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Case Studies

Benign Fibrous Histiocytomas of the Oral Mucosa: Report on Three Cases and Review of the Literature

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Key Words

Benign fibrous histiocytoma · Literature review · Management

Abstract

Benign fibrous histiocytomas (BFH) of the skin are common lesions, although they only rarely involve the oral mucosa. This article presents 3 additional cases of BFH of the oral mucosa, with a review of previously published cases. Although a malignant variant of BFH also exists, the present review focuses only on benign lesions. The clinical presentation, diagnosis, histopathological and immunohistochemical features of BFH are discussed. According to the present analysis, the majority of oral mucosal BFH have occurred in middle-aged and elderly patients, with a slight female predilection. Within the oral cavity, BHF may occur at any mucosal site, including the lips, tongue, buccal mucosa, mandibular and maxillary gingiva as well as the palate. Histopathology is essential to diagnose the lesion, while immunohistochemical investigations may be utilized to exclude the histopathological differential diagnoses such as juvenile xanthogranulomas and nevi. This review also revealed total excision as the treatment of choice for BFH, with a very good prognosis and an extremely low rate of relapse.

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Introduction

Benign fibrous histiocytoma (BHF) designates a group of quasi-neoplastic lesions that show both fibroblastic and histiocytic differentiation. Whether the lesions originate from histiocytic or fibroblastic tissues has not been clearly determined yet. Some experts hypoth-

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esize that the cells originate from the tissue histiocytes and then assume fibroblastic properties [1], while others argue that immunohistochemical evidence of factor XIIIa positivity favors a dermal dendrocytic cell origin [2]. In consequence of the controversies of origin, over the years, BFH have been designated by several different names, such as sclerosing hemangioma, histiocytoma cutis, fibroxanthoma and nodular subepidermal fibrosis [1].

Although BFH may occur anywhere in the body, including in visceral organs, skeletal system or sinuses, the majority arise on the skin of the extremities [2]. When BHF occur in the dermis, the lesions are designated as dermatofibromas. Furthermore, BFH are also classified as superficial and deep lesions, depending on the location [2].

Only rarely lesions may involve the oral mucosa or jaw bones [3–31]. In the oral mucosa, BFH show a predilection to the buccal mucosa and vestibule [1, 4–31]. Compared to oral mucosal lesions, intraosseous lesions that involve the jaw bones are extremely uncommon, with 7 cases of mandibular and 2 maxillary BFH reported to date [3].

The purpose of this article is to report 3 additional cases of BHF of the oral mucosa and to review the current literature on this topic.

Case Reports

Case 1

A 48-year-old female, in good general health, presented to our consultation 7 months after the onset of a lesion of the left lower lip. The lesion had appeared after the patient bit her lip and evolved by fluctuating in size, alternately growing and diminishing. It was painful, which motivated the patient's consultation. The mucosal appearance was banal (no picture available). It was completely excised under local anesthesia.

The macroscopic examination revealed a greyish mucosal sample measuring $0.8 \times 0.8 \times 0.3$ cm with central ulceration. The histopathological examination showed inflammatory ulceration of the labial mucosa with the deep aspect of the lesion located in a thickened submucosa. The ulcerated area was covered by a coating of fibrin, debris and leukocytes (fig. 1). The principal cell population consisted of an irregularly arranged compact proliferation of histiocyte-like cells with a clear cytoplasm and a nucleus containing a prominent nucleolus (fig. 2). The submucosa contained numerous small blood vessels collapsed by the turgescence of the endothelial cells. Between these vessels, there was a dense chronic and polymorphic inflammatory infiltrate also composed of few polymorphonuclear cells. The epithelium was hyperplastic. There were no sign of malignancy within the limits of the sample. Immunohistochemical stains showed positivity for CD68 (fig. 3) and vimentin, negativity for MNF116, S-100 protein, CD34, smooth-muscle actin (SMA) and desmin. The diagnosis rendered was BHF of traumatic origin.

