

# Benign neoplasms of gingiva and alveolar mucosa

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## ABSTRACT

Clinicians encounter a variety of oral lesions that can originate from various etiologies, such as from infective, idiopathic, inflammatory, reactive, and neoplastic changes. Neoplastic changes are rare compared with other affecting conditions, however, the oral cavity is one of the areas where tumors and tumor-like lesions most commonly develop and include both non-odontogenic and odontogenic lesions. Diseases affecting the oral mucosa are diverse and cover a broad spectrum of benign or malignant lesions. To make an accurate diagnosis, a clinician must take a comprehensive clinical history and have adequate information about the signs and symptoms, such as location, size, color, and morphology of the oral mucosal lesion. This review aims to describe the clinical, radiographic, microscopic, and treatment aspects of benign neoplasms that might affect the gingiva and alveolar mucosa.

**Keywords:** Benign lesions, gingiva, alveolar mucosa

## INTRODUCTION

The term neoplasia means new growth<sup>1</sup> and tend to grow independently of adjacent tissues. Neoplasms are often called tumors although not all neoplasm are malignant. The clinical characteristics of a tumor allow it to be categorized as benign or malignant.<sup>2</sup>

### Tumors have two main components:<sup>3</sup>

1. Parenchyma consisting of neoplastic cells
2. Supportive, host-derived, non-neoplastic stroma consisting of connective tissue and blood vessels, and host-derived inflammatory cells

The biological behavior of the tumor is determined by the parenchyma and the tumor is named after this component. The stroma serves as support for the growth of parenchymal cells.

## COMPARISON OF BENIGN AND MALIGNANT TUMOR CHARACTERISTICS<sup>4</sup>

Benign and malignant tumors vary from each other according to their degree of differentiation, growth rate, local invasiveness, and metastatic potential. While benign tumors are similar to the tissue from which they originate and show good differentiation, malignant tumors are poorly differentiated or are completely undifferentiated (anaplastic). Benign tumors grow slowly, while malignant tumors usually grow faster. Benign tumors are well circumscribed and have a capsule structure, whereas malignant tumors are poorly circumscribed and invade adjacent tissues. While benign

tumors remain localized at the site of origin, malignant tumors are locally invasive and can metastasize to distant sites.

## BENIGN NEOPLASMS OF THE GINGIVA AND ALVEOLAR MUCOSA<sup>5</sup>

- Squamous papilloma
- Fibroma
- Giant cell granuloma
- Traumatic neuroma
- Neurofibroma
- Schwannoma
- Leiomyoma
- Hemangioma
- Lymphangioma
- Congenital epulis
- Peripheral odontogenic tumor
- Fibromatosis

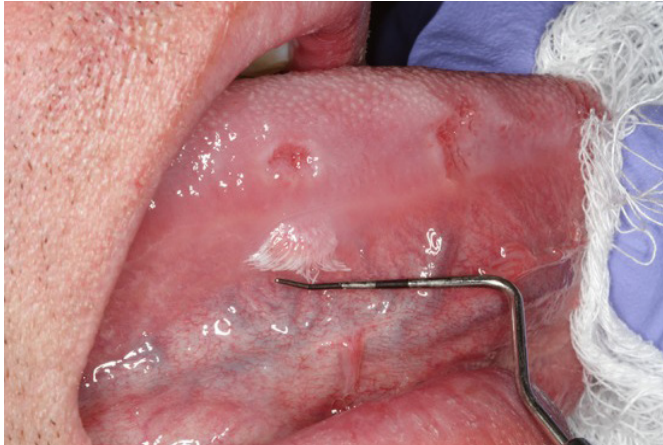
### Squamous Papilloma

This is a benign, asymptomatic, non-plaque-related gingival lesion with exophytic finger-like protrusions (Figure 1), thought to be caused by the human papilloma virus, formed by the proliferation of stratified squamous epithelium.<sup>6</sup> HPV type 6 and type 11 are associated with squamous papilloma<sup>7</sup> and

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it has also been suggested that this neoplasm can occur due to trauma.<sup>8</sup> In the intraoral region, it most commonly affects the palate, tongue, and lip mucosa.<sup>9</sup> Squamous papillomas are typically seen in individuals aged 30-50 years, but also reported in children under 10 years<sup>8,10</sup> and constituting approximately 8% of oral tumors in children.<sup>10</sup> Koilocytes are seen in the spinous layer of squamous papillomas and connective tissue shows varying degrees of keratinization.<sup>11</sup> They can exhibit as a pedicled lesion with a cauliflower-like surface.<sup>8</sup> They present as solitary masses rarely exceeding 5 mm and range from white to pink and red in appearance.<sup>11</sup>



