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Case Report

Gingival angioleiomyoma in children: a case report and review of the literature

Giovanna Ribeiro Souto[a,*], Leandro Junqueira de Oliveira[a], Martinho Campolina Rebello Horta[a], Ricardo Alves Mesquita[b], Paulo Eduardo Alencar de Souza[a]

[a] Department of Dentistry, Pontifícia Universidade Católica de Minas Gerais, Belo Horizonte, Brazil
[b] Department of Oral Surgery and Pathology, School of Dentistry, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

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ABSTRACT

Angioleiomyomas are common benign neoplasms in the extremities, but they are rare in the oral cavity, particularly in the upper gingiva and among children. Because of molecular genetic data, the WHO classification published in 2013 included angioleiomyomas under the heading for pericytic tumors for the first time. The aim of the present study was to report a rare case of angioleiomyoma in a child, with unusual location, together with histochemical and immunohistochemistry findings. A PubMed search to identify cases described in the English-language literature was also performed. Nine angioleiomyomas located in gingival sites, including the present case, have been related. Histologically, it is often difficult to differentiate angioleiomyomas from other types of spindle-cell tumors such as myofibromas and myopericytomas. Masson's trichrome stain and immunohistochemistry detection were shown to be useful. Due to infrequent reports of angioleiomyomas in this location and this early in life, it was important to record this case for further reference in the future.

1. Introduction

An angioleiomyoma is a common benign neoplasm in the extremities. However, they are rarely seen in the head and neck, and especially in the oral cavity [1,2]. Lesions usually develop between the fourth and sixth decades of life [1], with a slightly higher incidence in males [2]. Lesions usually present as small, slowly enlarging masses, and pain is reported by about half of the patients. Possible causes have been implicated including trauma, topical estrogen, hormonal imbalance, infection, arteriovenous malformation, venous stasis, and genetic translocation [3].

This type of tumor is characterized histologically by a circumscribed lesion with distinct eosinophilic spindle cells with blunt-ended, cigar-shaped nuclei and perinuclear vacuoles [2]. Angioleiomyomas are composed of mature smooth-muscle bundles with many vascular channels and classified as three histological variants: solid, venous, and cavernous subtypes [1]. It is suggested that myopericytomas and angioleiomyomas, particularly in venous- or cavernous-type tumors, are closely related because of morphological overlap and similar immunohistochemistry findings of smooth-muscle markers [2]. In the 2013 World Health Organization (WHO) Classification of Soft Tissue Tumors, the angioleiomyoma (vascular leiomyoma) was reclassified in the category of pericytic (perivascular) tumors, or the group of myopericytomas, which also included myofibromas/myofibromatosis [4]. The 2018 WHO Classification of Skin Tumours described the angioleiomyoma as a member of perivascular myoid family of tumors, together with myopericytoma, myofibroma and glomus tumour [5].

Although the angioleiomyoma represents a rare and benign tumor in the oral cavity, and surgery is almost always curative, it is important to recognize the differential diagnostic characteristics between angioleiomyomas and other smooth-muscle cell-like tumors, including myofibroblastic tumors. The aim of the present case report is to describe a rare case of angioleiomyoma in a child and to highlight its unusual location, together with histochemical and immunohistochemistry findings. In addition, a literature review of previous reports of gingival angioleiomyoma was performed and compared.

2. Case report

An 11-year-old boy was referred to the Department of Dentistry at the Pontifícia Universidade Católica de Minas Gerais (PUC Minas) for

* Corresponding author at: Departamento de Odontologia – ICBS/PUC Minas, Rua Dom José Gaspar, 500 – Prédio 45 – sala 111, Laboratório de Biologia Oral Coração Eucarístico, Belo Horizonte, MG, 30.535-610, Brazil.
E-mail address: grsouto@hotmail.com (G.R. Souto).