Case 2

A 75-year-old male presented with a 0.5×0.5 cm round lump of a hard consistency on the posterior palate. The lesion was excised under local anesthesia, and the histopathological examination revealed a mucosal nodule covered by orthokeratinized stratified squamous epithelium. A circumscribed but unencapsulated wedge-shaped lesion was evident in the corium, composed of spindle cells arranged in a storiform pattern in several foci (fig. 4). Histiocytes containing clear cytoplasm and central nuclei were also noted. Elsewhere, the stroma was densely fibrous and was composed of hyalinized eosinophilic collagen fiber bundles. Marked basal cell hyperpigmentation was also evident. This fact led us to exclude an intramucosal nevus using S-100 immunostain. Furthermore, SMA negativity was useful to exclude leiomyoma. Thus, the final diagnosis rendered was BFH.

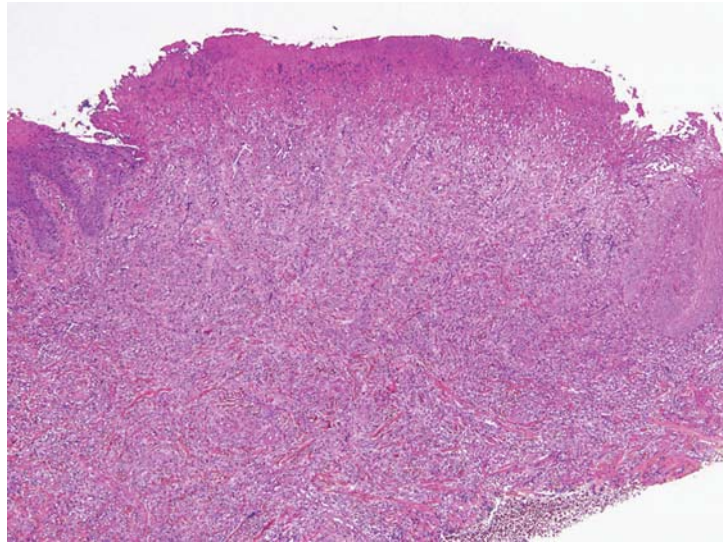


Fig. 1. The lesion with central ulceration. $\times 4$.

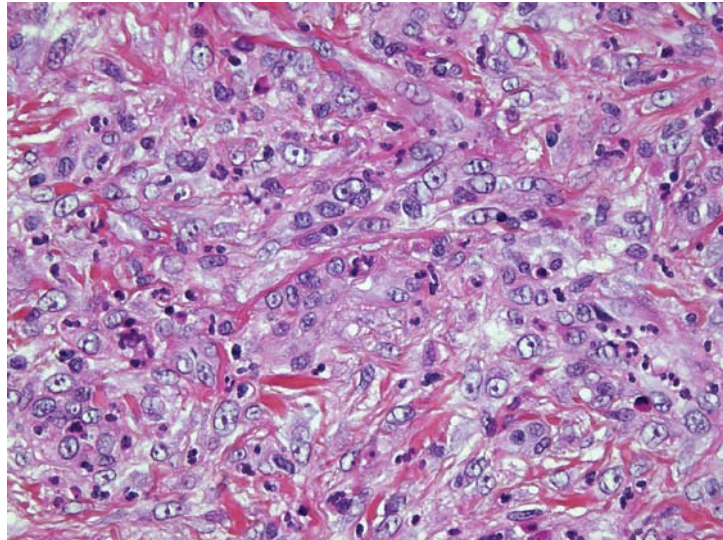


Fig. 2. Irregular disposition of histiocyte-like cells. $\times 40$.

