Final Diagnosis for The “Epulis”

Subjects: Others

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Epulis” is a widely used term to describe a localized gingival enlargement. However, a wide range of neoformations might present as localized, slow-growing, asymptomatic gingival masses. Histological examination, sometimes combined with immunohistochemistry, might reveal a wide spectrum of lesions, including hamartomatous lesions, non-neoplastic lesions, benign and malign neoplasms and metastases from distant cancers.

Keywords: epulis ; gingival overgrowth ; oral tumor ; provisional diagnosis ; reactive lesions ; histology ; immunohistochemistry

1. Introduction

Localized, slow-growing, asymptomatic gingival masses are commonly indicated as “epulis”. The usage of the term “epulis” as a diagnosis is well established among clinicians. However, the diagnosis of “epulis” is simplistic and inaccurate [1]. In fact, “epulis”, from the Greek ἐπουλίς, literally means “over the gingiva”. Thus, the term refers to the location of the neoformation and does not represent a specific pathological entity.

The occurance of masses over the gingiva may be due to different types of underlying pathological changes [2]. According to etiologic factors and pathologic changes, gingival enlargments can be classified as: inflammatory enlargements, drug-induced enlargements, enlargements associated with systemic diseases or conditions, neoplastic enlargements and false enlargements [3].

Localized enlargements can be further divided into three sub-types [3]:

- Isolated (enlargements limited to gingiva adjacent to one or two teeth);
- Discrete (isolated sessile or pedunculated enlargements);
- Regional (enlargements that involve gingiva around three or more teeth in one or multiple areas of the mouth).

Reactive lesions, or focal reactive overgrowth of the gingiva (FROG) [4], are the most common neoformations that lie beneath the so-called “epulis” [4][5].

Those neoformations are: pyogenic granuloma, peripheral giant cell granuloma, giant cell fibroma, fibrous hyperplasia and peripheral ossifying fibroma. They do not have a neoplastic origin and represent an exaggerated repairing and remodeling response to stimulus [6][7][8][9][10][11].

Drug-induced enlargements are mainly due to anti-convulsants, calcium channel blockers and immunosuppressants [12][13].

Systemic diseases or conditions exaggerate the usual gingival response to local irritation [2]. Localized gingival overgrowths that appear during pregnancy are often called “pregnancy tumor” or “granuloma gravidarum”. The pathogenesis is thought to be related to the increase in sex hormones that might stimulate the synthesis of angiogenic growth factors [12][14].

Localized gingival enlargemnts have been reported in patients with neurofibromatosis, Sturge–Weber syndrome and leukemia [12][15][16].

Neoplastic enlargements can be benign or malignant [1]. Among the benign entities are nerve sheath tumors, such as neuroma and schwannoma, and vascular tumors, such as hemangioma. Among the malignant entities are verrucous carcinoma, lymphoma, sarcomas and metastasis [1].

Masses originated from different pathological changes might look very similar in shape and color. They take the form of a discrete sessile or pedunculated mass which, in dentate patients, occurs on the interdental papilla, the buccal or the palatal/lingual surface of a tooth, whereas in edentulous or partially dentate patients, it occurs on the alveolar ridge and might be close to an ill-fitting prostheses. The color may vary considerably (pink, pale pink, red or blue) [2].

Thus, the histopathological exam and, when appropriate, an immunohistochemical evaluation are mandatory to make a correct diagnosis [1][17][18].

The management of the patient should never be underestimated and depends on the nature of the lesion. Based solely on the clinical aspect, local gingival enlargements might be misdiagnosed [19]. To rationally approach these neoformations, the clinician should own a comprehensive knowledge of the pathological entities that might occur over the gingiva.

2. Considerations from Provisional to Final Diagnosis

Localized chronic gingival enlargements are frequently detected by clinicians and the management requires a rational approach. These neoformations occur with the following characteristics [1][2][3][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35]:

- Develop on the buccal/palatal/lingual side or extent from buccal to palatal/lingual side along the interdental papillae;
- Self-limited and solitary growth;
- Progressively increasing in size over a variable period of time;
- Variable size (usually about 1 or 2 cm in diameter);
- Nodular/ovoid shaped;
- Smooth or irregular surface;
- Well-defined margins;
- The same color as the surrounding normal mucosa/pale pink/red/blue;
- Sessile or pedunculated;
- Soft/hard on palpation;
- Spontaneous bleeding/ulcerated surface might be present.

A careful collection of data regarding the medical history of the patient must always be the first step to take in the process that will lead the clinician to the final diagnosis. Sometimes the medical history might be not relevant at all, whereas at other times it might be of great help.

As regards the patient's medical history, the clinician should investigate the following aspects [36]:

- Systemic diseases;
- Medications taken;
- Pregnancy;
- Previous diagnosis of malignant tumors.

A previous diagnosis of a malignancy at a distant site should make the clinician consider the possibility that a metastasis occured over the gingiva [35][37].

Time of appearance, eventual recurrence, any change in shape, color and consistency and spontaneous bleeding and ulceration are relevant details.

