Vascular leiomyoma of the oral cavity. Clinical, histopathological and immunohistochemical characteristics. Presentation of five cases and review of the literature

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Abstract

Leiomyoma, a benign neoplasia arising from smooth muscle is an uncommon neoplasia of the oral cavity. The most common histological subtype in the oral cavity is the vascular one. To supplement information on vascular leiomyoma of the oral cavity (VLOC), we present cases of VLOC describing their clinical, histological, and immunohistochemical characteristics. Case reports. Five cases of VLOC (3 females; 2 males) from the Clinical and Experimental Pathology Laboratory, Dental School, National Autonomous University of México, are included. The most frequent clinical characteristic of VLOC was a single, asymptomatic, slow growing nodule. The age average of the cases was 40.6, however 3 out of our 5 cases were ≤ 40 years old at the moment of their diagnosis. The lesions were composed of fusiform cells arranged in bundles or fascicles. The neoplastic cells were characterized by eosinophilic cytoplasm and tapered nuclei. The presence of vascular spaces was prominent in all cases. The immunocharacteristics of VLOC neoplastic cells were: alpha smooth muscle (+); vimentin (+), desmin (+), CD34 (-) and S-100 protein (-). The endothelial cells of vascular spaces were CD34 (+). Differential diagnosis of VLOC with fusocellular neoplasm is discussed.

Key words: *Vascular leiomyoma, oral cavity.*

Introduction

Leiomyoma, a benign neoplasia arising from smooth muscle is an uncommon tumor of the head and neck region (1,2). Leiomyoma is a rare neoplasia of the oral cavity (1,2). It has been proposed that the origin of leiomyoma in the oral cavity arises from vascular smooth muscle and excretory ducts of salivary glands (3,4). The clinical characteristics of vascular leiomyoma of the oral cavity (VLOC) include: asymptomatic nodules of variable size and slow growth, located principally in the tongue, lips, palate and buccal mucosa (5). Most of the VLOC are diagnosed during the 5th decade of life (1-5). Surgical excision is an effective treatment for this neoplasia (5). With the aim of better understanding this particular neoplasm we present 5 cases of vascular leiomyoma of the oral cavity and additionally we performed a review of the scientific literature updating their clinical, histological and immunohistochemical features.

Case Reports

All the cases were referred to the Oral Pathology Service, Postgraduate Division, Dental School, National Autonomous University of México. In all cases, excisional biopsies were performed in the Maxillofacial and Oral Surgery service at the same institution. All of the surgical samples were fixed in 10% buffer formalin for a minimum

of 48 hours, embedded in paraffin and cut at 5 μm to be stained with Hematoxylin-Eosin technique. Additionally, histological slides were obtained to performed immunohistochemical technique.

Case 1

A 39 year old Hispanic female was referred by a private dentist because of a swelling in the retromolar area. On clinical inspection a unique asymptomatic, mobile, well delimited nodule was observed in the lower left retromolar area. The patient was not aware of an increase in the size of the nodule during the previous year. Macroscopically the specimen (0.9 x 0.6 x 1 cm) had an irregular oval shape, a smooth surface and a brownish color. Microscopically the lesion was composed of an abnormal proliferation of mesenchymal cells with a fusiform aspect, eosinophilic cytoplasm and tapered nuclei. Several vascular formations were observed. The stroma was characterized by fibrous connective tissue with inflammatory cells and focal hemorrhagic areas. We emitted a diagnosis of vascular leiomyoma.

Case 2

A 27 year old Hispanic female was referred by her private dentist because during a routine radiographic inspection a unilocular radiolucency located in the left mandibular region was found. The patient was not aware of the presence of the lesion. Macroscopically the specimen (1.4 x 1.3 x 1 cm) had an oval shape, a resilient consistency, and a brownish color with hemorrhagic areas on its surface. Microscopically the lesion consisted of a well circumscribed lesion formed by bundles of fusiform cells with elongated nuclei. The neoplastic cells were arranged around vascular spaces that were lined by endothelial cells. We emitted a diagnosis of an intraosseous vascular leiomyoma.