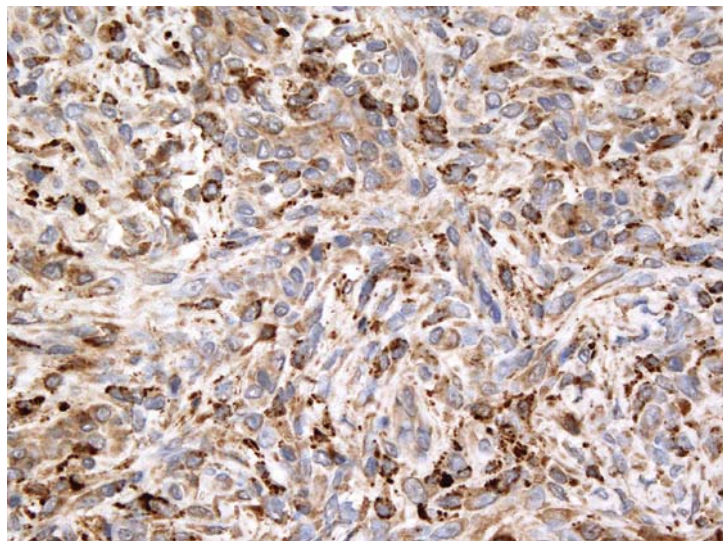


Fig. 3. Strong immunohistochemical positivity for CD68. $\times 40$.

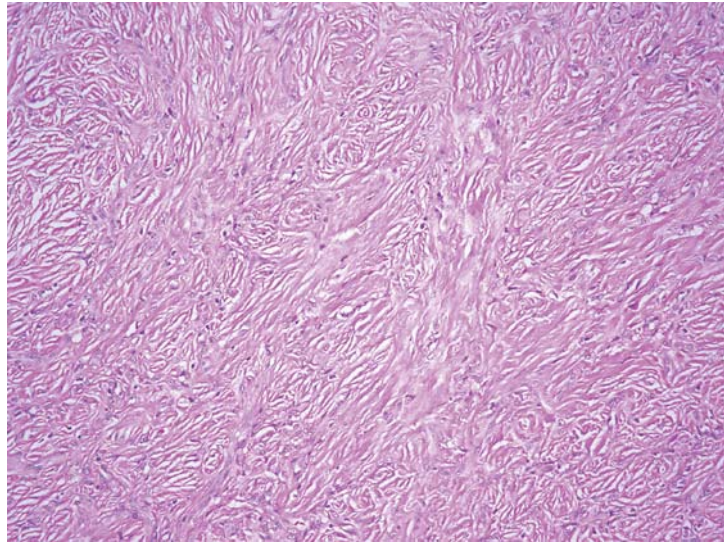


Fig. 4. Spindle cells arranged in a storiform pattern. $\times 10$.

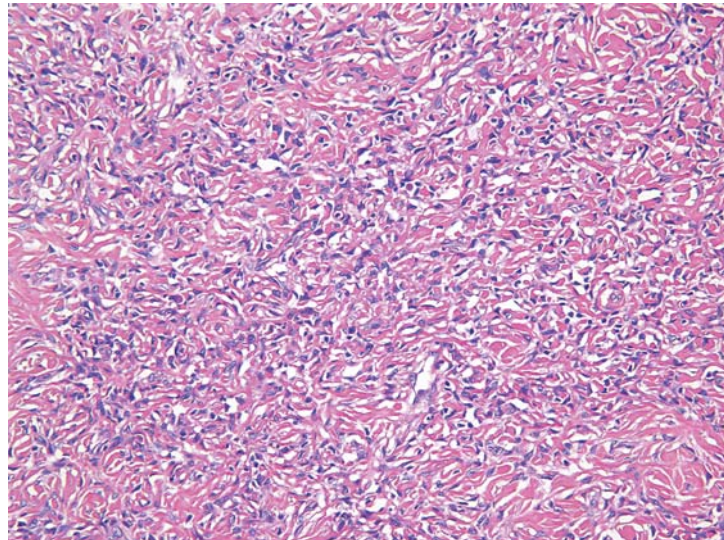


Fig. 5. Rich cellularity of the tumor mass. $\times 20$.

