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Aggressive angiolymphoid hyperplasia with eosinophilia of the tongue: A case report and review of the literature

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1. Introduction

Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon benign vascular lesion, characterised by proliferation of small to medium-sized vascular structures lined by plump epithelioid (histicytoid) endothelial cells surrounded by a mixed inflammatory infiltrate [1,2]. Although its aetiology and pathogenesis are still uncertain, some authors [3,4] have suggested that ALHE represents a heterogeneous group of benign vascular lesions and reactive or reparative vascular proliferation.

The lesions of ALHE vary in clinical appearance from intradermal papules to subcutaneous nodules, may be solitary or multiple, red to brown in colour, quite small in size and usually occur in young adults [1].

The lesions primarily occur in the skin and subcutaneous tissues of the head and neck [5], particularly in the pre-auricular area and scalp, although some authors have also reported muscle, bone and salivary gland involvement [6].

Surgical excision is considered the most effective treatment for this rare condition. However, it is suboptimal, as it is also associated with the highest rate of treatment failure versus other modalities such as administration of intralesional corticosteroids [7], cryotherapy [8], laser cauterisation [9], and treatment with oral retinoids [10] or pentoxifylline [11].

Intraoral lesions of ALHE are uncommon [12], and tongue involvement is extremely rare. A review of the English literature through a PubMed database search indicated that only 12 cases have previously been reported [5,12–19]. Here, we report an aggressive case of ALHE of the tongue, along with a review of the relevant literature.

2. Case report

A 60-year-old woman was referred to the Department of Maxillofacial Surgery of the University of Turin for evaluation of a painless lesion on the left lateral border of the tongue (Fig. 1). The lesion had already been biopsied elsewhere, and the results of histological examination indicated granulation tissue, hyperplasia, acanthosis and parakeratosis of the epithelium without dysplasia. Detailed evaluations revealed an accidental bite 1 year previously following which the patient noticed the swelling, which became enlarged very slowly until reaching the condition at presentation.

Physical examinations revealed a whitish, lobulated, non-tender mass on the middle one third left lateral border of the tongue, measuring 13 mm at the greatest dimension. The soft to firm mass was not attached to the adjacent structures and was therefore mobile. Digital pressure did not elicit pain. There were no associated medical findings or a relevant family history of any other

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concomitant diseases. No regional lymphadenopathy was palpable.

A new preoperative incisional biopsy was carried out and microscopic features were similar to those of the previous sample. Two weeks later, the patient underwent surgical resection of the mass under general anaesthesia. Intra-operative examination of frozen sections revealed a specimen of muscular tissue with mild interstitial fibrosis and chronic inflammation, without evidence of malignancy. The lesion was extended up to about 1 mm from the surgical margins. The patient was discharged from the hospital 2 days after the surgery without any complications.

Macroscopic examination of the specimen revealed a whitish 3.0 × 2.0 × 1.5 cm mass that was soft to firm, with a white lobular greyish surface. Microscopic examinations indicated proliferation of vascular structures lined with epithelioid-like endothelial cells, with vesicular nuclei that protruded into the lumina and large vacuolated acidophilic cytoplasm. A dense cellular inflammatory infiltrate surrounding the vessels, which consisted mostly of eosinophilic granulocytes, was observed (Fig. 2a, b, 2c). No mitosis or nuclear atypia was found, and surgical margins were unimpaired. Immunohistochemical investigations using antibodies against CD31, a marker of endothelial differentiation, showed intense positive staining of numerous vascular structures (Fig. 2d).

Based on the microscopic and immunohistochemical findings, the lesion was ultimately diagnosed as ALHE.

The lesion recurred in the same area 2 months after the operation with the same clinical appearance, measuring 10 mm in the greatest dimension. Therefore, a second attempt at surgical resection of the mass under general anaesthesia was made, with removal of about 3 mm of tissue from the lesion. At an 8-month follow-up, the lesion had recurred in the same area once again, measuring 8 mm in the greatest dimension. As the patient refused further surgical treatment, she was followed up on an outpatient basis. The lesion has since remained unchanged for 1 year.