Clinical examination must include a good descriptive evaluation of the neoformation as well as the assessment of oral hygiene and the presence of traumatic factors [32]. With the sole clinical examination, a provisional and not a definitive

diagnosis might be formulated. The term “epulis” can be provisionally used to describe the overgrowth that occurs over the gingiva. Surgical treatment should be preceded by cause-related therapy and elimination of plaque retentive factors in attempts to modify etiological factors. The choice between an excisional or incisional biopsy might be challenging. Incisional biopsy instead of complete excision of the lesion should be taken into consideration when one or more of the following features are present [17][23][25][26][28][30]:

- Persistent ulceration;
- Multiple and irregularly spherical in shape enlargements;
- Induration or fixation over time;
- Unusual pigmentation;
- Lymphadenopathy;
- Unexplained tooth mobility,
- Paraesthesia;
- Irregular bone loss at radiographic examination;
- History of cancer.

A detailed investigation through a histopathological examination is mandatory for the final diagnosis. Immunohistochemical evaluation is also of great help, especially in the most challenging scenarios.

The microscopic evaluation might reveal a wide spectrum of lesions, including hamartomatous lesions, non-neoplastic lesions, benign and malign neoplasms and metastases from distant cancers.

Hamartomas are rare findings in the oral cavity and may derive from various tissues [38].

ALQahtani et al. [20] and Raghunath et al. [27] diagnosed an oral leiomyomatous hamartoma that arised over the gingiva. ALQahtani et al. [20] reported that the patient was in good health and the lesion appeared as a polypoid, pedunculated, light pink and soft swelling. A complete excision of the lesion was performed. The diagnosis was made thanks to histological and immunohistochemical investigations. Masson’s trichrome staining allowed the authors to distinguish the smooth-muscle cells (red-stained) from the surrounding collagen fibers (blue-stained). Smooth-muscle bundles stained positive for smooth-muscle actin and desmin.

Raghunath et al. [27] reported that the patient’s medical history was not relevant for the final diagnosis and the lesion appeared 6 months earlier, measured about 1.5 × 2 cm and was smooth surfaced, sessile, ovoid and soft. The lesion was completely excised. Van Gieson stain was used to differentiate the smooth muscle bundles, which stained yellow, from the collagen bundles, which stained red.

The oral cavity is an uncommon site for metastatic colonization. The development of tumor metastases in the oral cavity accounts for 1 to 3% of all the malignancies of the head and neck region [39].

Oral metastasis might be the first indication of an occult malignant tumor [40]. The sites of the primary tumor might be lung, kidney, liver and prostate for men, and breast, female genital organs, kidney and colo-rectum for women [41]. Oral metastatic lesions are divided into mucosal and jawbone metastases. The jawbones are more affected than the oral soft tissues [42].

Mucosal metastases over the gingiva might resemble a reactive lesion [17]. Fukuda et al. [37] suggested that the criteria for considering an oral malignant neoplasm as metastatic are: a primary tumor with histologic verification, a second oral lesion histologically relevant to the primary tumor, a histopathologic appearance of the oral lesion distinct from that of a typical oral malignancy and exclusion of a possible direct extension from the primary tumor.

Kawamura et al. [23], Moser et al. [26], Wu et al. [33], Shah et al. [28] and Chiarelli et al. [21] reported the occurrence of gingival metastasis. Kawamura et al. [23] treated a patient who previously underwent a surgical procedure for poorly differentiated rectal carcinoma. The gingival mass presented as a red and tender swelling. The histology of the mass was

similar to the histology of the primary tumor. Immunohistochemical examination revealed positive staining for cytokeratin 20 and negative staining for cytokeratin 7, estrogen, progesterone and thyroid transcription factor-1.

Moser et al. [26] reported a gingival metastasis that occurred in a patient who was diagnosed with epitheloid mesothelioma 2 years earlier. The compact, painless and ulcerated swelling appeared 6 weeks before the patient was referred to their department and increased in size during that period. There was no objective paresthesia of the mental nerve nor was lymphadenopathy discernible. Orthopantomography and a CT scan showed no signs of osteolytic activity. Microscopic examination showed a morphology very similar to the one of mesothelioma. The mesothelial marker calretinin was strongly positive in tumor cells. Positive staining for cytokeratins 5/6 and negative staining for Ber-EP4 ruled out the diagnosis of adenocarcinoma.

3. Conclusions

“Epulis”is a non-specific term used for localized gingival enlargements. These enlargements might hide various pathological entities. Thus, the diagnosis cannot be based only on clinical impressions. Histological and immunohistochemical examinations help clinicians to formulate the right diagnosis. A clear medical history is necessary to rule out possible association with systemic diseases, medical treatments and pregnancy. Metastatic spread of a malignancy must also be considered. Sometimes medical history reveals nothing meaningful, even in the presence of a gingival metastasis, since it might be the first indication of a cancer of unknown origin. The clinical examination must comprise an accurate evaluation of the characteristics of the neoformation (location, extension, shape, size, margins, color, surface, consistency) and the general status of the oral cavity (level of oral hygiene, plaque retentive and traumatic factors).

Clinicians should not worry about surgical approach and prognosis of hamartomatous lesions, non-neoplastic lesions and benign neoplasms. On the contrary, the management of patients diagnosed with a malign tumor or metastasis is much more troubling. Furthermore, the clinical presentation of a malign tumor or a metastasis in the oral cavity can be deceiving, leading to a misdiagnosis. CT of the mandible/maxilla must be used to detect any bone-destructive activity under masses, although bone involvement might not always be present. Moreover, when a malign neoplasm is diagnosed, it is mandatory to detect any systemic spread of the primary neoplasm.

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