence of enlarged multinucleated stromal giant cells [23]. Rare examples of pleomorphic lipoma involving the tongue have been reported [24, 25], however, none of the cases in the present series exhibited the characteristic atypical pleomorphic or floret-like giant cells. Similarly we did not encounter any lingual examples of lesions described as pseudoangiomatous [26] or low fat/fat free [27] variants of spindle cell lipoma recognized at other soft tissue sites.

By immunohistochemistry, the spindle cells in spindle cell lipoma are consistently positive for CD34. CD34 expression is, however, a ubiquitous finding in various other lipomatous and nonlipomatous soft tissue tumors; thus, this marker has a somewhat limited role in the diagnosis of spindle cell lipoma. The lesional spindle cells are negative for S-100 protein and actins, but may occasionally be positive for desmin [28]. Overall, the immunohistochemical profile of spindle cell lipoma is not unique, so the diagnosis is established based primarily on histologic findings.

When considering a diagnosis of lingual spindle cell lipoma it is important to exclude the possibility of an atypical lipomatous tumor/well differentiated liposarcoma. A recent review of oral cavity atypical lipomatous tumor/well differentiated liposarcoma showed the tongue specifically to be involved in 55 % of cases [29]. Similar to spindle cell lipomas, liposarcomas affecting the tongue typically present clinically as painless, slow growing masses [29, 30]. Histologically, atypical lipomatous tumor/well differentiated liposarcoma can exhibit a spindle cell component that can lead to confusion with spindle cell lipoma [29, 30]. Features that distinguish atypical lipomatous tumor/well differentiated liposarcoma from spindle cell lipoma include significant variation in adipocyte size and shape, fibrous septa with atypical stromal cells exhibiting nuclear hyperchromasia, and the presence of more than an occasional lipoblast [29, 30]. Rare lipoblasts may occur in spindle cell lipoma but are never a prominent finding. Pseudo-lipoblastic changes attributed to atrophy resulting in adipocytes with decreased cytoplasmic lipid and more prominent nuclei are not uncommon in oral cavity spindle cell lipomas [13, 16] and should be distinguished from true lipoblasts that exhibit enlarged, hyperchromatic, irregularly shaped nuclei.

Spindle cell lipoma, when accompanied by a predominantly myxoid stroma, can be potentially mistaken for myxoid liposarcoma. Spindle cell lipoma lacks the rich arborizing capillary network and small signet ring lipoblasts that are characteristic features of myxoid liposarcoma. Conversely, the presence of thick collagen bundles and areas of prominent spindling point to a diagnosis of spindle cell lipoma, as these findings are typically absent in myxoid liposarcoma. In difficult cases, molecular assays to detect the presence of a *FUS-DDIT3* fusion can be employed to confirm a diagnosis of myxoid liposarcoma.

When the myxoid background is prominent, a pleomorphic adenoma with lipomatous change/metaplasia may also be included in the differential diagnosis. However, the

lack of a plasmacytoid appearance, epithelial and myoepithelial elements, along with immunoreactivity with p63, pan-cytokeratin, S-100 protein and GFAP, should help with this distinction.

Two otherwise typical cases of spindle cell lipoma in the present series showed an abundant myxoid matrix accompanied by areas of small multivacuolated cells creating an appearance reminiscent of chondroid lipoma. The latter tumor, however, is generally devoid of spindle cells and lacks the conspicuous ropey collagen fibers of spindle cell lipoma [31].

While the morphologic appearance of spindle cell lipoma is characteristic and easily recognized in most instances, variations in the quantity and distribution of the spindle cell component of the tumor can lead to the consideration of alternative diagnoses. Once liposarcoma has been excluded, the principle entities in the differential diagnosis of spindle cell lipoma are non-lipomatous neoplasms characterized by the presence of spindle cells and a component of mature adipose tissue, which include fat-forming solitary fibrous tumor (previously known as lipomatous hemangiopericytoma), mammary-type myofibroblastoma, and cellular angiofibroma. Lingual examples of each of these lesions have been reported, though are exceedingly rare [32–34].

Similar to spindle cell lipoma, fat-forming solitary fibrous tumor is composed of an admixture of lipomatous and CD34 positive spindle cell elements [35, 36]. In contrast with fat-forming solitary fibrous tumor, blood vessels are generally inconspicuous in spindle cell lipoma; in particular, the presence of a prominent ectatic branching vasculature, while a characteristic feature of fat-forming solitary fibrous tumor, would be unusual for a spindle cell lipoma. In problematic cases, studies have shown STAT6 to be a potentially useful immunohistochemical marker for solitary fibrous tumor, reflecting the recent discovery of *NAB2–STAT6* gene fusions in the majority of these neoplasms [37]. Nuclear overexpression of the STAT6 protein has been shown to be typically absent in neoplasms that histologically mimic solitary fibrous tumor, including spindle cell lipoma [37].

Although presently recognized and categorized as clinicopathologically distinct tumors, some regard spindle cell lipoma, mammary-type myofibroblastoma, and cellular angiofibroma to be morphologic variants of a single entity based on the demonstration of shared histologic and genetic features [38–40]. The latter include alterations of chromosome 13 leading to deletion of 13q14 and loss of the *RB1* and *FOXO1* loci [38–40]. Microscopically, intersecting fascicles of spindle cells and more prominent, thickened, hyalinized bands of collagen are findings that would favor a mammary-type myofibroblastoma over spindle cell lipoma [41]. Although both tumors express CD34, desmin positivity is more consistently observed in mammary-type myofibroblastoma.

Intralesional fat is common in cellular angiofibroma, which along with the spindle cell component, results in some morphologic overlap with spindle cell lipoma [39, 42, 43]. The latter, however, lacks the conspicuous, thick walled, hyalinized vessels characteristic of cellular angiofibroma. In addition, the stromal collagen of spindle cell lipoma is more eosinophilic and ropey as compared with that of cellular angiofibroma, which has a more delicate and wispy appearance [39, 42, 43]. Immunohistochemical studies do not reliably separate the two entities, as cellular angiofibromas show variable immunoreactivity for CD34, as well as desmin and smooth muscle actin.

In summary, spindle cell lipomas arising in the tongue are rare. The present series of cases serves to further elucidate the clinical and pathologic features of this uncommon variant of lipoma affecting this particular anatomic site. Spindle cell lipoma is histologically distinctive, but may be easily mistaken for other lipomatous and non-lipogenic neoplasms, both benign and malignant. Lingual spindle cell lipoma follows a benign clinical course with no risk of recurrence. As such, these lesions are best managed by simple local excision.

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