Exophytic soft tissue traumatic lesions in dentistry: A systematic review

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Abstract
Aim: The aim of this work is to provide an overview of the only most frequent exophytic soft tissue lesions with traumatic etiology found in the daily outpatient clinic.

Background: The term oral exophytic lesions represent any pathological growth that projects above the normal contours of the oral surface epithelium. This kind of lesion are often related to traumatic insults. The most common are fibrous nodule, traumatic and peripheral ossifying fibroma, morsicatio buccarum, pyogenic and peripheral giant cell granuloma, mucocele and ranula.

Review Results: About morsicatio buccarum a work by Woo et al. examined 584 white lesions, with a temporary diagnosis of leukoplakia, and pointed out that 56 of these were actually morsicatio buccarum. Santana Santos et al. did an epidemiological study on traumatic fibromas and pointed out that on 1290 oral soft tissue lesions, 193 were traumatic fibromas, about 15%. Mucocele is often a masticatory trauma that causes a laceration of the minor salivary glands with the formation of a cystic lesion that tends to increase. From a work by Jafarzadeh et al. It has emerged that about 1/3 of the pyogenic granulomas are related to trauma, and poor oral hygiene acts as an accelerating factor.

Conclusion: Exophytic traumatic soft tissue lesions must be well identified by the clinician because of their high frequency. These lesions often have similar clinical characteristics but different evolution. Therefore, histological confirmation is essential after excision.

Clinical Significance: These lesions can also cause a lot of concern to patients, so they need to be well treated to prevent complications. Furthermore, some of these lesions recurred more frequently than others, especially if it did not exit completely, such as in the case of the peripheral ossifying fibroma. For this reason, specific follow-up must also be set depending on the lesion diagnosed.

Keywords: Exophytic lesion, fibroma, fibrous nodule, narrative review, pyogenic granuloma, traumatic etiology

Introduction
The soft tissues of the oral cavity are often subject to traumatic injuries. These lesions can occur with different clinical forms; in this article only exophytic lesions will be considered. Oral exophytic lesions represent a pathological growth that projects above the contours of the oral surface epithelium [1]. Exophytic lesions account for 26% of all oral lesions and the differential diagnosis is not simple. There are several underlying mechanisms responsible for oral exophytic lesions such as hypertrophy, hyperplasia, neoplasia, and pooling of the fluid [2]. Exophytic soft tissue lesions’s correct diagnosis is decisive as these can show very similar clinical features. Therefore, the correct diagnosis of these lesions is decisive, indeed, an initial diagnostic error could cause subsequent errors in the therapeutic choices [3].

Review Results
An electronic MEDLINE (Pubmed) search was carried out for clinical studies including articles published from January 1, 1980 up to January 1, 2020.

Inclusion criteria were:
- Scientific contributions written in English language;
- Reviews and systematic reviews with well-structured experimental designs;

The exclusion criteria were:
- Scientific contributions written in non-English language;
The search used the following keywords “exophytic” “oral” “lesions” of the oral cavity, finding 280 results. The same procedure was used for an initial research using the following keywords: “traumatic oral lesions” of the oral cavity finding 129 results. Once the most frequent lesions were found, more detailed researches of the individual lesions were carried out, by typing the following keywords and thus obtaining the indicated number of articles: (Graph 1):

- “Oral fibrous nodule”: finding 98 results;
- “Traumatic fibroma”: finding 36 results;
- “Peripheral ossifying fibroma”: finding 245 results;
- “Morsicatio buccarum”: finding 21 results;
- “Oral pyogenic granuloma”: finding 610 results;
- “Oral peripheral giant cell granuloma”: finding 948 results;
- “Mucocele”: finding 93 results.

Therefore, the total searches yielded 2460 potentially relevant articles. Of these, 307 were duplicates and were thus removed. Subsequently, two authors (PG and AO) independently analyzed the titles resulting from this extensive research. If the title and abstract were not sufficient to decree their inclusion, full-text was analyzed. Any disagreements were resolved through discussion in order to reach consensus. After screening the titles and abstracts, 1996 items were found irrelevant, as they were out of context. After full-text evaluation, the remaining 157 articles were obtained and reviewed. After full-text evaluation, 124 studies were excluded because they did not meet the inclusion criteria. Therefore, the remaining 33 studies were included in this systematic review (Graph 2). Despite the inclusion of articles published in the past 40 years, two previous works were still mentioned in this systematic review (Eversole and Obermayer), due to their historical significance, as they were the first authors to describe respectively the reactive lesions of the oral cavity and the morsicatium buccarum. As stated by Santosh et al. [1] and Babu et al. [4] fibrous nodule, traumatic and peripheral ossifying fibroma, morsicatium buccarum, pyogenic and peripheral giant cell granuloma, mucocele and ranula are some of the most frequent traumatic exophytic lesion of oral cavity.

