Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Case report

Immune cell infiltration in gingival epithelioid angiomatous nodule: Case report and immunohistochemical analysis☆,☆☆

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ARTICLE INFO

Article history:
Received 9 April 2017
Received in revised form 5 June 2017
Accepted 9 June 2017
Available online xxx

Keywords:
Oral mucosa
Gingiva
Vascular neoplasms
Immunohistochemistry
Cellular immunity

ABSTRACT

Epithelioid angiomatous nodule (EAN) is a rare benign vascular proliferation, regarded as part of the morphologic spectrum of benign and malignant epithelioid vascular lesions. EAN is a rare lesion affecting the oral mucosa and, to date, only three cases have been reported in the English-language literature. We report the second EAN case affecting the gingival mucosa of a 69-year-old female patient. Oral examination revealed an asymptomatic, well-defined nodule exhibiting a smooth and erythematous surface, measuring 0.8 cm in greater diameter. The lesion was fully excised and histopathological study showed a mucosal epithelioid proliferation with solid and organoid growth patterns, and vascular lumens scattered focally throughout the lesion. The large epithelioid cells showed intracytoplasmic vacuoles and vesicular nuclei with prominent nucleoli, surrounding by scarce extravasated erythrocytes. Immunohistochemistry showed positivity for vimentin, α-SMA, CD34, focally for D2-40, and Ki-67 was 15%. Noteworthy, numerous immune cells (HLA-DR+/CD68+/CD163+/FXIIIa+) scattered throughout the lesion, were detected. To the best of our knowledge, this is the first report, which highlights the immune cell population, with M2-like phenotype, as an important component of EAN, suggesting the participation on their etiopathogenic mechanisms.

1. Introduction

Epithelioid angiomatous nodule (EAN), is a rare benign vascular proliferation, firstly described in the skin by Brenn and Fletcher, and clinically characterized by a nodule or papule well circumscribed [1,2]. The color can vary from erythematous to violaceous, and it can be painful [3]. EAN primarily affects young adults, aged between 15 and 45 years, with no gender preference; however, one study has noted male predominance [3–5]. In the first descriptions, trunk and extremities were reported as the sites most commonly affected [5]. Currently, the head and neck region is considered the most predominant anatomic site [5]. The etiology of EAN is unknown, but its rapid and ultimately self-limited growth suggests that it is probably a reactive or benign process [6]. To date, no EAN case showing recurrence, progression or metastasis has been reported [3].

EAN is regarded as part of the morphologic spectrum of benign and malignant epithelioid vascular proliferations that includes epithelioid hemangioma (EH), epithelioid hemangioendothelioma (EHE) and epithelioid angiosarcoma (EA) [3,6]. Microscopically, EAN is characterized by a solid and clearly circumscribed proliferation of epithelioid cells that may present vacuoles in the cytoplasm, without cellular atypia or pleomorphism, but some degree of typical mitosis can be visualized [7]. In the oral mucosa, EAN is a rare lesion, with only three previously published cases, in which one

☆ This case was the subject of a poster presentation at the Brazilian congress of Oral Medicine and Oral Pathology, Annual Meeting, Manaus, AM, 4–8, July, 2016.
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http://dx.doi.org/10.1016/j.ajoms.2017.06.002
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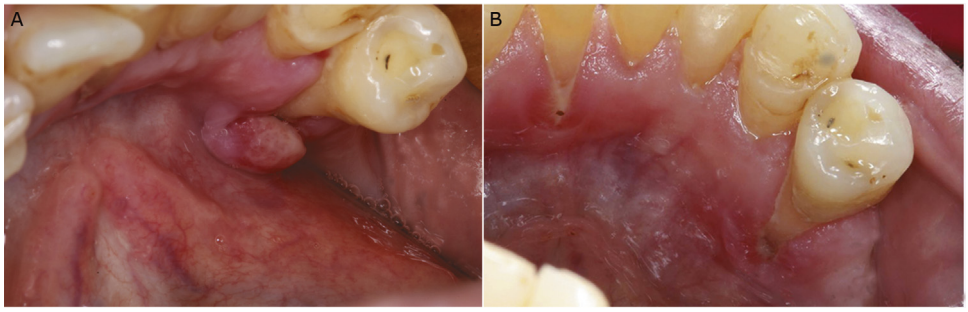

Fig. 1. Clinical aspects of EAN. Clinical view showing a well circumscribed nodule on the mandibular gingiva at level of the right first premolar, diagnosed as EAN (A). Clinical view 1 year after excisional biopsy (B).