**Figure 1.** Squamous papilloma and finger-like protrusions<sup>11</sup>

Differential diagnosis includes verruca vulgaris, verruciform xanthoma, condyloma acuminatum, giant cell fibroma, and squamous cell carcinoma.<sup>12</sup> Verruciform xanthoma is distinguishable as they are not parakeratinized. Condyloma acuminatum is mostly larger than squamous papilloma.<sup>11</sup> Treatment of squamous papilloma usually involves complete excision, but there remains the potential for recurrence.<sup>6</sup>

### Fibroma

Fibromas are benign, reactive lesions resulting from prolonged irritation in the oral cavity that are often found on the buccal mucosa, lips, or along the lateral edges of the tongue.<sup>13</sup> Clinically, oral fibroma appear as a hard, smooth swelling that is similar in color to the surrounding soft tissue<sup>14</sup> (Figure 2). Fibromas have a dome-shaped structure, but can be pedunculated.<sup>13</sup> Although usually seen in older people, fibromas can occur at any age, but rarely affect adults.<sup>15</sup>



**Figure 2.** Irritation fibroma<sup>16</sup>

A biopsy should be performed after excision to eliminate other possible pathologies. Studies have shown the incidence of fibroma to range between 5% and 8.4% compared with similar oral pathologies. Conservative excision is preferred as a treatment and recurrence is not expected.<sup>17</sup>

### Giant cell fibroma

First described by Weathers and Calliham in 1974, oral giant cell fibroma is a benign tumor characterized by the presence of star-shaped and giant multinucleated cells in the subepithelial fibrotic connective tissue.<sup>18</sup> It constitutes 2-5% of fibrous lesions in the oral cavity and idiopathic stimulation might have a role in its etiology<sup>19</sup>, however, there are debates about its etiology.<sup>20</sup> Giant cell fibroma is generally more common in patients under age 30 years and predominant in women.<sup>21</sup>

Although it is most observed in the gums, the tongue and buccal mucosa are the most common sites.<sup>22</sup> It is seen as an asymptomatic exophytic lesion in the oral cavity, less than 1 cm in size, and can have a pedicle<sup>21</sup> (Figure 3). Surgical excision is the preferred treatment and recurrence is not expected.<sup>22</sup>



**Figure 3.** Giant cell fibroma<sup>21</sup>

### Neurofibroma

Neurofibroma is a benign tumor originating from Schwann cells and perineural fibroblasts.<sup>23</sup> It is most commonly considered a skin lesion, but can also occur as an oral lesion. Neurofibroma is most commonly seen intraorally on the tongue and buccal mucosa, but studies report neurofibroma formation on the lips and gums.<sup>24</sup> These neoplasms present clinically as solitary or as a component of neurofibromatosis. The solitary type, which is more commonly found in younger people, appears as slow-growing, soft, painless lesions ranging from small nodules to larger masses.<sup>25</sup> Although neurofibromas can be seen centrally, they are rare. In rare cases, it can present in various forms on radiographic findings ranging from well-circumscribed to poorly circumscribed and with a unilocular or multilocular appearance (Figure 4).<sup>26</sup>

Histologically, neurofibromas are circumscribed and unencapsulated tumors consisting of spindle-shaped cells with elongated, thin nuclei and scant cytoplasm, surrounded by a collagen matrix located in a myxoid stroma.<sup>28</sup> Surgical excision is the preferred treatment and recurrence is not expected.<sup>25</sup>

### Schwannoma

Schwannoma is a slow-growing, single, encapsulated tumor originating from the Schwann cells of the peripheral nerve sheath.<sup>29</sup> Of all nerve sheath tumors, schwannoma is the most common, accounting for approximately 89% of cases<sup>30</sup>, however, its incidence in the oral cavity is rare.<sup>31</sup> The regions with the highest incidence of schwannoma lesions are the tongue, palate, floor of the mouth, buccal mucosa, lips, and gums<sup>32</sup> (Figure 5). Except for any peripheral, olfactory, and ocular cranial nerves containing Schwann cells that form the myelin sheath, other cranial nerves or autonomic neurons can be responsible for its etiology.<sup>29</sup>



Figure 4. Neurofibroma on the floor of the mouth<sup>27</sup>



Figure 5. Schwannoma lesion on the floor of the mouth<sup>33</sup>

Approximately 90% of schwannomas are sporadic and may develop together with neurofibromatosis type 1 (NF1), NF2, and schwannomatosis.<sup>34</sup> It is more common between the ages of 20-50 years and there is no gender predominance. Histopathological examination commonly shows an encapsulated tumor consisting of two different histopathological areas. Antoni A tissue has hypercellular spindle cells that palliate eosinophilic areas (verocay bodies) and is S100 positive. Antoni B tissue is hypocellular with loose connective tissue.<sup>30</sup> Schwannoma are generally solitary, smooth, mobile, slow-growing, and minimally invasive tumors. To eliminate the risk of recurrence, total surgical excision is the preferred treatment.<sup>30</sup>

