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Palatal atypical histiocytic granuloma

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Abstract

In this report, we examine a clinical entity called atypical histiocytic granuloma (AHG), which is characterized by ulceroproliferative lesions that clinically simulate a squamous cell carcinoma or specific granulomatous lesions. AHG histologically shows a histiocytic proliferation and is characterized by specific mitotic activity, which has the potential to be confused with malignant processes of a lymphoid origin. There are few cases reported in the literature, and an adequate knowledge of the process is required in order to avoid a misdiagnosis, especially as regards malignant processes. To our knowledge, a case of this type of lesion in the palate has not yet been described. We present a case of an atypical histiocytic granuloma which occurred in the form of an ulcerated pediculated lesion in the palatine mucosa (an uncommon localization that not yet has been researched). This case histologically showed a histiocytic infiltration with an increase in the mitotic index, eosinophils and an accumulation of haemosiderin. The lesion resolved spontaneously after the biopsy, without recurring after a period of five years. This report stresses the important value of immunohistochemistry in diagnosing the lesion and also discusses the similarities and differences between other lesions that may be confused, potentially leading to a misdiagnosis.

Key words: *Atypical histiocytic granuloma, traumatic granuloma, pseudolymphoma, lymphoproliferative diseases.*

Introduction

In 1985, Eversole et al (1) described 4 cases of oral ulcerous lesions which histologically were characterised by an intense histiocytic infiltration, with moderate pleomorphism and mitotic activity. They did not show any signs of systemic disease and all the lesions were resolved after biopsy, there being no re-occurrences after a follow up period of 2 to 4 years. The lesions were clinically similar to squamous carcinomas or specific granulomatous ulcerations, whilst from the histopathology point of view, they led to diagnostic confusion with

malignant lesions of lymphoid origin (lymphomas). The authors believed that these lesions had not been reported before and suggested the term Atypical Histiocytic Granuloma.

This entity is included within a group of lesions which have in common a lymphohistiocytic infiltration with a certain level of atypia, which could be confused both clinically and histologically with lymphoid type malignant processes, particularly with lymphomas, for this reason being called "pseudolymphomas". Among the entities which are grouped within this concept would

be eosinophil granuloma of the oral cavity (2), angiolymphoid hyperplasia with eosinophilia (3), ulcerated granuloma eosinophilicum diutinum (4), benign follicular lymphoid hyperplasia of the palate (5), traumatic granuloma (6), etc. An erroneous interpretation of any of these lesions means an erroneous diagnosis of malignant lymphoma and therefore leads to incorrect over-treatment, which is harmful and expensive for the patient.

We present a case of atypical histiocytic granuloma situated in the palate (an uncommon localization that not yet has been informed), probably caused by trauma, and where the histochemical study was able to confirm the removal of the histiocytic infiltration, thus excluding the initial suspicion of malignant lymphoma.

Case Report

A 45 year old woman, without any significant medical history was seen in our oral surgery clinic for the evaluation of a lesion localized in mucosa of the hard palate, under the removable complete dentures that the patient was using. The lesion was situated in the left frontal area of the palate, in the rough palatine area. It was 6 mm in diameter and was pediculated, emerging from a normal mucosa and making a slight prominence on the palatine mucosa. It was greyish-brown in appearance and had a slight, non-bleeding ulceration on part of its surface (Fig.1). It was not painful to palpation. No other significant oral lesion was detected, and the extra-oral examination did not show up any clinically detectable cervical lymph-adenopathy.

The patient was a wearer of complete upper prostheses for fifteen years and there was no mention of any history of alimentary trauma in the area which could justify the lesion. The lesion had begun to be noticed with the tongue two years ago, without causing any problem. She decided to come to us due to having a small bleed under the dentures, which was attributed to the lesion. The radiological examination showed the complete loss of upper teeth but without any evidence of bone abnormality.



Fig. 1. Atypical histiocytic granuloma. An oval 6 mm erythematous elevated nodule of palatal mucosa.

With the suspected diagnosis of traumatic granuloma, but not discounting any other possible diagnosis, given its small size, the complete elimination of the lesion by excision biopsy was carried out, and it was sent to pathologist for rapid histological examination. The anatomy-pathology report showed up a polypoid formation covered by a keratinised stratified squamous epithelium, with focal ulceration and acute inflammation. Under the epithelium, a proliferation of cells with histiocytic properties appeared with an increase in the mitotic index and nuclear pleomorphism, presence of eosinophils, abundant vascularisation and frequent accumulations of haemosiderin (Fig.2).