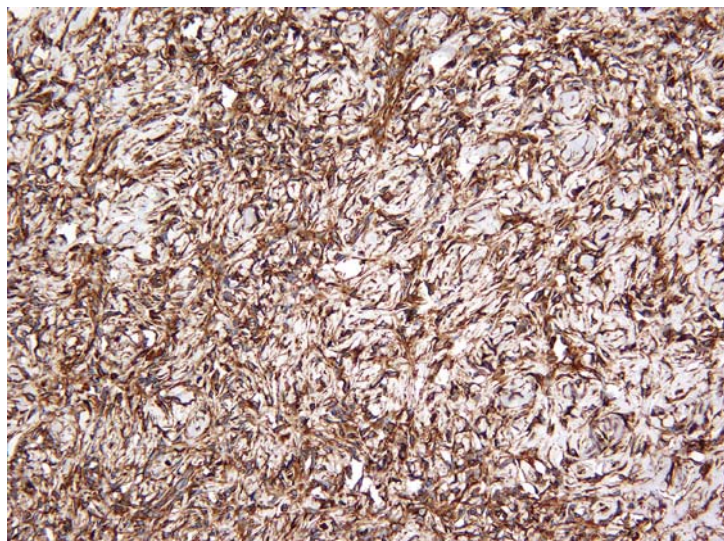


Fig. 6. Vimentin-positive staining of the lesion cells. $\times 20$.

Case 3

An 81-year-old male presented with a firm pedunculated 3 × 3 cm lump on the hard and soft palate junction of 6 months duration. The overlying mucosa was pink in color and without ulceration. No significant radiological changes were evident. Histopathology revealed a mucosal nodule covered by atrophic orthokeratinized stratified squamous epithelium. A few foci of the tumor were richly cellular (fig. 5), composed of spindle cells arranged in a storiform pattern. Some cells showed pleomorphic nuclei with smudged chromatin and minimal cytoplasm. Elsewhere, densely sclerotic stroma composed of collagen fiber bundles was noted. Immunohistochemical investigations with SMA, S-100 and vimentin revealed tumor-cell positivity to vimentin (fig. 6) and sparsely for CD68. Thus, the final diagnosis was BFH. The lesion did not recur during the 6-year follow-up period.

Table 1 shows the clinicopathological presentations of 47 cases of oral BFH published until 2014.

Discussion

Based on the literature review and the present cases, BFH of the oral mucosa were found to clinically present as slowly growing, painless masses [5]. Although these lesions do not produce any repercussion on the patients' general health, they may have local consequences, for example interfere with mastication and compress or displace anatomical structures. Rarely, multiple BFH may occur due to immunosuppression [2], but none of the oral BFH reviewed had presented as multiple lesions [4–31]. The overlying mucosa remains most often intact but can show periods of ulceration [4] due to traumatism, in which case lesions may become painful. Majority of the lesions are freely mobile and have no associated lymphadenopathy.

Oral mucosal BFH most often occur in middle-aged to older adults [4–31] compared to the cutaneous counterpart, which occurs predominantly in young adults [2]. Oral mucosal BFH are slightly more often encountered in female patients, similar to dermatofibromas. Macroscopically, BFH are generally round to oval-shaped, whitish to yellowish and firm. The lesions are well demarcated from surrounding tissues but not properly encapsulated [4–31].

Histologically, there is a dual cell population of fibroblasts and histiocytes. Occasional multinucleated giant cells, lipid-containing xanthoma cells and lymphocytes can be found [1, 2]. The fibroblasts are spindle-shaped and arranged in a storiform pattern or short fascicles [2]. The cells do not show any sign of malignancy, and mitoses are extremely rare. The stroma is densely fibrous and may show areas of myxoid change or focal hyalinization [1]. Variants of BFH include cellular fibrous histiocytomas, epithelioid fibrous histiocytomas, aneurysmal fibrous histiocytomas as well as clear cell, lipidized, palisading, myxoid and granular cell types [2]. In addition, Han et al. [32] classify dermatofibromas as fibrocollagenous, histiocytic, cellular, aneurysmal, angiomatous, sclerotic, monster, palisading and keloidal dermatofibromas. According to their classification, the BFH described in the present report can be classified as fibrocollagenous BFH (case 1) and sclerotic BFH (cases 2 and 3).

