Benign oral mucosal lesions: Clinical and pathological findings

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Learning objectives
After completing this learning activity, participants should be able to recognize key clinical features of common benign oral mucosal neoplasms; correctly identify clinically benign oral mucosal lesions; and choose the most appropriate next step in management of each particular lesion.

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A diverse spectrum of benign oral mucosal lesions exists, presenting as either isolated oral findings or in association with dermatologic conditions. Oral lesions can closely resemble one another; therefore, it is important for clinicians to be able to recognize their distinctive features, to be able to recognize benign versus malignant disease, and to recognize when obtaining a biopsy specimen is warranted. The first article in this continuing medical education series reviews oral anatomy, the clinical attributes of several benign lesions of the oral cavity, and appropriate management and therapeutic modalities. (J Am Acad Dermatol 2019;81:43-56.)

Key words: benign lesions of the oral cavity; benign pigmented lesions; granular cell tumors; neurofibromas; neuromas; oral hemangiomas; peripheral giant cell granulomas; peripheral ossifying fibroma; physiologic hyperpigmentation; pyogenic granuloma.

INTRODUCTION

A diverse spectrum of benign oral mucosal lesions exists, presenting as either isolated oral findings or in association with dermatologic conditions. Oral lesions can closely resemble one another; therefore, it is important for clinicians to be able to recognize their distinctive features, to be able to recognize benign versus malignant disease, and to recognize when obtaining a biopsy specimen is warranted.[1]

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Abbreviations used:

GC:	granular cell tumors
NF:	neurofibroma
OH:	oral hemangioma
PEN:	palisaded encapsulated neuroma
PG:	pyogenic granuloma
PGCG:	peripheral giant cell granuloma
PH:	physiologic hyperpigmentation
POF:	peripheral ossifying fibroma

BASIC ORAL ANATOMY

Key points

- **The oral cavity consists of lip lining, mucosa, buccal mucosa, gingiva, anterior two-thirds of the tongue, the floor of the mouth, and the hard palate**
- **The mucosal lining of the oral cavity is a stratified squamous epithelium with histologic variations that adapt to specific functionality**

The oral cavity extends from the lips to the posterior oropharynx and contains 3 main regions: the oral cavity proper, the oropharynx, and the vestibule. The oral cavity proper is the area between the dental arches that is bordered by the palatoglossal arch posteriorly (Fig 1). The oropharynx is positioned behind the palatoglossal arch and is comprised of the visible posterior pharyngeal wall, palatine tonsils, posterior one-third of the tongue, and the soft palate. The vestibule is the region of space between the dentition and the lips or cheeks. Within the vestibule, the labial frenula, midline mucosal folds in the maxilla, and mandible attach the lips to the thinner alveolar mucosa and thicker gingiva mucosa.[2]

Lining the entire oral cavity is a moist oral mucosa, divided externally from the skin of the face at the vermillion border. A mobile squamous stratified nonkeratinized mucosa is the primary epithelial type lining the buccal regions and floor of the mouth. A more durable keratinized mucosa lines the dorsal surface of the tongue, gingiva, and hard palate in order to withstand the force of mastication. The nonkeratinized mucosa lining the oral cavity represents about 60% of the total surface area. The tougher masticatory mucosa and specialized mucosa on the dorsum of the tongue comprise 25% and 15% of the lining, respectively.[3] The epithelium is attached to the underlying connective tissue and periosteum for enhanced support. Oral mucosa progenitor cells regenerate within the stratum basale. The mucosa lining the vestibule and floor of the mouth connects to the gingiva at the mucogingival junction.

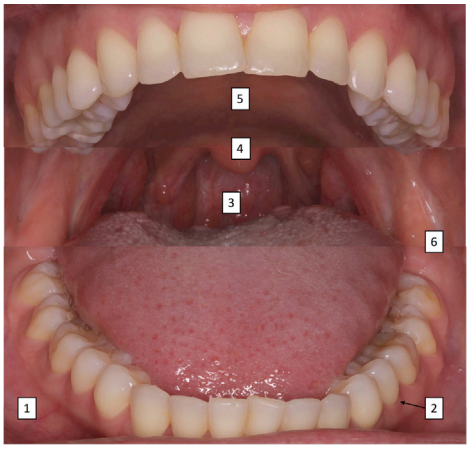

Fig 1. Basic oral anatomy. *1*, Vestibule; *2*, gingiva; *3*, oropharynx; *4*, uvula; *5*, hard palate; *6*, retromolar trigone.