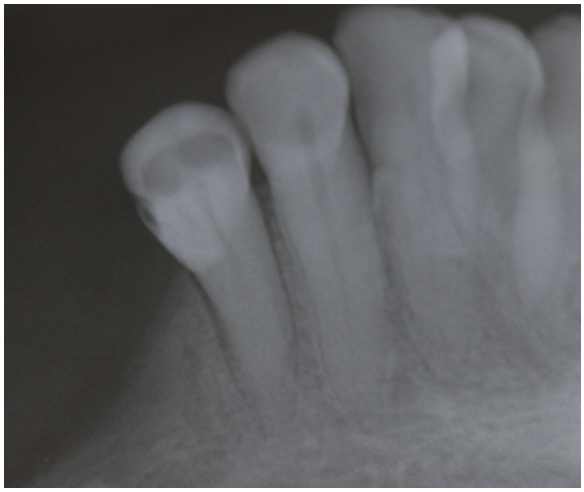

Fig. 2. Radiographic aspects of EAN. A radiographic view showing preservation of the periodontal tissues, confirming restriction to soft tissue.

of them affected the gingival mucosa [5,8]. Moreover, there are two EAN cases affecting each one the skin of upper and lower lip [5]. The distinction of EAN from other epithelioid vascular lesions can be made on the basis of the clinical and morphological features. However, in some cases, immunohistochemistry is helpful for establishing the correct diagnosis, which highlights the endothelial cells and smooth muscle cells, as the major components of the lesion. Interestingly, infiltrating non-neoplastic immune cells in EAN has not been reported so far. Thus, the aim of this paper is to report the second case of EAN located in the gingival mucosa and to review the English-language literature. To the best of our knowledge, this is the first report which highlights the intralesional immune cell population, with a M2-like phenotype, as an important component of EAN, suggesting participation on their etiopathogenic mechanisms.

2. Case report

A 69-year-old, otherwise healthy, Brazilian woman was referred presenting a lesion of 2-month evolution on the lingual marginal gingiva of the mandibular right first pre-molar. Intraorally, was observed an asymptomatic well-defined nodule, with a smooth and erythematous surface, measuring 8 millimeters in greater diameter, which clinically was diagnosed as pyogenic granuloma (PG), peripheral giant cell lesion (PGCL), peripheral ossifying fibroma (POF) or peripheral odontogenic tumor (Fig. 1A). Periapical radiograph shows no bone involvement (Fig. 2). An excisional biopsy was performed, and histopathological analysis showed a mucosal epithelioid proliferation with solid and organoid growth patterns, which exhibited scattered throughout the lesion, small vascular lumens of varying caliber. In fact, intralesional vascular channels, lined by a monolayer of epithelioid endothelium, were frequently observed. In high-power view, the large epithelioid cells showed intracytoplasmic vacuoles and vesicular nuclei with prominent nucleoli, admixed with scarce granulocytes and extravasated erythrocytes, and supported by fine connective tissue network (Fig. 3). Immunohistochemistry showed positivity for vimentin, α-SMA, CD34, focally for D2-40, and Ki-67 labeling index was 15%. CD138 evidenced few plasma cells and discreetly the cellular stroma, while that desmin highlighted focally the vascular wall. AE1/AE3 pan-cytokeratin, EMA, p53, p63 and Bcl-2 were negative (Fig. 4). Noteworthy, numerous immune cells (HLA-DR+/CD68+/CD163+/FXIIIa+), scattered throughout the lesion, in perivascular pattern, were visualized. Moreover, CD1a and CD207 markers were practically negative, whereas scarce S100 positivity was detected, indicating absence of Langerhans cells (Fig. 5).

At present, the patient is under clinical follow-up, and after 1 year, no recurrence or alteration has been observed.

3. Discussion

Epithelioid angiomatous nodule is a rare benign vascular proliferation, firstly described by Brenn and Fletcher in 2004, in a series of 15 cases [1]. EAN is extremely rare on the oral mucosa. Since this lesion was initially described, only three oral EAN cases have been reported [5,8] and the current case appears to be the second affecting the gingiva. Table 1 summarizes the clinical features presented in case reports described to date in the literature Moreover, there are two EAN cases affecting each one the skin of the upper and lower lip [5]. In the oral cavity, two lesions were located in the tongue and one in the maxillary gingiva. The size varied from 0.3 to 0.8 centimeters and the time the evolution from two weeks to one month. There were two women and one man, being the mean age 27.6 years (range, 13–49 years). Clinically, EAN is characterized by a nodule or papule well circumscribed. The color can vary from erythematous to violaceous and it can be painful [3]. In the present case, the lesion was an asymptomatic well-defined nodule, located on the mandibular gingiva, measuring 0.8 centimeters in greater diameter, and with 2-month evolution, which clinically was diagnosed as PG, PGCL, POF or peripheral odontogenic tumor. The radiographic analysis did not show alterations, showing that the lesion was restricted to gingival mucosa. Clinically, PGs are reactive lesions and occur often in traumatized areas as face and oral cavity. Histologically are constituted by a lobular proliferation of capillaries consisting of endothelial cells, surrounded by pericytes in a loose stroma, which contains numerous inflammatory cells. In the periphery, ulceration is frequent [6,9]. For both, EAN and PG, the treatment consists in simple local excision [5]. PGCL is a reactive lesion, originates from the periosteum or periodontal ligament [10,11]. Histologically is constituted by numerous multinucleated giant cells admixed with mononuclear cells, hemorrhagic focuses

Please cite this article in press as: Ortega RM, et al. Immune cell infiltration in gingival epithelioid angiomatous nodule: Case report and immunohistochemical analysis. J Oral Maxillofac Surg Med Pathol (2017), http://dx.doi.org/10.1016/j.ajoms.2017.06.002