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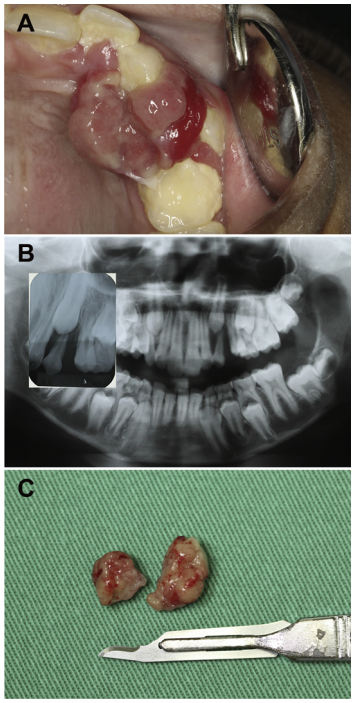

Fig. 1. Clinical aspect. (A) Intraoral examination showed a firm mass in upper gingival. (B) panoramic and periapical radiograph showing no bone changes. (C) macroscopic aspect of excised specimen.

treatment of a symptomatic swelling of the gingiva that had been present for approximately two months. Medical and socioeconomic conditions were not contributory. Intraoral examination found a firm mass in the gingiva in the region of the upper-left lateral incisor, deciduous canine, and first premolar. The tumor was pedunculated, and the overlying mucosal surface presented an ulcerated area with reddish color. The tumor was 15 mm at its longest measurement (Fig. 1A). The panoramic and periapical radiographs revealed no bone changes (Fig. 1B). Differential diagnosis at the time of the clinical examination included pyogenic granuloma, peripheral ossifying fibroma, peripheral giant-cell lesion, and fibrous hyperplasia.

The patient was submitted to an excisional biopsy (Fig. 1C), and the specimen was sent to the Oral Pathology Service. Sections stained with hematoxylin and eosin (H&E) showed a solid and uniform tumor, composed mostly of spindle-shaped cells and multiple small to large dilated vascular channels. Intervascular areas showed spindle cells with eosinophilic cytoplasm and elongated, blunt-ended, cigar-shaped nuclei with perinuclear vacuole (Fig. 2A–C). The microscopic features were suggestive of angioleiomyoma and solitary fibrous tumor, and Masson's trichrome stain and immunohistochemistry were performed to confirm the diagnosis.

Masson's trichrome stain showed minimal delicate blue fibrous tissue surrounding the red smooth-muscle cells (Fig. 2D). Immunohistochemistry analysis included alpha-smooth muscle actin (α-SMA, dilution 1:150, Dako Corporation, Carpinteria, CA, USA), muscle-specific actin (MSA) (HHF-35, dilution 1:500, Dako Corporation, Carpinteria, CA, USA), h-Caldesmon (h-CA, dilution 1:100, Dako Corporation, Carpinteria, CA, USA), Calponin (dilution 1:50, Dako Corporation, Carpinteria, CA, USA), Desmin (dilution 1:50, Dako Corporation, Carpinteria, CA, USA) and CD34 (dilution 1:25, Novocastra, Newcastle, United Kingdom). Serial sections of 3 μm in thickness from paraffin-embedded blocks were deparaffinized and dehydrated. Antigen retrieval was conducted with a 10-mM citrate buffer (Labsynth, Diadema, SP, Brazil), pH = 6.0, for 20 min at 98 °C. Endogenous peroxidase activity was blocked using 0.3% hydrogen peroxide. Primary antibodies were incubated at room temperature for 1 h. Detection was

