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Giant cell angiofibroma of the oral cavity: A case report and review of the literature

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Abstract

Giant cell angiofibroma is a well-circumscribed, normally encapsulated, distinctive orbital soft tissue tumor. However, it is now recognized that this lesion can also present in other locations, including the oral cavity. The morphological hallmark is a richly vascularized, patternless spindle cell proliferation containing pseudovascular spaces and floret-type multinucleate giant cells. CD34 immunoreactivity, although not specific, represents the only immunohistochemical finding of potential diagnostic value. We present a case of a 44-year-old male Caucasian patient complaining of painless solitary nodule arising on the right buccal mucosa, which was diagnosed as giant cell angiofibroma. To the best of our knowledge, this is the third case of oral giant cell angiofibroma reported in the English-language literature.

Key words: *Giant cell angiofibroma, mouth, immunohistochemistry.*

Introduction

Giant cell angiofibroma (GCA) was first described in 1995 by Dei Tos et al. (1) as a distinctive orbital tumor occurring exclusively in male adults. GCA is a benign, mesenchymal lesion showing histological features intermediate between, but distinct from, solitary fibrous tumor (SFT) and giant cell fibroblastoma (GCF) of soft tissue. However, it is now recognized that this lesion can also occur in other locations, including the oral cavity. There are only two cases of oral GCA reported in the mouth (2,3), and we describe one case affecting the buccal mucosa, emphasizing the histopathological and immunohistochemical (IHC) features.

Case Report

A 44-year-old Caucasian male was referred to the Oral Diagnosis Clinic, University Center Hermínio Ometto – UNIARARAS, São Paulo, Brazil, complaining of a painless solitary swelling in the right side of the mouth. The patient was otherwise healthy, and the general medical history was noncontributory. He is a cigarette smoker for the last 26 years and refers daily beer consumption. Extraoral examination revealed reactive regional lymphadenopathy on the side right of the neck. Intraorally there was a painless, well-delimited, submucous nodular lesion of fibroelastic consistency. This was covered by normal mucosa, measuring 0.5 cm in diameter and it was located in

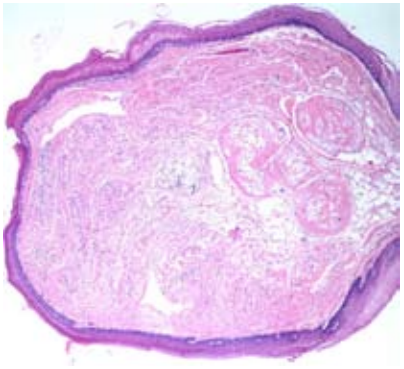

Fig. 1. Giant cell angiofibroma of the cheek. Low-power microscopic view showing a well-demarcated nodular tumor (H&E, OM X2,5).

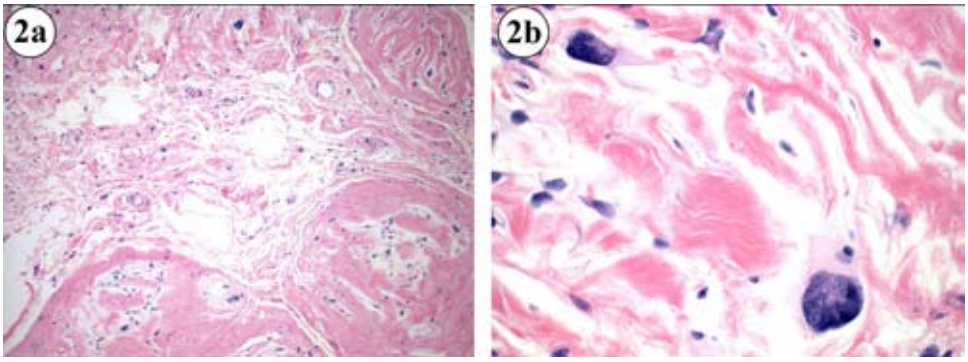

Fig. 2a. Higher magnification of figure 1, showing areas of sclerosis and hyalinized nodules, intermingled with variable amounts of blood vessels and pseudovascular spaces (H&E, OM X10). 2b. Multinucleated giant cells scattered among spindle- and stellate-shaped tumor cells (H&E, OM X40).

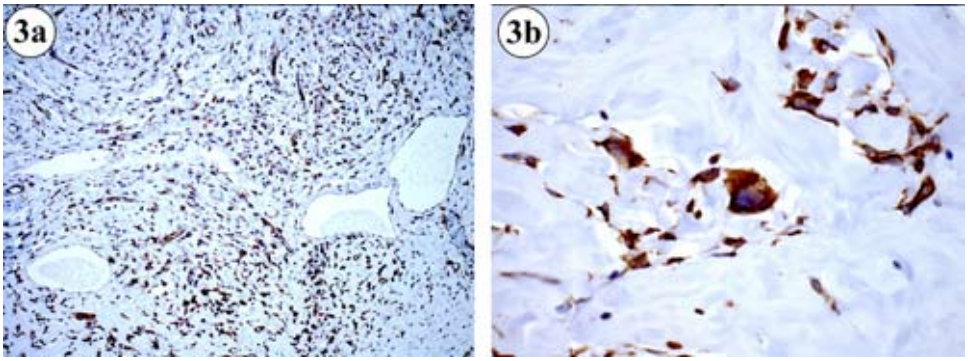

Fig. 3a. GCA showing immunoreactivity for vimentin in mononucleated tumor cells (IHC, OM X10), and multinucleated giant cells (3b) (IHC, OM X40).