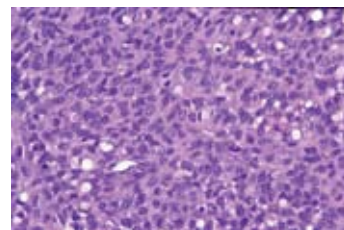


Fig. 2. Histological image in which an abundant histiocytic infiltration is seen with a high mitotic index. (Hematoxylin and eosin, 40x).



Fig. 3. Microscopic image which shows an intense positivity for CD68, confirming the extirpation of the histiocytic infiltration. (Staining for Antibody CD68, 10x).

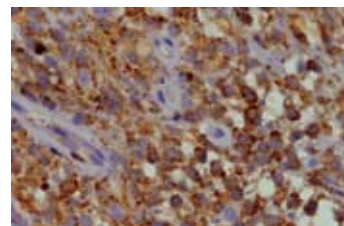


Fig. 4. Microscopic image which shows an intense positivity for CD68, confirming the extirpation of the histiocytic infiltration. (Staining for Antibody CD68, 63x).

In view of these histological findings, the pathologist decided to confirm the histiocytic infiltration and discount any suspicion of malignancy. He carried out immunohistochemical techniques which showed an intense positivity for CD68 (monoclonal antibody produced against macrophages and histiocytes), which confirmed the cell proliferation of the histiocytic extirpation, as well as negativity for factor VIII (Fig.3 and 4). The histological image was negative for malignancy. All this helped to suggest the diagnosis of atypical histiocytic granuloma.

After the biopsy, the patient was recommended to get a new set of complete dentures made, to avoid the possibility of a trauma factor due to the old dentures. The patient was reviewed a week after the extirpation, for the removal of the sutures. She was subsequently seen at one month, six months and one year after the intervention, to be subsequently seen once a year. The mucosa of the zone where the lesion was situated is now completely normal, with no sign of recurrence to date (five years).

Discussion

Benign histiocytic granuloma, clinically as well as anatomy-pathologically, can suggest malignancy, which can provoke a diagnostic error and an incorrect aggressive therapeutic approach. Hence the importance of understanding the clinical picture and using all means avail-

able for its diagnosis, which should eliminate any doubt of its possible malignancy. In some of the cases reported in the literature they were suspected or were diagnosed as malignant processes (1, 7-12).

In clinical pictures found in the literature (Table 1), here is a great number of localizations for this entity. Localization in the lingual mucous and mandibular gum are predominant (4 cases, 28,4%). The lip, so much upper, as lower, or the commissure, in a joint way, they also reach 4 cases (2 at level of the lower lip, one case at level of the upper lip and one in the labial commissures). Cases localized in other less frequent fields exist (mucous yugal, 1 case) or with multiple localizations.

However, in our case the lesion was located in the hard palate. This location not having been reported in any of cases reviewed (1, 5-12). However, there are reported cases of lymphoproliferative affection of the hard palate, which is different from atypical histiocytic granuloma (AHG) due to the predominance of infiltrated lymphoid which replaces the sub-mucosal tissue and does not demonstrate the pathological-anatomical peculiarities of histiocytic granuloma, despite being similar in its potentially malignant aspect (16,17).

The GHA happens in a comprehensive age range, between the 16 and 91 years, with a mean age of 55 year-old (1,10). The distribution per sexes is equalized (7 men in front of 7 women, among the 14 cases published before the one that occupies us).

Table 1. Summary of the cases of atypical histiocytic granuloma published in the international literature.

Author, year	Age, sex	Localization	Time in which cured (weeks)	Follow up free of recurrence
Ruckley et al, 1984 (9)	50, M	Dorsal tongue	4	11 months
Eversole et al, 1985 (1)	81, M	Mandibular gum	4	2-4 years
	75, F	Mandibular vestibule	8	2-4 years
	91, F	Mandibular gum	6	2-4 years
	60, M	Lower and upper lip. Alveolar mucosa.	3-4	2-4 years
Godfrey et al, 1985 (10)	16, M	Lip commissures	3	5 years
	22, F	Lateral of the tongue	4	2 years
Ankjaergaard et al, 1988 (11)	41, F	Lower lip	8	5 months
Kabani et al, 1988 (12)	42, F	Anterior maxillary mandibular	Not provided	20 months
Morrison et al, 1990 (7)	39, M	Dorsal tongue	3	5 months
De Vicente et al, 1991 (13)	67, F	Dorsal tongue	3	11 months
Van Doorne et al, 1994 (14)	65, M	Upper lip	2	Not provided
Del Rio et al, 1997 (15)	62, M	Buccal mucosa	16	2 years
Thronson et al, 2001 (8)	77, F	Lower lip	4	19 months
Case presented	45, F	Hard palate	-	5 years