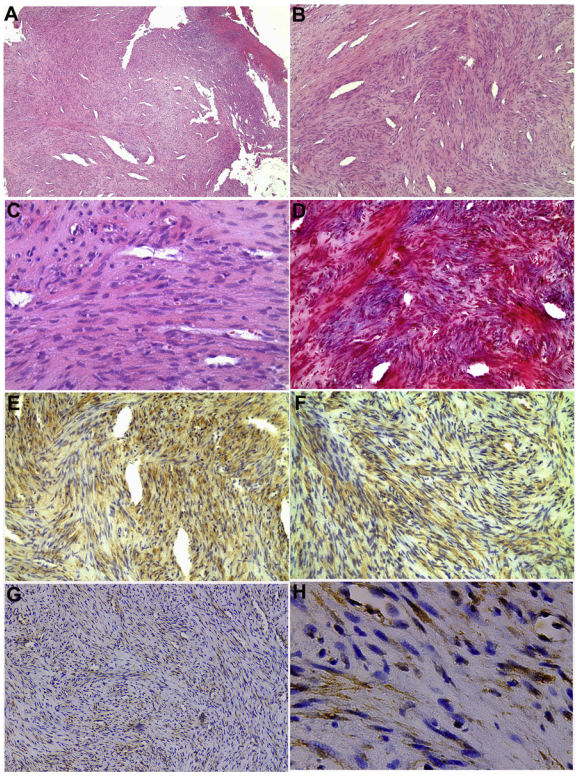

Fig. 2. Section stained in H&E. (A) solid and uniform tumor (×50). (B) fascicles of spindle-shaped cells between slit-like vessels (narrow) (×100). (C) and spindle cells with eosinophilic cytoplasm and elongated, blunt-ended, cigar-shaped nuclei (narrow) with perinuclear vacuole (×400). (D) section stained in Masson's trichrome (×100). (E) immunoreaction for MSA (HHF-35) and (F) α-SMA (IHQ stain, ×100). Immunoreaction for Calponin (G) (IHQ stain, ×100) and (H) (IHQ stain, ×400).

performed using the LSAB system (Dako, Carpinteria, CA, USA). Subsequently, 3,3'-diaminobenzidine tetrahydrochloride chromogen (DAB, Sigma–Aldrich, St. Louis, MO) and Mayer's hematoxylin were used for counter-staining. Appropriate positive and negative controls were included in the immunohistochemistry assays. The spindle-shaped cells were immunoreactive for HHF-35 (Fig. 2E), α-SMA (Fig. 2F), Calponin (Fig. 2G and H) and negative for h-Caldesmon and Desmin. The endothelial cells along the walls of the prominent vascular channels were immunoreactive for CD34. The final diagnosis was angioleiomyoma, and the patient presented no further complications following four years and three months of follow-up (Fig. 3).

3. Discussion

Angioleiomyomas are benign tumors rarely found in the oral cavity, particularly in children [1,6]. The lip, palate, and tongue are the most common sites in the oral cavity for angioleiomyomas [6]. Lesions in gingival location are rare. In the present literature review, eight cases of gingival angioleiomioma have been reported. The age ranged from 14

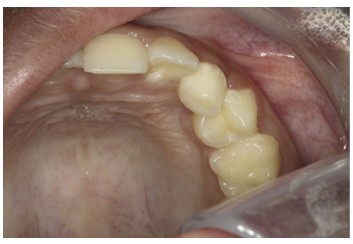

Fig. 3. Clinical features 30 months after surgical treatment.

Table 1
Clinical data, immunohistochemical analysis and histochemical stain of gingival angioleiomyomas reported in the English-language literature from 1964 to date.

Author (Year)	Site (gingival)	Gender	age	Symptoms	Immunohistochemical analysis							Histochemical stain	
					Vim	Desm	SMA	HHF-35	Calp	CD34	h-Ca	Masson's trichrome	Van Gieson
1. Liu et al. [2]	NI	M	20	Symptomatic	++	+	++	NR	NR	+*	NR	†	†
2. Brooks et al. [6]	NI	F	68	NI	NR	NR	NR	NR	NR	NR	NR	†	NR
3. Utz et al. [8]	NI	F	29	Asymptomatic	NR	NR	NR	NR	NR	NR	NR	†	NR
4. Menditti et al. [14]	upper	M	14	Asymptomatic	NR	NR	NR	++	NR	NR	NR	NR	†
5. Ranjan and Singh [15]	lower	F	45	Asymptomatic	NR	NR	++	NR	NR	NR	NR	NR	NR
6. Bajpai et al. [16]	lower	M	39	Asymptomatic	NR	NR	NR	NR	NR	NR	NR	NR	NR
7. Arpag et al. [17]	lower	M	25	Asymptomatic	NR	NR	++	NR	NR	NR	NR	NR	NR
8. Arpag et al. [17]	upper	F	55	Asymptomatic	NR	NR	++	NR	NR	NR	NR	NR	NR
Present case	upper	M	11	Symptomatic	NR	–	++	++	+	+*	–	†	NR

NI: no information; M: male; F: female; Vim: vimentin; Desm: desmina; SMA: smooth muscle actin; HHF-35: muscle specific actin; Calp: calponin; h-Ca: h-Caldesmon; ++: reaction diffusely positive; +: reaction focally positive; -: negative reaction; NR: no reaction. +*: vessels stained positively; †: Intense red staining.

to 68 years (average age, 34 years old), and there was a slightly higher incidence in men (male-to-female ratio is 5:4) (Table 1). This article reported a case of angioleiomyoma located in the upper gingiva of a 11-year-old patient. The tumor in the case reported presented as a nodular, soft-tissue mass 1.5 cm in size that was pediculated, firm, and painful, with slow growth over two months.