Discussion

Pyogenic Granuloma: Pyogenic granuloma is an inflammatory hyperplasia [5] characterized by a nodular growth of the mucosa with inflammation and granulation tissues [6]. Pyogenic granuloma is a very frequent pathology, although it can occur in all ages, it is predominant in the second decade of life in young adult females [5]. This lesion is considered as a reactive tumour-like lesion (Fig. 1a) [2]. Clinically, it’s a smooth or lobulated, compressible to palpation, sessile or pedunculated exophytic lesion [2-5]. Also in this case, the dimensions are very variable (from a few millimeters to several centimeters in diameter), as well as its color which can vary from pale pink to red and purple [3]. In 75% of cases this lesion affects the gingiva and in the remaining ones the labial, lingual and buccal mucosa [5]. The causes of its development can be multiple. However, as Jafarzadeh et al. said approximately one third of the lesions occur after an oral trauma [5]. Furthermore, a recent systematic literature review correlates pyogenic labial granuloma especially with chronic trauma [6]. The term “pyogenic granuloma” is confusing because the etiopathogenesis of this lesion is not infectious [7]. It is fundamental in the presence of these lesions to evaluate the possible differential diagnoses with histological examinations [8]. Indeed, histological examination shows a highly vascular proliferation similar to granulation tissue. Numerous small and large channels filled with red blood cells and coated with endothelial cells are formed [5]. Being a strongly vascularized lesion, pyogenic granuloma bleeds very easily [2]. The main treatment of this lesion is excisional however if the lesion is small and asymptomatic monitoring and follow up are indicated [9]. Differential diagnosis mainly includes: peripheral giant cell granuloma, peripheral ossifying fibroma, metastasis, hemangioma and hyperplastic gingival inflammation [5]. Unfortunately, recurrence is not uncommon [2].

Peripheral giant cell granuloma: Peripheral giant cell granuloma is the most frequent giant cell lesion of the jaws [10]. It develops from the periodontal membrane or from the connective of the periosteum in response to irritation or chronic trauma [11]. The lesion usually develops between the fifth and sixth decades of life and shows a slight female predilection [12]. Clinically it manifests as a solid red-blue nodular lesion located on the gingival mucosa, fundamentally in the lower jaw [13]. Peripheral giant cell granuloma does not show neoplasia, but it can be considered rather a benign hyperplastic reactive lesion [14]. Indeed, there are many local etiological factors: complicated tooth extractions, non-congruent restorations and prostheses, dental malposition, bacterial plaque and calculus [14]. Furthermore, a recent systematic review, included in the present study, associates dental implants with the peripheral giant cell granuloma. Most of them are located in the posterior mandible. As a result of the lesser hygiene in these sectors due to the reduced accessibility there is a greater probability of occurrence of peripheral giant cell granuloma associated to dental implants. According to this study, peripheral giant cell granuloma related to dental implants shows a high recurrence rate, which requires surgical removal of them [15]. Histological exam is fundamental to establish the definitive diagnosis because there are many disorders that should be considered in the differential diagnosis like pyogenic granuloma, peripheral ossifying fibroma, traumatic fibroma [16]. Treatment consists of complete surgical resection of the entire lesion [10]. Histological features include an non-encapsulated tissue mass consisting of reticular and fibrillar connective stroma with multinucleated giant cells and connective fusiform cells [11]. According to Eversole et al. recurrence is observed only in 5% and 11% of cases [17].