Clinically, the lesion normally appears as an ulcer in the oral mucosa, generally on the lip, gums or tongue, with a variable period of evolution, but always more than two weeks. Cases of non-ulcerated lesions have also been reported, such as that published by Kabani et al. (12) in which it appeared as a sub-mucosal mass at the bottom of the maxillary mandibular. Our case presented as a pediculated lesion in the palate, which probably eroded and bled due to traumatic aggression from the complete prostheses which completely covered it.

The cause of AHG is unknown, the aetiological factor not being known in the majority of cases. In ours, just like that reported by Kabani et al. (12), the lesion is produced in intima related to the presence of a removable prosthesis, which we could call a reactive symptom, in view of the irritant factor which the dentures produced. In one case a high level of antibodies against the Epstein-Barr virus has been described, although it could have been just a casual finding. In fact, of the cases of AHG published, none of them showed clinical findings which suggested an underlying systemic viral infection. (10)

Equally, the possibility of an infection due to *Candida Albicans* has been suggested, by mechanisms of hypersensitivity, could be implicated in these types of lesions, especially in cases related to removable prostheses; in fact, it is well known that the presence of these types of dentures create a favourable environment for infections by these types of micro-organisms. However, we agree with Kabani et al. (12) in that, although it is possible to have a concomitant infection due to *Candida* in these patients, its aetiological implication is not justified; in fact, in our case there were no sign of infection beneath the dentures of the patient.

Lastly, the case reported by Thronson et al. (8), presented as history the use of topical tobacco for more than 60 years in the area of the lesion, although this circumstance has not been reported in any other case of AHG published.

As treatment its extirpation followed by pathological-anatomical study is recommended; whenever it is possible, it is better to carry out an excision biopsy with the complete removal of the lesion, although some authors have reported the recovery spontaneously of lesion after an incision biopsy. (1,11,13) This statement is discussed by authors such as Thronson et al. (8) who claim that the carrying out of a surgical procedure such as the taking of an incision biopsy cannot strictly be seen as an absence of treatment, and that even a minor surgical intervention could stimulate local repair and growth factors which favour healing. Analyzing other published cases the recurrence happened to the 5 weeks of follow up (range: 2 to 16 weeks).

AHG shares clinical and anatomy-pathology features with other clinical profiles such as eosinophil granuloma

of the oral cavity (2), diutinum ulcerated eosinophil granuloma (3), Wegener granulomatosis (18), angiolymphoid hyperplasia with eosinophilia (19), histiocytosis X (20), benign follicular lymphoid hyperplasia of the palate (5), traumatic granuloma (6), histiocytosis of the Langerhans cells, fibrous histiocytoma, allergic granulomatosis, etc... (21,22). A detailed study of the clinical and histological characteristics should be sufficient to differentiate between them, traumatic granuloma being the one that presents with more similarities and therefore more possibilities of diagnostic confusion. The fundamental difference lies in the absence of atypias in the infiltration of the traumatic granuloma, unlike that which occurs in AHG (1,8).

With regard to the eosinophil granuloma, this one affects predominantly 20-year-old minor males (unlike the presented case). The osseous affection is a clinical fact typical of the different forms of histiocytosis of Langerhans's cells (histiocytosis X), that helps it differ of entities as the presented one in this article. The differences with other lesions that must be included in the differential diagnosis, as the fibrous histiocytoma (fibrous injuries located in soft tissues and especially of jaw location), are more evident to anatomopathologic level, and the above mentioned study must be the key in the differentiation of these entities.

Therefore, we think in presence of a slightly common lesion, in our case located in a place not informed in the literature previously, but that it presents a fundamental characteristic: the high possibility of getting confused, in his diagnosis, with a linfoma. Of there the importance of a complete diagnostic study in this class of entities. Also we must highlight the importance of using immunohistochemical test that confirm the histiocytic extirpate of the cells, diminishing enormously the possibility of the diagnostic mistake that it can lead to an aggressive and unnecessary treatment bearing the reactive character of the lesion.

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