3. Discussion

ALHE was first described by Wells and Whimster [2] in 1969, while the term epithelioid haemangioma (EH) was proposed by Enzinger and Weiss [19] in 1983 to describe the same lesion. Many other terms have been applied to these lesions, including inflammatory angiomatous nodule, pseudo- or atypical pyogenic granuloma and histiocytoid haemangioma [13]. However, the term ALHE is the most commonly used nomenclature for these lesions in the English literature.

Intraoral lesions of ALHE are uncommon and the most frequent anatomical site is the lip, followed by the tongue and buccal mucosa [14]. Tongue involvement is extremely rare, with only 12 cases reported to date (Table 1), consisting of eight males and four females ranging in age from 23 to 82 years (mean, 52.5 years).

These lesions appear as solitary or multiple intradermal papules or subcutaneous nodules, which are sometimes ulcerated [1]. All patients presented with single or multiple lesions, measuring between 0.4 and 4.3 cm in the greatest dimension; five patients with an ulcerated lesion, six patients with a nodule, as in our case; and one patient with a macule. Regional lymphadenopathy was found in only one case.

With regard to the pathogenesis of ALHE of the tongue, there is controversy whether ALHE represents a vascular neoplasm [4] or a reactive inflammatory condition related to traumatic phenomena, such as masticatory bites [5,14]. We found a history of trauma to the involved area in only one previous case [5], in addition to our case.

Histopathology is essential to confirm the diagnosis, characterised not only by proliferation of small to medium-sized vascular structures but also by epithelioid (histiocytoid) endothelial cells with eosinophilic often vacuolated cytoplasm and vesicular or occasionally indented nuclei that protrude into the lumina forming the characteristic ‘tombstone’ appearance [6]. They are uniformly positive for CD34 and CD31, while factor VIII-related antigen can be either positive or negative [1].

In our case, ALHE was not suspected pre-operatively, both because tongue involvement is rare and because of its clinical behaviour mimicking a malignancy. However, the histological results of both pre-operative incisional biopsies were not suggestive of malignancy. Therefore, we performed surgical resection with conservative margins, diagnosed as lesion-free.

Despite surgical excision remaining be the most effective treatment option, ALHE has a recurrence rate of 44,2% [20].

According to our review of ALHE of the tongue, in cases in which follow-up was reported, recurrences have been described in three of nine cases, which were treated successfully by re-excision in only two cases. Here, we reported the only case of a second recurrence, despite further wider local excision.

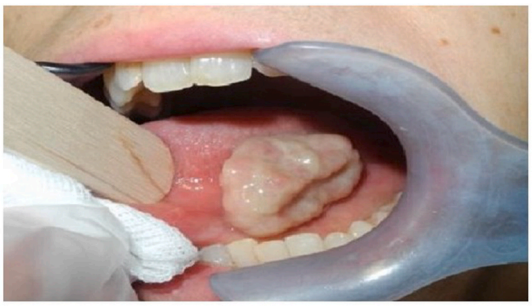

Fig. 1. Clinical view showing a well circumscribed nodule measuring 13 mm in the greatest dimension on the left lateral border of the tongue in a 60-year-old woman.