Traumatic fibroma: Traumatic fibroma is the most common tumour-like lesion of the oral cavity with the prevalence of 1-2% in general population [2]. The epidemiological study of Santana Santos et al. pointed out that on 1290 oral soft tissue lesions, 193 were traumatic fibromas, about 15% [18]. This lesions have an high frequency in female adults as stated by Zarei et al. [19] Traumatic fibroma is a reactive hyperplasia of connective tissue in response to local irritation or trauma (Fig. 1b). It is an exophytic lesion with a pedunculated or sessile structure. The color is similar to those of the surrounding mucous membranes and the surface is typically smooth, hyperkeratotic or ulcerated [2] Usually, irritation traumatic fibroma or focal fibrous hyperplasia have an average diameter of 1.5 cm, but, if left untreated, they can reach considerable
dimensions. The most common intraoral site is along the occlusal line of the buccal mucosa, which is an area typically subjected to masticatory trauma, but it can appear also on the tongue, the lower lip and hard palate (Fig. 1c). The etiological factors are local irritative factors, such as prostheses, but also the chronic habit of biting the lips and cheeks. Furthermore, de Santana Santos et al. suggest that female hormones contribute positively to an increase in the synthesis and accumulation of collagen by fibroblasts in the presence of a chronic lesion. Histologically, this lesion is characterized by an uncapsulated nodular mass of dense and sometimes hyalinized fibrous connective tissue. These lesions have clinical features very similar to other traumatic exophytic lesions such as pyogenic granuloma, peripheral giant-cell granuloma and peripheral ossifying fibroma for this reason a diagnostic confirmation is required with histological examinations. Furthermore, recent studies show excellent outcomes even after removal by diode laser. They are benign and asymptomatic lesions and the initial treatment involves the identification of the causative local irritative factor, their elimination with subsequent monitoring and finally surgical excision. The recurrence rate is very low.

Peripheral ossifying fibroma: Peripheral ossifying fibroma also called epulis of the ossifying fibroid, fibroblastic calcifying granuloma or peripheral fibroid with calcification is a benign hyperplasia of the gingival mucosa which shows areas of calcification or ossification. This lesion accounts for 2% to 9% of all gingival lesions and 3% of all oral biopsy specimens. These lesions appear as a small focal mass with a sessile or pedunculated base, usually originating from an interdental papilla in the anterior maxilla. The color is typically pink, similar to the adjacent mucosa. Usually, the lesions have an average diameter of 2 cm and when the size increases, tooth mobility, tooth migration and bone loss may arise. The etiopathogenesis of these lesions mainly depends on the proliferation of cells of the periodontal ligament due to chronic trauma, microorganism, calculus and plaque. According to a recent study, the primum movens derives from the expression of the SATB2 gene by stromal cells located in the periodontal ligament. Peripheral fibroma with calcification occurs in younger patients more often than fibrous hyperplasia, and thus may represent a stage in the development of traumatic fibroma. Histologically it is made up of well-vascularized hypercellular connective tissue, containing plump mesenchymal cells and numerous multinucleated giant cells. Consequently, histological analysis is necessary for diagnostic confirmation. In fact, the differential diagnosis includes fibrous hyperplasia, pyogenic granuloma and peripheral giant cell granuloma. Treatment includes local surgical excision and follow-up because of the recurrence rates. Also in this case, a recent review highlights alternative therapies to surgical excision, such as the use of the laser diode, with excellent results and advantages (greater surgical visibility, absence of bleeding and less morbidity). Recurrence is caused by incomplete excision or by persistence of local factors. Indeed, recurrence rate is estimated between 8% and 20%. Although these diseases have very similar clinical characteristics, some of them can direct the clinician towards a more precise differential diagnosis, although the confirmation is always histological. The detection of the causative factor through the medical history and physical examination plays a key role in the initial diagnostic process. Some lesions, in particular traumatic fibroma, can be identified mainly by their site and by the relationships with the adjacent structures: the case of prostheses and incongruous restorations is typical, moreover, the lesion is typically pink and on palpation it’s elastic. Instead, an easily bleeding, purplish-red mass, and soft on palpation suggests a pyogenic granuloma, especially in a female patient. As for the peripheral giant cell granuloma and the peripheral ossifying fibroma, both can be locally invasive, inducing dental mobility and bone resorption, however the second one is hard on palpation and the mucous membrane is generally pink while the second more frequently has a darker color and is softer on palpation.

Fibrous nodule: Fibrous nodule are nodular benign lesions resembling small fibromas. In fact, they present clinical, histological characteristics similar to traumatic fibromas. Clinically, they appear as single or multiple pinkish-white nodules or papules on the gingiva of both dental arches. On average they measure between 1 and 4 mm and are asymptomatic. Histologically it has a non-ulcerated physiological stratified squamous epithelium and underlying connective tissue with collagen fibers and some fibroblasts. Gingival fibrous nodule is essentially a variation of normal oral structures that may be mistaken for disease. The differential diagnosis for this condition includes: fibroma, papilloma, focal epithelial hyperplasia, hamartomas, gingival cyst and exostosis. Indeed, fibrous nodules do not show any kind of evolution, the patients in most cases are not aware of their existence, so their removal is not necessary. In fact, if they are removed, they may recur.