Case 3

A 43 year old Hispanic female was admitted at the Oral Pathology service because of the presence of a well circumscribed, firm, asymptomatic and mobile nodule in the lower lip. The patient had been aware of the lesion for 9 months. Macroscopically the specimen (0.7 x 0.5 x 0.4 cm), had an irregular oval shape, a smooth surface and a resilient consistency. Microscopically the lesion consisted of a well defined proliferation of fusiform cells with eosinophilic cytoplasm and tapered nuclei with rounded endings. The neoplastic cells were arranged in intercalated fascicules. We observed several blood vessels. We emitted a diagnosis of vascular leiomyoma.

Case 4

A 36 year old Hispanic male, was referred by his private dentist because of the presence of a unique, firm, well circumscribed nodule in the mucosa of the upper lip mucosa (Figure 1). The lesion had been asymptomatic during 7 years, since the patient noticed the lesion. Macroscopically the specimen (1.5 x 1.0 x 1.0 cm) had an irregular shape, a light brown color with hemorrhagic areas and a firm consistency. Microscopically it consisted of a partially circumscribed neoplasia with a biphasic cellular pattern: areas of fusiform cells characterized by elongated nuclei (cigar-like shape) with eosinophilic cytoplasm and areas of epithelial-like cells with cells characterized by basophilic nuclei. The vascular component was predominant in the fusiform cell area. Based on these characteristics, we emitted a diagnosis of vascular leiomyoma.

Case 5

A 48 year old male was referred by his private dentist because of a swelling in his upper lip. On clinical inspection, an asymptomatic swelling, covered by mucosa with inconspicuous characteristics was found. Macroscopically the specimen (1.7 x 1.0 x 1.0 cm) had an ovoid shape and a brownish color. Microscopically fusiform cell proliferation, with elongated nuclei and eosinophilic cytoplasm was observed. Several blood vessels lined by a thin layer of endothelial cells were observed intercalated in the fascicules. The neoplasia was well circumscribed and evidenced recent hemorrhage in the periphery. We emitted a diagnosis of vascular leiomyoma.

Figure 1 and 2 show the most striking clinical and histological characteristics of VLOC reported in the present paper.

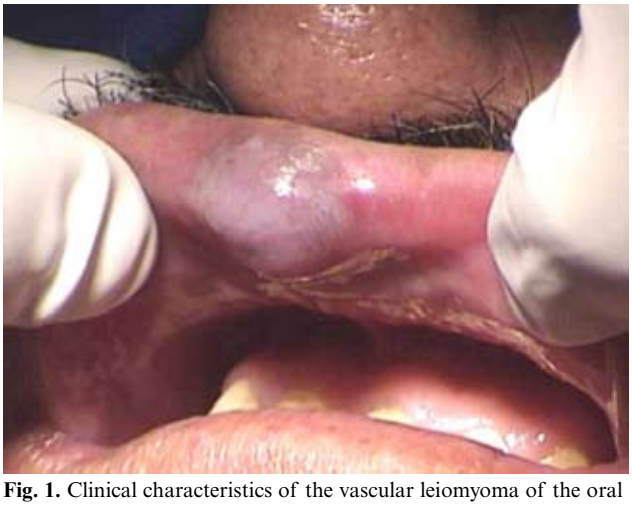

Fig. 1. Clinical characteristics of the vascular leiomyoma of the oral cavity.

This microphotography shows the typical clinic aspect of vascular leiomyoma, e.g. a single, asymptomatic, slow growth nodule (Case 4).