According to the literature, BFH show different patterns of positivity with immunohistochemical stains. Most lesions show a strong tendency for positivity with vimentin and CD68. Positivity for SMA and factor XIIIa is often reported [1]. Further, the immunohistochemical features may vary over time, with early lesions of dermatofibromas showing reactivity for CD68 and factor XIIIa, which may diminish progressively. CD56 and neuron-specific enolase are variably expressed, and S-100 protein is only exceptionally expressed [19]. Lysozyme can also be positive. In our cases, the positivity for vimentin and CD68 and the negativity for MNF116 (keratin), S-100 protein (neurological marker), CD34 (vascular marker), SMA and desmin confirmed the diagnosis of BFH.

Table 1. Literature review based on the clinicopathological presentations of 47 cases of oral BFH

First author [ref.], year, case	Age	Gender, origin	Localization, mucosal lesion	Size	Previous traumatism	Immunohistochemical stains	Treatment	Follow-up	Recurrence
Hillis and Beasley [4], 1975	52	male white	Left lower lip, intact mucosa	5 × 10 mm			Complete excision	1 year	no
Del Hoyo et al. [5], 1976	68	male	Internal left cheek, intact mucosa				Complete excision	14 months	no
Hoffman and Martinez [6], 1981, case 1	8	male	Left cheek, intact mucosa	0.6 × 0.5 × 0.4 cm	Bite 1 month earlier		Complete excision	10 months	no
case 2	12	female white	Gingiva lingual to the lower right first and second molars, ulcerated mucosa	2.3 × 1.3 × 0.8 cm	Injury of the inter-proximal area with a toothpick		Complete excision	10 months	no
Weerapradist and Punyasingh [7], 1984	50	female Thai	Left retromolar area, reddish oral mucosa	3 cm			Complete excision		
Thompson and Shear [8], 1984, case 1	49	female	Retromolar region	T3			Excision	10 months	no
case 2	36	male	Maxillary anterior labial gingiva	T1			Excision	12 months	no
case 3	44	female	Base of the tongue	T1			Excision	11 years	no
case 4	49	female	Palate	T1			Excision	7 months	no
case 5	17	male	Left buccal mucosa	T1			Excision	7 months	no
Triantafyllou et al. [9], 1985	70	male	Tip of the dorsum of the tongue, intact mucosa	1 × 0.8 × 0.6 cm	Local traumatism 1 week earlier		Excisional biopsy	3 years	no
Fieldman and Morrow [10], 1989	11	male Hispanic	Soft palate, intact mucosa	3 cm			Wide excision	8 months	no
McLeod and Jones [11], 1992	22	female white	Midline of the lower lip sloughing of the surface	2 cm	Injury 1 month earlier		Incomplete excision at the lateral margins	5 years	no
Gray et al. [12], 1992, case 1	45	male Hispanic	Right upper lip at the nasolabial angle, intact mucosa	2–3 cm			Excision		no
case 2	42	male	Right buccal mucosa						no
case 3	65	male	Right buccal mucosa						no
case 4	37	female	Left side of the tongue						no
case 5	50	female	Right dorsum of tongue						no
case 6	71	female	Left buccal mucosa						no
case 7	45	female	Right lower lip						no
case 8	49	male	Right maxillary vestibule						no
case 9	70	female	Left buccal mucosa						no
case 10	60	male	Left mandibular vestibule						no
case 11	68	female	Right buccal mucosa						no
case 12		female	Left mandibular vestibule						no
case 13	66	female	Left mandibular vestibule						no
case 14	37	female	Right anterior maxillary gingiva						no
Bielamowicz et al. [13], 1995, case 1	25	male	Right buccal mucosa with extension to the vermilion border, intact mucosa	3 cm		N: keratin, desmin, SMA, factor VIII-related antigen; P: KP1 and S-100 protein	Complete excision	2 years	no
case 2	49	male	Right submandibular region	2 cm			Complete excision	17 years	no
Hong et al. [14], 1999	74	female	Floor of the mouth, intact mucosa	6 × 6 × 4.5 cm		P: vimentin (fibroblasts), CD68	Complete excision	9 months	no
Femiano et al. [15], 2001	32	male	Right cheek, intact mucosa	6–7 cm		P: CD68	Complete excision		no