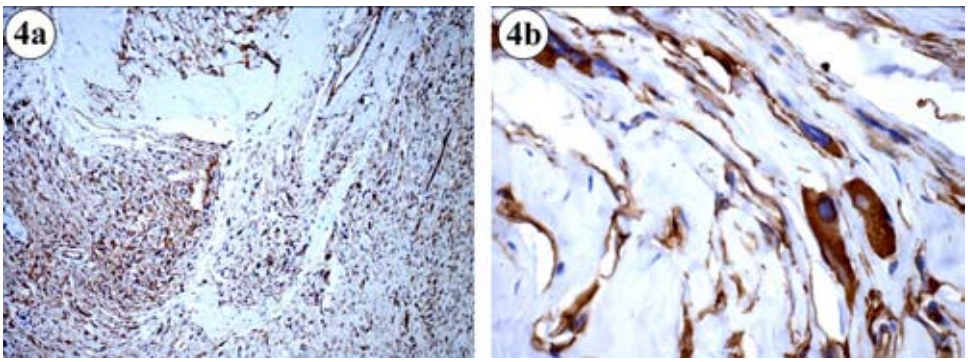

Fig. 4a. GCA showing strong immunoreactivity for CD34 in spindle and dendritic tumor cells (IHC, OM X10), and also multinucleated giant cells (4b) (IHC, OM X40).

Table 1. Antibodies used for immunohistochemical evaluation of giant cell angiofibroma of the oral cavity.

Antibody	Clone/Source	Dilution
Cytokeratin-cocktail	AE1/AE3, Dako®*	1:500
Vimentin	Vim3B4, Dako®*	1:400
Alfa-smooth muscle actin	1A4, Dako®*	1:400
Muscle specific actin	HHF35, Dako®*	1:800
S100	Polyclonal, Dako®*	1:12000
Desmin	D33, Dako®*	1:1000
CD68	PG-M1, Dako®*	1:400
CD34	QBEnd10, Dako®*	1:50
Bcl-2	124, Dako®*	1:50

* Dako, Dako Corporation, Carpinteria, Calif.

the right buccal mucosa, next to retromolar pad area. Our clinical diagnosis was of a benign glandular/mesenchymal neoplasia or fibrous hyperplasia. An excisional biopsy was carried out under local anesthesia, and the specimen was submitted to histopathological analysis.

Microscopic examination revealed a non-encapsulated, well-circumscribed nodule (Fig. 1), and two histological patterns could be distinguished. In the more superficial areas, the lesion showed increased cellularity, with elongated, spindled, and wavy cells, intermingled with variable amounts of blood vessels, pseudovascular spaces, and scarce multinucleated giant cells. The second pattern, in the deep zones of the lesion, revealed small hyalinized nodules containing small blood vessels, discreet pseudovascular spaces and scattered multinucleated giant cells with peripherally arranged nuclei that imparted a floret-like appearance (Figs. 2a and 2b). In addition, there was prominent sclerosis around blood vessels. A preliminary diagnosis of a benign spindle cell neoplasm with multinucleated giant cells was provided.

IHC analysis for pan-cytokeratin, vimentin, alfa-smooth muscle actin, muscle specific actin, S100, desmin, CD68, CD34, and bcl-2 was performed (Table 1). The mononucleated and multinucleated giant cells were diffusely positive for vimentin (Figs. 3a and 3b), CD34 (Figs. 4a and 4b), and weakly positive for bcl-2. CD34 highlighted in the mononuclear dendritic cells strands of thin stellate cytoplasm. Immunoreactivity for other antibodies used were uniformly negative. The final diagnosis was of GCA. After one year of follow-up no recurrence was observed.

Discussion

GCA is a distinctive benign, mesenchymal orbital tumor occurring exclusively in male adults. However, it is now recognized that this lesion can also present in other locations, and 18 cases were reported in extra-orbital sites as submandibular, parascapular, retroauricular, thigh, mediastinum, back, scalp, retroperitoneum, vulva, hip, forearm, groin, parotid, and neck (4-6). The mean age of affected patients was 45 years, with a range of 18 to 81 years. Interestingly, the extraorbital lesions predominantly affect women, corresponding to 66% of the cases. Only two cases arising in the oral cavity, both affecting the buccal mucosa, have been reported. One case in a 46-year-old woman, and the other in a 60-year-old man (2,3). Although benign, it is considered that GCA has the potential for local recurrence, especially after incomplete resection (1,7).