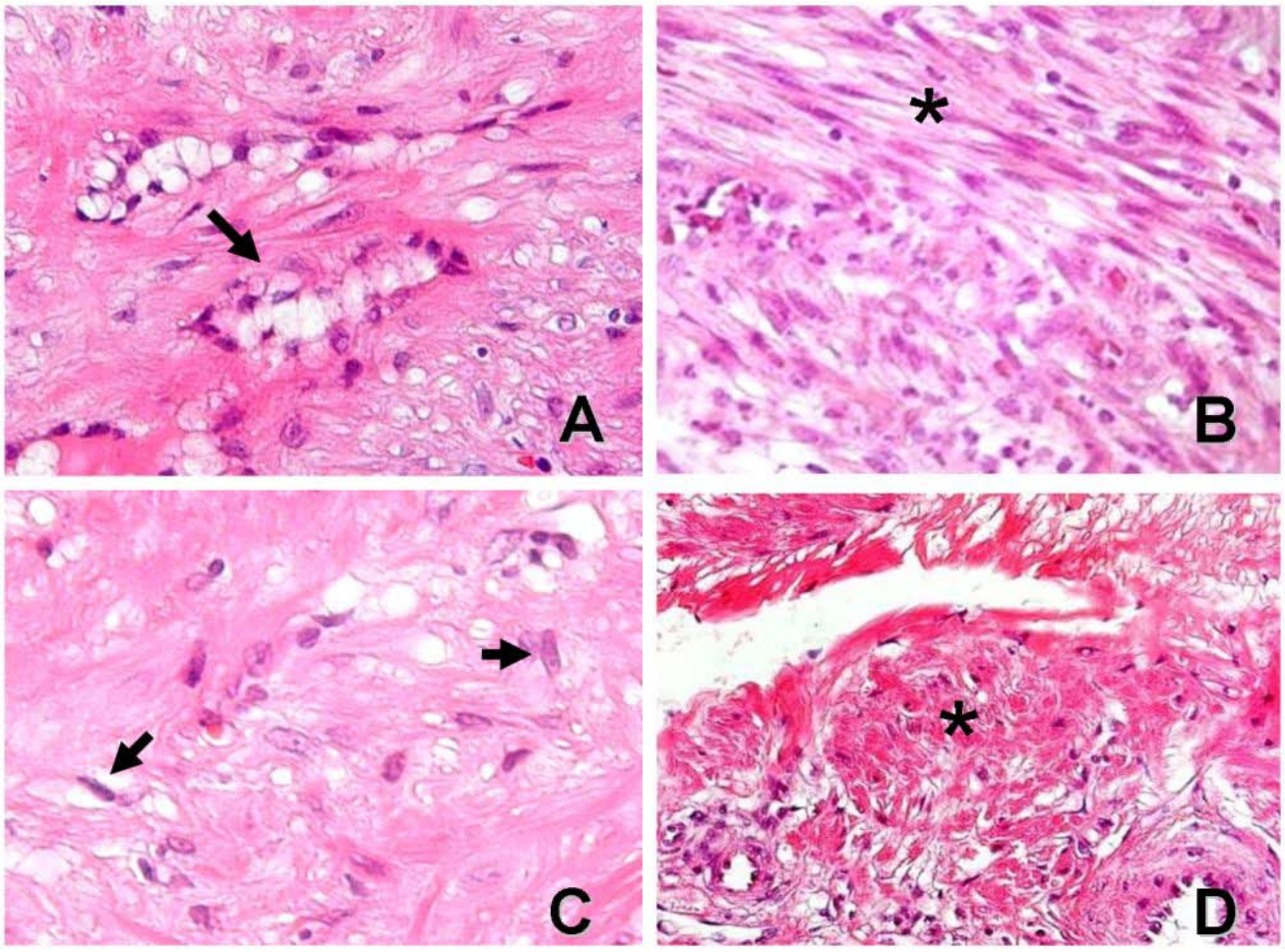

Fig. 2. Histopatological characteristics of the vascular leiomyoma of the oral cavity.

A).- Observe the vascular spaces (arrow) in relation to stromal oedema.
Case 1, H-E- X200.

B).- This microphotography show the fusocellular pattern (*) of vascular leiomyoma.
Case 2. H-E X400

C).- In this microphotography it can observes tapered cells with a cigar-shape nuclei (arrows), conspicuous characteristic of vascular leiomyoma neoplasm cells.
Case 3; H-E X400

D).- This microphotography show a heterogeneous cellular area, specifically an the epithelial-like cells area (*). Case 4; H–E X200.