Histologically, it is often difficult to differentiate angioleiomyomas from other types of spindle-cell tumors, especially myofibromas and myopericytomas [6]. Myofibromas reveal diffuse sheets of dense, cellular tissue with an occasional nodular arrangement. The amount of stroma is variable, and hyalinized dense collagen may also be found. However, spindle cells of myofibromas/myofibromatosis are remarkably similar and often indistinguishable from smooth-muscle cells. Therefore, myofibromas may be confused with smooth-muscle lesions [7]. Histochemical analysis such as Masson's trichrome stain and immunohistochemical detection are useful in differential diagnosis [2], as reported in the current case. However, in the current literature, only one case found in gingiva used a complete immunohistochemical panel [2], and only four cases used Masson's trichrome stain in the diagnosis [2,6,8]. With Masson's trichrome stain, the smooth-muscle cells' cytoplasm was stained red, while the collagenous fibrous tissue was stained blue. Myofibromas are composed of much more collagenous stroma intermixed with spindle cells, while smooth-muscle lesions showed only minimal delicate fibrous tissue surrounding the smooth-muscle cells and in the septa between the smooth-muscle masses [9]. In the present case, a red mass of smooth-muscle tumor surrounded by blue fibrous tissue was observed. In regard to immunohistochemistry detection, in the case reported, positive expression of α-SMA, HHF-35 and Calponin demonstrated the presence of smooth-muscle cells, and the positive expression of CD34 demonstrated the presence of vascular endothelium. Positive expression of α-SMA, HHF-35 and Calponin confirmed the smooth-muscle nature but was not conclusive. These markers are observed in myofibromas, myopericytomas, and smooth-muscle lesions including leiomyomas and leiomyosarcomas [6,10]. Tumor cells in angioleiomyomas are diffusely and strongly reactive to SMA, MSA (HHF-35) and Calponin [5,11] as well as variably immunoreactive to h-Caldesmon [5]. Although desmin is expressed in most cases of angioleiomyoma [5,11], it was negative in the case reported. H-Caldesmon is a protein that has been thought to be expressed exclusively in vascular and visceral smooth-muscle cells (SMC). H-Caldesmon demonstrated to be a specific marker of both SMC and its neoplasms, and it may facilitate the differential diagnosis between lesions of smooth muscle and other tumors with SMC-like differentiation, including myofibroblastic tumors [12]. In the present case, h-Caldesmon presented a negative reaction, which may confirm the pericytic nature in the case related.

Differentiation between angioleiomyomas and other types of spindle-cell tumors, such as myofibromas, is very important. There are two major reasons why proper diagnosis has obvious implications for patients. First, myofibroma lesions could indicate myofibromatosis that has a multicentric nature, and thus, further investigation of visceral organ involvement might be indicated in order to prevent a misdiagnosis of tumor metastases. Second, misdiagnosis may lead to inappropriate treatment. The differential diagnosis in the present case of angioleiomyoma demonstrated this importance because the lesion was observed in a child and was in an unusual location in the gingiva. These two clinical characterizations are more frequently observed in myofibroma lesions [13].

In conclusion, the case reported represents an angioleiomyoma located in the gingiva found in the youngest patient thus far. In this case, Masson's trichrome stain and immunohistochemistry detection were demonstrated to be important methods in the differentiation between angioleiomyoma and myofibroma, since both lesions demonstrate different characteristic patterns. In the present case, misdiagnosis could have led to inappropriate treatment.

Ethical approval

The authors wish to declare that all experiments on human subjects were conducted in accordance with the Declaration of Helsinki. Patient consent was obtained.

Conflicts of interest

The authors declare there is no conflict of interest in this paper. The decision was not influenced by other or secondary interest.

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