The characteristic and diagnostic features of GCA include (a) absence of infiltrating growth pattern; (b) solid and pseudovascular areas; (c) fibroblastic spindle cells mingled with collagenous stroma; (d) multinucleated giant cells; (e) prominent vascularity; and (f) tumor cells that are intensely positive for CD34 and negative or minimal staining for muscle, nerve, and epithelial markers (7). In our case, besides these histopathological features, small hyalinized nodules containing prominent sclerosis around small blood vessels, discreet pseudovascular spaces and scattered multinucleated giant cells with floret-like appearance were observed. IHC analysis showed that the mononucleated and multinucleated giant cells were positive for vimentin, CD34, and bcl-2. CD34 immunoreactivity, although not specific, represents the only IHC finding of potential diagnostic value (4).

A variety of soft tissue lesions share the microscopic and IHC features of GCA. Among those are SFT, GCF, dermatofibrosarcoma protuberans (DFSP), pleomorphic hyalinizing angiectatic tumor (PHAT) of soft parts, multinucleate cell angiohistiocytoma (MCAH), benign fibrous histiocytoma (BFH), and angiomyolipoma (AML).

Various cases of SFT were described in the oral cavity. Clinically it presents most often as a slowly growing mass in middle-aged adults. The lesion is well-circumscribed and is composed of a short storiform pattern of monomorphic positive spindle-shaped cells deposited in a matrix with prominent wire-like collagen. A hemangiopericytoma-like vascular pattern is often focally present. The tumor cells are vimentin, CD34, and bcl-2 positive (8), complicating its distinction from GCA. However, pseudovascular spaces and lining by multinucleated giant cells are not seen in SFT.

GCF most often presents in early childhood as a slow-growing infiltrative soft tissue mass, at a wide variety of sites and is characterized by a high rate of local recurrence. Several studies have emphasized the relationship between GCF and DFSP, and interestingly in this context a case was reported with synchronous GCA and DFSP areas (4). Thus, it seems that GCF, GCA, and DFSP are closely related tumours. Morphologically, however GCF is much more infiltrative and lacks the prominent vascular pattern characteristic of GCA.

PHAT arises as a superficial subcutaneous tumour on lower extremities of adults. Microscopically there are similar features between SFT and GCA, including pseudovascular spaces and multinucleate giant cells. However,

in PHAT substantial cellular atypia is present which is not a feature of GCA. Nevertheless, the expression of CD34 in half of PHAT cases, and the overlapping histological features raise the possibility that PHAT may belong to the same family of tumours (9). To our knowledge, there is only one typical case of PHAT described in the oral cavity, affecting the buccal mucosa (10). It should be pointed out that this case was initially regarded as Schwannoma with advanced degenerative changes, until it was re-examined immunohistochemically. The diagnosis of PHAT was supported by the absence of S100 protein expression, and positivity for CD34 in the tumor cells. Therefore, it is possible that some cases of ancient Schwannoma defined prior to the advent of immunohistochemistry may be reclassified as PHAT.

MCAH is a benign fibrohistiocytic vascular lesion that appears as multiple brown-red papules located on the skin of the extremities, mimicking Kaposi's sarcoma. A solitary lesion appearing as a pink nodule on the upper lip of a 44-year-old man was diagnosed as MCAH (11). Microscopically, MCAH shows loosely arranged connective tissue, interspersed with numerous blood vessels, cells, multinucleated giant cells, and scattered thick collagen bundles. The histiocytoid and multinucleated giant cells stain positively with vimentin, variably for factor XIIIa, but it is negative for CD34. Distinction of MCAH from GCA is based on the more prominent perivascular lymphohistiocytic infiltration that is observed in MCHA. Furthermore, MCHA is less cellular than GCA (2).

BFH has a strong predilection for the skin of the extremities and areas exposed to the sun; however, it can affect other sites including the oral mucosa. Histopathologically, it shows a biphasic cell population of histiocytes and fibroblasts arranged in a storiform pattern or dispersed in fibrous areas. Other histological features frequently described are the presence of multinucleated giant cells, abundant vascularity, and inflammatory infiltrate. IHC analysis shows positivity for vimentin, actin, CD68, and factor XIIIa (12).

AML is a tumour that usually occurs in the kidney associated with tuberous sclerosis. Oral AML differs in several ways from the renal counterpart. It is not associated with tuberous sclerosis, and presents as a well-demarcated small and solitary mass. Microscopically it is composed of groups of mature adipose tissue intermixed with convoluted thick-walled blood vessels, and irregularly arranged sheets of smooth muscle. The smooth muscle cells are positive for vimentin, actin, and desmin, and adipocytes express S100 protein. HMB-45 is negative (13).

Thus, CD34 immunoreactivity of the spindle and multinucleated giant cells in GCA argue in favour of a fibroblastic interstitial dendritic cell histogenesis. Because overlapping histologic features and CD34 expression are shared by SFT, GCA, GCF, DFSP, and PHAT, it is possible that all these tumors may be histogenetically related.

In summary, we report the third case of GCA affecting the oral cavity, and based on these reports, the buccal mucosa is the site of predilection for this lesion. It is important to recognize this condition in order to avoid misdiagnosis with others fibrous tumors associated with giant cells.

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