Immunohistochemistry

All cases were analyzed by a immunohistochemical technique using the following immunemarkers: anti-vimentin (Bio SB®, Santa Bárbara, CA), anti-actin (Biogenex®, San Ramón, CA), anti-CD34 (Biogenex®, San Ramón, CA) and anti-S-100 protein (Bio SB®, Santa Bárbara, CA) antibodies. In all of the cases we were able to observe a strong anti-actin immunoreactivity of the cellular membrane of the neoplastic cells (Fig 3-A). Regarding to anti-desmin antibody we observed a positive immunoexpression of the cytoplasm of neoplastic cells in all cases (Fig 3-B). In regard to CD34 antibody, there was positive immunoreactivity of the endothelial cells that lined the vascular spaces (Fig 3-C). In all cases the neoplastic cells showed positive immunoreactivity against vimentin, the cytoplasm of the fusiform cells was the site of immunoexpression (Fig 3-D). We did not observe immunoreaction to anti-CD34 in any neoplastic cell. The epithelia-like cells (case 4) expressed positive immunoreaction for smooth muscle actin and vimentin. We did not find evidence of positive immunoreaction to protein S-100 in any neoplastic cell from any case.

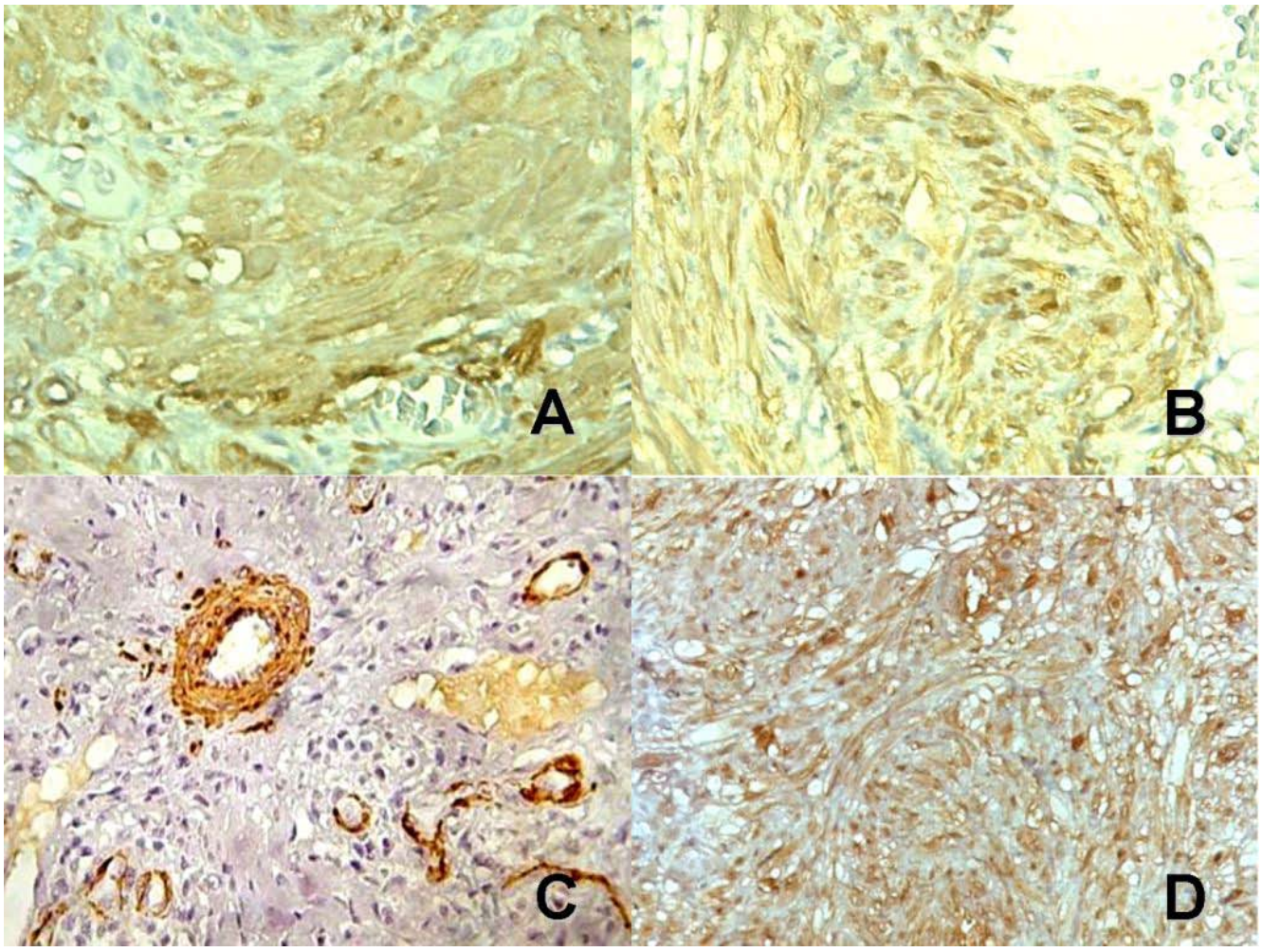

Fig. 3. Immunohistochemical characteristics of the vascular leiomyoma of the oral cavity.

A).- Positive immunoreactivity against anti alpha-actin smooth muscle antibody showed by cellular of neoplastic cells. X100.

B).- Positive immunoreaction against anti-desmin antibody showed by cytoplasm of neoplastic cells. X200.

C).- Positive immunoreaction against anti-CD34 antibody showed by the endothelial cells lined the vascular spaces. X100.

D).- Positive immunoreaction against anti-vimentin antibody showed by cytoplasm of fusiform cells. X200.

Discussion

Benign neoplasms that arise from smooth muscle are uncommon in the oral cavity region (1, 2). The VLOC is characterized clinically by asymptomatic solitary nodules, of long evolution and slow growth (6, 7). None of our cases was over 2cm diameter. The mucosa that covers them is similar to the adjacent mucosa.