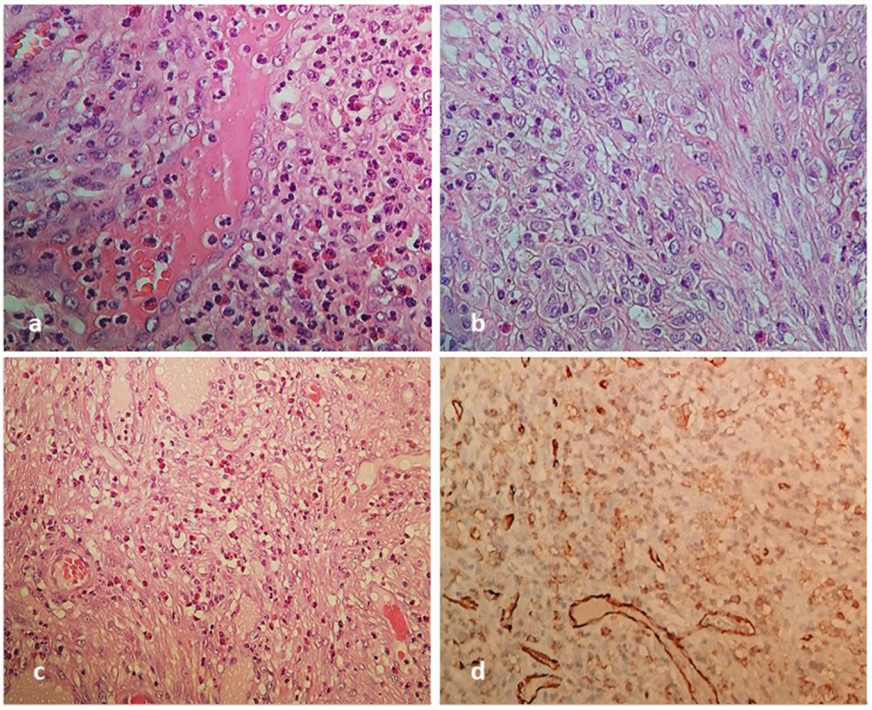

Fig. 2. Main features of ALHE: a) Proliferation of small vessels lined by plump endothelial cells with a hobnail/tombstone appearance (H&E, original magnification x400). b) Sheet of epithelioid cells among vessels (H&E, original magnification x400). c) Prominent stromal infiltrate with lymphocytes and abundant eosinophils (H&E, original magnification x200). d) CD31 immunoreactivity both in the endothelial cells and in the epithelioid cells (original magnification x200).

Table 1
Summary of the previous cases of angiolymphoid hyperplasia with eosinophilia of the tongue.

	Sex	Age	Lesion	Size[a]	Location	Preoperative diagnosis	Treatment	Recurrence
[17]	M	31	macule	1,0 cm	left sublingual region	NS	excision	no for 1 year
[12]	M	82	ulcer	2,0 cm	right dorsal surface	squamous cell carcinoma	spontaneous remission after incisional biopsy	no for 6 months
[15]	M	48	nodule	3,0 cm	left ventral surface	NS	excision	after 5 weeks
[5]	F	43	nodule	1,0 cm	midline	NS	excision	no for 3 years
[4]	M	23	ulcers	1,0 cm and 0,4 cm	left lateral border	malignant tumor	excision	after 3 weeks
[13]	M	56	ulcer	1,5 cm	right lateral border	NS	excision after incisional biopsy	no for 6 months
[18]	M	59	nodule	4,3 cm	right posterior one-third and floor of mouth	Rhabdomyoma	excision	no for 2 months
[14]	M	52	nodules	NS	NS	vascular tumor	excision	NS
	F	65	nodule	NS	NS	pyogenic granuloma	excision	NS
	F	32	ulcer	NS	NS	squamous cell carcinoma	excision	after 3 months
	M	48	nodule	1,5 cm	bottom	vascular tumor	excision	NS
[16]	F	75	ulcer	0,5 cm	right lateral border	NS	excision	no for 1 year
Current study (2020)	F	59	nodule	1,3 cm	left lateral border	malignant tumor	excision	after 2 months and 8 months

NS: not stated.
[a] Largest diameter of the lesion.

Although ALHE is a benign disease, its therapeutic management can be challenging considering the frequency of recurrence. Therefore, it is essential to carry out examination of the complete margins of the surgical specimen to achieve local control and close monitoring of the patient is required to detect possible recurrence.

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certificate, please see:
http://www.textcheck.com/certificate/JSNc42.

Proof of consent

Since formal consents are not required for the use of entirely anonymised images from which the individual cannot be identified, no appropriate permission was requested from the patient.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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