Morsicatio buccatum: Morsicatio buccatum is a form of chronic oral mucosa lesion caused by habitual cheek or lip biting. According to Obermayer this disease can be considered a real compulsive neurosis. Morsicatio buccatum prevalence is in 750 out of everyone million individuals, with females being more affected than males, especially during pregnancy. The most frequent lesions are transverse ridges along the lines of occlusion, soft nodules termed “diapneusie buccale”, fibrosis of the oral mucosa, white lesions resembling leukoplakia or lichen planus, red lesions resembling leucoplakia or lichen planus. Histologically the epithelial shows acanthosis, hyperkeratosis and orthokeratosis often accompanied by a slight inflammation in the subepithelial stroma. In most cases, patients are unaware of their habit, making the clinician’s diagnosis very complex. This habit lead to development of several lesions that can be confused with other dermatological disorders leading to misdiagnose, indeed, there are cases of morcicatio buccatum incorrectly treated with corticosteroid drugs because they had been mistaken for pemphigus. A work by Woo et al. examined 584 white lesions with a diagnosis of leucoplakia and found out that 56 of these were actually morsicatio buccatum lesions. Indeed, differential diagnosis includes dermatological diseases such as oral lichen planus, pemphigus, benign mucous pemphigoid, alba line, oral white sponge nevus or leukoplakia. It’s therefore important to keep this possibility in mind and to intercept it early to undertake dental (protective screening devices) and psychological therapy.

Mucocle and Ranula: Mucoceles, by definition, are cavities filled with mucus. Mucocele is the most common disease of the accessory salivary glands. As a confirmation of this, Barros et al., in a recent retrospective 11-year study on lip lesions, revealed that the mucocele was the most frequently
detected lesion in all age groups \[^{34}\]. Mucoceles are most common in patients in the first four decades and develop more often on the lower lip \[^{35}\]. Clinically, they present as asymptomatic and soft lesion coloured blue or with the normal colour of the mucosa. It’s a non-malignant lesion caused by a masticatory trauma that leads to a laceration of the salivary glands with the extravasation of mucus and the formation of a cystic lesion that tends to increase. Ranulas are variant of mucoceles which develop on the oral floor. Histologically, the mucous extravasation is lined with granulation and connective tissue with variable inflammation and vascular congestion \[^{33}\]. It’s important to differentiate them from vascular lesions such as angiomas that have similar characteristics but if they are removed they cause significant bleeding \[^{36}\]. The most common treatment are the surgical excision and the marsupialization. The choice of treatment depends mainly on the size of the lesion and the risk of damaging anatomical structures. The removal of the sublingual gland associated to a ranula reduce the risk of recurrences though it is very invasive \[^{33}\]. As regards alternative treatments, cases of excision through the use of the laser are frequently described in the literature \[^{37}\], particularly indicated in cases of very small patients \[^{38}\].

As regards the working classification, the first step is represented by the medical anamnesis, with particular regard to the pharmacological one, in order to exclude gingival hypertrophies caused by drugs. Subsequently, an objective examination of the oral cavity and perioral region must be performed. Later, assess whether the lesion is single or multiple, the diseases examined in this systematic review, with the exception of the fibrous gingival nodules, are single. Following factors must be evaluated: any relationships with local irritants (suggest traumatic fibroma), mobility in the underlying planes (typically positive for mucocele and ranula) color, local invasiveness, texture on palpation, anatomical location and age of the patient.

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**Graph 1**: Pie chart of search results.

**Graph 2**: Flow chart of the search performed.
Conclusions
There are many different exophytic traumatic lesions of the oral cavity with different clinical behaviors. They are often difficult to distinguish, it is therefore essential to know them and carry out diagnostic tests through histological examinations that are the only ones that allow a certain diagnosis. These lesions have different treatment possibilities and risk of recurrences that must be known by the dentist. It is important to recognize the causes of these lesions in the early stage so that they are still moderate in size and may undergo spontaneous healing without the need for surgery. The surgical excision must then be carried out correctly in order to obtain complete excision of the lesion and avoid the development of recurrences.

Clinical Significance
Exophytic soft tissue traumatic lesions are frequently found in daily clinical practice in all patients, of any age group. An accurate knowledge of these pathologies by the clinician is crucial for the differential diagnostic process, in order to carry out a correct treatment. Furthermore, if untreated, these lesions can develop into more severe forms, causing a aggravation of the life's quality of patients. Finally, the correct treatment is necessary because many of these lesions show higher recurrence fees than others, such as the peripheral ossifying fibroma, especially if not completely removed. For this reason, following the histological confirmation, specific follow-up will have to be scheduled depending on the diagnosed lesion.

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