The highest prevalence of head and neck leiomyoma is observed in 4th and 5th decade of life, with a peak of prevalence between 40 and 49 years of age (8). In our cases, the average age was 40.6 years; however 60% of our patients were under 40 years of age at the moment of their diagnosis. 3 of our cases were in female patients. The gender preference for female is agreement with the literature (1- 6).

It is important to highlight the case of an oral intraosseous leiomyoma (case 3); to date and to the best of our knowledge only 15 cases of oral intraosseous leiomyoma have been reported. Radiographically the oral intraosseous leiomyoma is characterized by an uni or multilocular radiolucency, generally with a sclerotic border without cortical displacement. It has been suggested that oral intraosseous leiomyoma arises from the muscle layer of the intramandibular blood vessels or from embrionary rests

of smooth muscle trapped in the mandibular region (for a review see 9, 10).

Several histological types of leiomyoma have been reported in the literature: solid, vascular (angiomyoma or angioleiomyoma) and epithelioid (11). Cases with predominant granular cells whose immunophenotype is in accordance to the leiomyoma have also been reported (12). The vascular variant is the most frequent in the oral cavity; 75% of all cases correspond to this histological type (1 – 6). Smooth muscle is scarce in the oral cavity, however this region is rich in blood vessels. Therefore it has been proposed that media layer of blood vessels may be the origin of oral cavity vascular leiomyoma (1).

The vascular leiomyoma is characterized by a well defined proliferation of mesenchymal tapered cells with eosinophilic cytoplasm and elongated basophilic nuclei that show tapered endings (cigar like shape nuclei). The vascular spaces which are lined by a single layer of endothelial cells (2-6, 11) are a constant feature in vascular leiomyoma. It is not uncommon to observe vascular leiomyoma with an heterogenic cell population; two or more different histological patterns could be interlaced in the same lesion, as in case 4.In this particular case, fusiform and epithelial-like cells areas were observed.