### Leiomyoma

Leiomyoma is a tumor of smooth muscle origin that is mostly associated with the gastrointestinal tract, uterus, and skin.<sup>35</sup> The oral cavity lacks smooth muscles other than the blood vessel wall, so its incidence in the mouth and maxillofacial region is low.<sup>36</sup> Intraoral lesions are most commonly found in the lips, tongue, buccal mucosa and palate, gingiva, and mandible.<sup>36</sup> Leiomyoma is characterized by an asymptomatic, slow-growing hard mass with average dimensions ranging from 1-2 cm and a history of less than one year<sup>37</sup> (Figure 6).



Figure 6. Leiomyoma<sup>38</sup>

Leiomyoma is usually seen in the oral cavity between the ages of 30-50 years.<sup>36</sup> Histologically, it contains small cells with eosinophilic cytoplasm and basophilic nuclei.<sup>38</sup> Diagnosis is difficult due to its nonspecific clinical appearance, therefore, histopathological examination and electron microscopy are used for definitive diagnosis. Complete excision is the preferred treatment.<sup>39</sup>

### Hemangioma

Hemangiomas are a spectrum of congenital, benign vascular tumors recognized in neonates, infants, and children.<sup>40</sup> Occasionally, hemangiomas might not be noticed at birth, but presents the first 8 weeks of life.<sup>41</sup> There can be a period of remission in adulthood.<sup>42</sup> These lesions are characterized by hyperlocalized proliferation of endothelial cells with a central lumen.<sup>40</sup> It is especially common in the head and neck regions of women. Oral hemangiomas are most commonly seen on the lips, buccal mucosa, tongue, and palate.<sup>43</sup>

Clinically, oral hemangiomas usually appear as asymptomatic, reddish-blue or dark blue, soft, well-circumscribed, lobulated, sessile, or pedunculated (Figure 7). The sizes of these lesions can range from a few millimeters to a few centimeters.<sup>44</sup>

Differential diagnosis is supported by advanced imaging methods, such as Doppler ultrasonography or magnetic resonance imaging.<sup>45</sup> In cases where imaging methods are not sufficient, histopathological evaluation is considered the most reliable diagnostic method of oral hemangiomas.<sup>44</sup> When intraoral hemangioma lesions were examined by ultrasound, all lesions were submucosal, well-circumscribed,

lobulated, unencapsulated, hypoechoic, had hyperechoic foci (echogenic septa), and heterogeneous lesion areas were detected.<sup>46</sup>



**Figure 7.** Submucosal hemangioma in the right molar region of the buccal mucosa<sup>45</sup>

### Lymphangioma

Lymphangiomas are benign, hamartomatous malformations resulting from lymphatic tissue sequestration that is twice as common in men than women.<sup>47</sup> They are rarely seen in the oral cavity and when they do occur, are more common on the dorsum of the tongue, followed by the palate, buccal mucosa, gums, and lips.<sup>48</sup> Superficial lesions consist of raised nodules that are pink or yellowish in color (Figure 8). Deeper lesions appear as soft, diffuse masses with normal color.<sup>49</sup>



**Figure 8.** Blister-like lesions on the tongue<sup>47</sup>

Lymphangioma is a common cause of macroglossia in children, which is associated with swallowing and chewing difficulties, speech disorders, airway obstruction, mandibular prognathism, and open bite.<sup>48</sup> Tasca, Myatt and Beckenham<sup>50</sup> stated in their study that Ludwin's angina might develop depending on the infected base of the tongue lymphangioma.

Histopathologically, they are divided into three groups: capillary, cavernous, and cystic. Marked dilatation of lymphatic vessels is evaluated by histopathology. With microscopic evaluation; small capillary-sized vessels are seen in the capillary type, large dilated lymph channels are present in the cavernous type, and large macroscopic cystic spaces are seen in the cystic type.<sup>51</sup> The cavernous type has the highest intraoral incidence.<sup>52</sup>

It is reported that lymphangiomas are associated with Turner syndrome, Noonan syndrome, trisomies, cardiac anomalies, fetal hydrops, and fetal alcohol syndrome.<sup>53</sup> Surgical excision is the preferred method in treatment. Alternatively, radiation therapy, cryotherapy, electrocautery, sclerotherapy, steroid application, embolization and ligation, Nd-YAG and CO<sub>2</sub> laser surgery, or radiofrequency tissue ablation techniques can also be used.<sup>48</sup> Lymphangioma is difficult to completely remove due to its unencapsulated structure and infiltrating character, which increases the incidence of recurrence. Although large lesions in the neck and tongue can result in airway obstruction and death, the prognosis is mostly positive for patients.<sup>54</sup>