Table 1 (continued)

First author [ref.], year, case	Age	Gender, origin	Localization, mucosal lesion	Size	Previous traumatism	Immunohistochemical stains	Treatment	Follow-up	Recurrence
Ide and Kusama [16], 2002	50	female	Gingival of the left mandibular second molar, ulceration of the mucosa	1.2 × 1 × 0.7 cm		P: vimentin, CD68, factor XIIIa, S-100 (granit cells) N: pancytokeratin, alpha-SMA, desmin, CD31, CD34	Complete excision	20 years	no
Yamada et al. [17], 2002	6 months	male	Upper lip, intact mucosa	1.3 cm		P: vimentin and factor XIIIa; N: S-100 protein, synaptophysin, alpha-SMA, desmin, CD31, factor VIII, CD68	Excision		
Alves et al. [18], 2003	26	female	Left anterior buccal mucosa, intact mucosa	1 cm		P: vimentin, factor XIIIa; N: desmin, S-100 protein, CD68, CD34	Excisional biopsy	24 months	no
Hidaka et al. [19], 2005	2 years 8 months	male	Gingival in left maxillary deciduous molar region, erosion of epithelium	4 × 2 × 2 cm	Context: sialidosis type 2	P: CD68, lysozyme; N: CD34, CD31, S-100, alpha-SMA, HMB-45	Excision	4 months	yes
Toyohara et al. [20], 2008	76	Japanese female	Upper lip, intact mucosa	1 cm		P: alpha1-ACT, lysozyme, CD68, vimentin; N: S-100 protein, NSE	Excisional biopsy	4 years	no
Menditti et al. [21], 2009, case 1	44	male white Caucasian	Lingual mucosa of the left mandible in the premolar area, intact mucosa	3 × 2.5 cm		P: vimentin, CD68; N: S-100 protein, CD34, factor XIIIa, SMA	Complete excision	10 years	no
case 2	34	male white Caucasian	Right side of the tongue, intact mucosa	3 × 2.5 cm		P: vimentin and CD68; N: S100, CD34, factor XIIIa, SMA	Complete excision	10 years	no
Lee et al. [22], 2010	41	female	Upper lip, intact mucosa	1 cm		P: CD34 (vessels), factor XIIIa (dendritic cells), CD68 (histiocytes), SMA (fibroblasts)	Excisional biopsy		
Giovani et al. [23], 2010	36	male	Right buccal mucosa	2.4 cm		P: vimentin, CD34, CD68 N: desmin, alpha-SMA, S-100 protein, Leu7, CD117	Complete excision	12 months	no
Bags et al. [24], 2010	59	female	Right cheek	7 × 5.5 cm			Complete excision	14 months	no
Lopez-Jornet et al. [25], 2011	8	female	Dorsal surface of the tongue	0.4 mm	no	P: vimentin; N: factor XIIIa, CD68, SMA	Complete excision		no
Bindhu et al. [26], 2012	20	female	Left hard palate medial to 25; 26; 27, intact mucosa	3 × 3 cm	Trauma with a fish bone 2 weeks earlier		Incisional biopsy		
Rullo et al. [27], 2012	9 months	male	Left lower border of the tongue	2.5 × 2 cm		P: lysozyme; N: S100 and SMA	Complete excision		
Caldeira et al. [28], 2012	29	female	Hard palate	3.5 × 2 cm	none	P: vimentin, factor XIIIa; N: S-100, HHF35, CD1a, CD56, CD57, EMA, CD34, HMB-45	Complete excision		
Rajathi et al. [29], 2013	23	male	Gingiva	1 × 1 cm	none	P: vimentin; N: factor XIIIa, CD68, SMA	Complete excision		no
Priya et al. [30], 2013	30	female	Dorsal surface of the tongue	3 × 3 cm	no	P: CD34 focal; N: CD68, SMA, S-100	Complete excision	3 years	no
Pandey et al. [31], 2013	26	male	Ventral surface of the tongue	6 × 5 cm	no	P: vimentin, factor XIIIa; N: S-100, EMA, CD34, HMB-45	Complete excision		
	0–25 years = 11 26–50 years = 24 51–75 years = 11 >75 years = 1	male = 23 female = 25	tongue = 8; buccal mucosa = 13; palate = 3; lip = 7; gingival = 7; other = 9		history of trauma = 5				recurrence present = 1