Scientific literature about the immunohistochemical characteristics of leiomyoma is scarce (3, 7, 13). The importance of assessing their immunocharacteristics is to contribute to differential diagnosis, specifically to rule out other neoplasia of the soft tissue, mostly mesenchymal lesions with predominance of fusiform cells (14). Smooth muscle actin corresponds to the alpha fraction of the actin chain (15); it is a specific immunomarker of smooth muscle although it could also have an immunoreaction in skeletal muscle (15). In all our cases the neoplastic cells showed positive immunoreaction to actin. Vimentin is a structural protein of the cytoplasm filaments of mesenchymal cells (15). Its expression in our VLOC cases was observed in the cytoplasm of the neoplastic cell population. CD34 is a transmembrane protein that is broadly expressed by vascular endothelium (15). In all of our cases, the endothelial cells presented immunoreactivity against anti-CD34 antibody.

Differential diagnosis of VLOC should include soft tissue neoplasias characterized by fusiform cells (16, 17). The solitary myofibroma of the oral cavity is a benign neoplasm characterized by proliferations of fibroblasts and myofibroblasts (18, 19). It is mostly observed between the 1st and 2nd decades of life, in contrast to leiomyomas which are frequent in the adult population. Histologically the solitary myofibromas are well defined lesions with a cellular component of fusiform cells with a tapered nucleus and undefined cytoplasm borders (18, 19). The solitary myofibroma has an important vascular component; therefore this neoplasm could show an angiopericytoma-like aspect with a peripheral desmoplastic reaction (18, 19). The typical immunophenotype of myofibroma is very similar to the leiomyoma: positive immunoreactivity against actin and vimentin. However, VLOC is S-100 negative and desmin positive, while myofibroma is S-100 positive (18, 19). Another differential diagnosis of VLOC is oral cavity myopericytoma (17). The oral cavity myopericytoma shares clinical and histological characteristics with VLOC. The myopericytoma belongs to the myoid and pericytoid neoplasms. The histological characteristics include a tapered cellular population, with elongated nucleus with round endings (cigar shape) similar that to observed in vascular leiomyoma (20). The intravascular variant of myopericytoma is a rare variant characterized by an intravascular mass similar in appearance to vascular leiomyoma (21). On the other hand, the oral inflammatory myofibroblastic tumor is a controversial lesion characterized by fusiform cells arranged in whirls (22, 23). The immunophenotype of oral inflammatory myofibroblastic tumors share some characteristics with vascular leiomyoma. Both lesions are vimentin positive, but leiomyoma are alpha-actin smooth muscle positive and desmin positive; while oral inflammatory myofibroblastic tumors show variable immunoreactivity against alpha-actin smooth muscle and against desmin (22, 23). A comparison of the immunophenotype of vascular leiomyoma versus some soft tissue fusocellular neoplasias is shown in table.

In conclusion, the oral cavity leiomyoma is a benign neoplasm characterized by a small (<2 cm), solitary, asymptomatic, nodular mass, located more frequently in

Table 1. Immunohistochemical profile of several fusocellular neoplasms, including the vascular leiomyoma.

Neoplasia	Antibodies				
	Vimetin	Desmin	Actin	CD34	S-100
Leiomyoma	+	+	+	-	-
Myofibroma	+	-	+	-	-/+
Myopericytoma	+	-	+	-	-
Inflammatory Myofibroblastic Tumor	+	+/-	+	-	-
Histiocytoma	+	+	+/-	-/+	-

the lower lip with predilection for 35 – 49 years old women. Histologically it is characterized by tapered cells, with undefined cytoplasm borders, hyperchromatic nucleus with rounded endings (cigar shape) where the vascular component is secondary to the cellular one. The immunophenotype of the neoplastic cells is: alpha-smooth muscle actin (+), vimentin (+), desmin (+), CD34 (-) (although the endothelium of the vascular spaces is CD34 +); and S-100 protein (-).

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