### Epulis

Epulis is also called congenital granular cell epulis.<sup>55</sup> The color of these lesions usually resemble the oral mucosa and can be pedicled or sessile. Their size can vary between a few mm and 1 cm and are more common in female babies (~8-10:1).<sup>56</sup> Although more common in the maxilla than in the mandible, epulis occurs in the gingival mucosa of the alveolar crest in the anterior region (maxilla:mandibula ratio 3:1).<sup>57</sup> While most are single lesions, they can occur as multiple lesions in approximately 10% of cases.<sup>58</sup> Large or multiple lesions can cause airway obstruction and difficulty when feeding<sup>59</sup> (Figure 9).



**Figure 9.** Epulis<sup>60</sup>

Histologically, these lesions have large and round polygonal cells, eosinophilic granular cytoplasm, and round or oval slightly basophilic nuclei are seen.<sup>57</sup> Histopathologically, this lesion is similar to granular cell tumors seen in adults and is difficult to differentiate using a light microscope.<sup>61</sup> Immunohistochemical staining of S-100 often helps

distinguish between the two, with granular cell tumor having positive staining.<sup>61</sup> Babies with airway and digestive tract obstruction should undergo surgery as soon as possible after birth.<sup>62</sup> From histopathological examination, numerous islands of proliferative squamous epithelium are observed and are clearly separated from the surrounding stroma by a flattened cell layer at the periphery.<sup>63</sup> Complete surgical excision is generally the preferred treatment and is successfully treated with local excision.<sup>64</sup> Epulis is usually asymptomatic and is detected by routine radiographic examinations or when tooth eruption is delayed.<sup>65</sup>

### Fibromatosis

Fibromatosis is a benign lesion characterized by slowly progressing localized and generalized fibrous growth of the gingiva that does not exceed the mucogingival border. Fibromatosis could be hereditary, syndrome-related, drug-related, or due to inflammation.<sup>66</sup> It can be attributed to various etiological factors, such as poor oral hygiene, plaque accumulation, malabsorption, hormonal stimulation, various blood dyscrasias, or long-term use of certain drugs, such as phenytoin, nifedipine, or cyclosporine.<sup>67</sup> The hereditary type is an autosomal dominant condition with high genetic heterogeneity.<sup>68</sup> Hereditary gingival fibromatosis can be idiopathic or associated with other syndromes, such as Zimmermann-Laband syndrome or hypertrichosis; juvenile hyaline fibromatosis; Rutherford, Jones, and Ramon syndrome; and tuberous sclerosis.<sup>69,70</sup> Fibromatosis affects 1:175,000 people and there is no gender predominance.<sup>70</sup> Connective tissue defects due to gene mutations play a role in the pathogenesis of the disease.<sup>71</sup> Sex hormones and epidermal growth factor also play a role in the abnormal proliferation of gingival fibers.<sup>72</sup>

Fibromatosis appears asymptomatic and non-hemorrhagic, with a firm consistency and normal gingival color. Gingival enlargement can be either generalized or localized. It is usually observed as an idiopathic gingival fibromatosis type generalized lesion. Idiopathic gingival fibromatosis involves overgrowth of all parts of the gingiva on both the maxilla and the mandible (Figure 10).



Figure 10. Gingival fibromatosis<sup>66</sup>

Fibromatosis can cause functional and aesthetic problems.<sup>66</sup> Gum overgrowth is a large hard, flexible and dense fibrous tissue that expands over the teeth. It can cause negative aesthetic and psychological effects on patients by causing malocclusion; delayed eruption of permanent teeth; and speech, articulation, and chewing disorders.<sup>73</sup> Periodontal disease develops in fibromatosis patients.<sup>74</sup> The clinical and histological features of non-syndromic and syndromic gingival fibromatosis are similar.<sup>75</sup>

Treatment methods such as electrocautery-laser are used, but the most effective treatment is conventional gingivectomy.<sup>74</sup> Good oral hygiene should be maintained to reduce recurrence. However, genetic predisposition might also be a reasons for recurrence, therefore, even with good oral hygiene, the long-term treatment effects are unpredictable.<sup>69</sup>

### CONCLUSION

The oral cavity is an area that is often inadequately examined in general practice. Oral lesions are relatively common conditions, but clinicians can find it difficult to distinguish benign from malignant lesions. Increased knowledge of common symptoms of oral lesions could increase the practitioner's confidence in performing oral examinations and managing any identified pathology. More importantly, physicians should keep in mind the red flags in oral pathology that could indicate malignancy.

### ETHICAL DECLARATIONS

#### Reviewer Evaluation Process

Externally peer-reviewed.

#### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

#### Financial Disclosure

The authors declared that this study has received no financial support.

#### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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