Age is expressed in years, unless otherwise indicated. NSE = Neuron-specific enolase, P = positive; N = negative; T1 = <2 cm; T3 = >4 cm.

Although factor XIIIa is a marker that has been considered to confirm the diagnosis of BFH, it may also show positivity in other mesenchymal tumors [2]. At present, there are no specific immunohistochemical markers to diagnose fibrohistiocytic lesions, including BFH. Thus, BFH are diagnosed by the exclusion of entities with similar features such as juvenile xanthogranuloma (S-100, CD1a positive), leiomyomas (SMA positive), dermatofibrosarcoma protuberance (DFSP; CD34 positive) as well as by the absence of positive staining with immunohistochemical markers other than vimentin, factor XIIIa and CD68 [23]. However, it is also important to remember that cellular BFH may show focal reactivity to CD34, in which case it may be relatively difficult to differentiate it from DFSP [2]. However, with regard to oral lesions, this problem may not arise as DFSP is a primarily cutaneous lesion.

Even though it is not possible to highlight such an event in every case reported, BFH can sometimes be related to a previous local injury or infection. There remains a long controversy about the origin of BFH, and it is not clear yet whether BFH arise as true neoplasms on sound mucosa or as a reaction to a previous traumatism [22]. Only in 5 cases of our review (2 cases in [6], [11, 13, 24]) and in case 1 of the present series, which appeared after a bite, such a traumatism is clearly mentioned.

Out of the BFH of the oral mucosa, only a small number involves the lips: 8/51 cases (taking our patient into account); 3 of the lesions occurred on the lower lip [4, 11, 12], 4 on the upper lip [12, 17, 20, 22] and 1 additional case involved the buccal mucosa with extension to the vermillion border of the lower lip [13].

Our case 1 presented with an ulceration of the overlying mucosa, which is less common than an intact mucosa. Out of the 51 cases of our review, 19 had a normal overlying mucosa, 26 were not specified and only 6 showed mucosal alterations, varying from moderate inflammation [23] or erythematous mucosa [7] to proper ulceration [6, 1, 19].

Fibrous histiocytoma has a malignant form, which is more often encountered in the literature. An intermediately aggressive variant (angiomatoid variant) has also been recognized since 1995 [27] and is described as having a local aggressiveness and a low rate of metastasis [27, 12].

In accordance to the other cases reported in the literature since 1975, the lesions had no consequence on the good general health of our patients and showed a slow growing pattern. Treatment of BFH consists of complete excision and has an excellent prognosis as recurrence is exceptional. Out of the 43 selected patients, only 1 case of recurrence is described in a two-year-old infant [19]. Forty-three cases were disease free at follow-up, which was between 7 months and 20 years, and for 7 cases, follow-up was not specified.

Conclusion

As BFH has a banal appearance, diagnosis or distinction from other types of nodules is impossible on a clinical basis. Histological examination is mandatory as it is the only way to confirm the benignity of the lesion. The cases we reported were relatively typical, and the clinical course corresponded to that of the other cases found in the literature, confirming the low risk of recurrence after complete excision.

Disclosure Statement

The authors declare no conflicts of interest.

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