BENIGN LESIONS OF THE ORAL CAVITY

Pyogenic granuloma

Key points

- **Pyogenic granuloma is a common hyperplastic reactive lesion that is caused by traumatic injury, inflammation, hormonal changes, or drugs**
- **Surgical excision is the standard treatment**

Background. Pyogenic granuloma (PG) is a common benign vascular-inflammatory lesion that can occur within the oral cavity. The term PG is a misnomer because the lesion is not caused by bacteria nor is it a true granuloma. Many factors may stimulate PG formation, including trauma, chronic local inflammation, hormonal influences, or medications.[4] One third of PGs are associated with traumatic injury and about 5% occur during pregnancy, most commonly during the second or third trimesters. PG is commonly seen in women and young adults in the second decade of life.[5]

Clinical features. PG presents as a red to red-purple, smooth papule or nodule, ranging in size from several millimeters to about 2.5 cm.[4] Lesions can be solitary or multiple and sessile or pedunculated (Fig 2, *A*). There is typically a period of rapid growth before a PG will stabilize.[6] Trauma typically causes PGs to bleed. The most common sites are the skin and the oral cavity. About 75% of PGs in the oral cavity develop on the anterior maxillary gingiva, the lips, tongue, and buccal mucosa.[5]

Histopathologic examination reveals a proliferation of granulation tissue and enlarged capillary channels filled with red blood cells and lined by protruding endothelial cells. There may be a lobular arrangement of these capillaries in association with inflammatory cells, including neutrophils, plasma

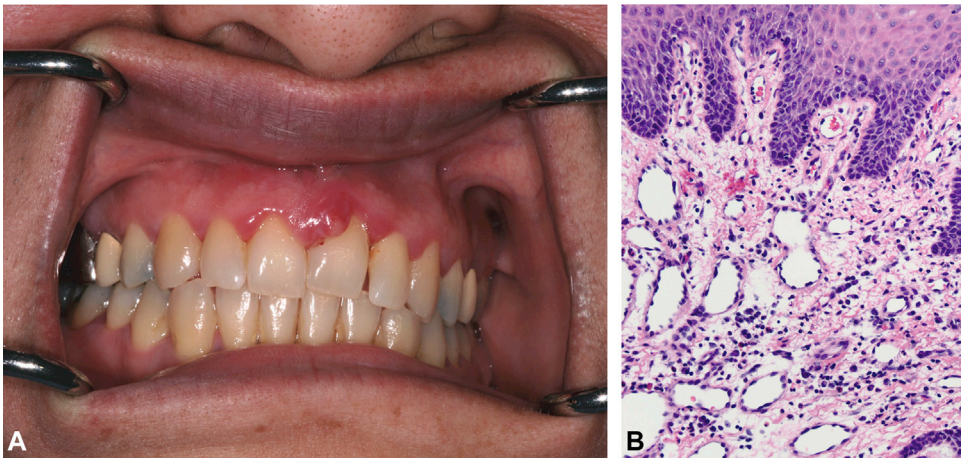

Fig 2. Pyogenic granuloma. **A**, Elevated hyperemic polypoid lesion involving the maxillary mucosa (*black arrow*). **B**, A mucosal nodule covered by keratinizing squamous epithelium and supported by loose reticular collagen and granulation tissue. The granulation tissue is composed of dilated vascular channels, acute and chronic inflammatory cells, hemorrhage, and proteinaceous debris. (*A*, Courtesy of John McDowell, DDS.)

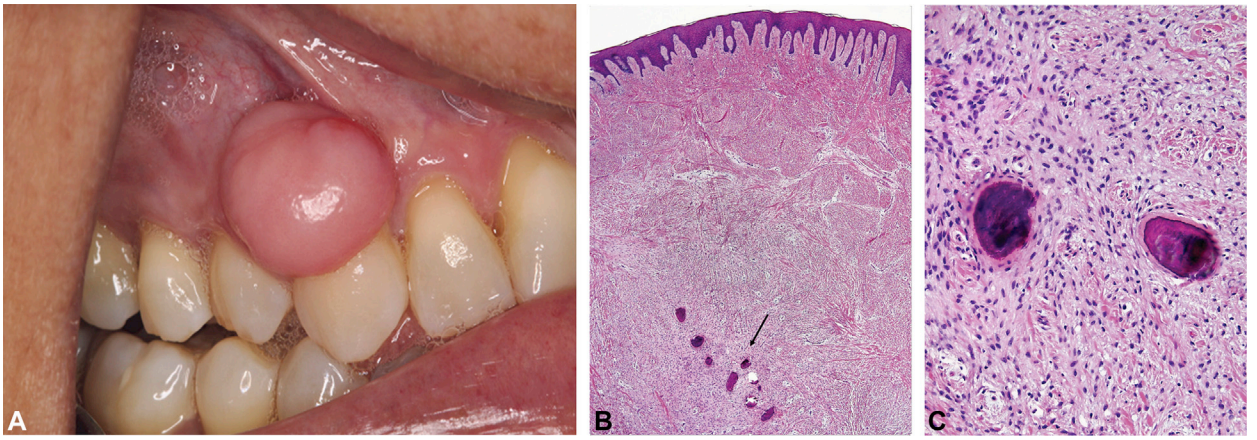

Fig 3. Peripheral ossifying fibroma. **A**, Nodular polypoid growth extending from the interdental papilla between the cuspid and first bicuspid teeth. **B**, Keratinizing squamous epithelium supported by mature connective tissue and streaming fibrous tissue bands. Aggregated within the fibrous connective tissue matrix there are nodular aggregates of bone (black arrow). **C**, Higher power image of bone aggregates. (*A*, Courtesy of John McDowell, DDS.)

cells, and lymphocytes (Fig 2, *B*). Histopathologic examination helps differentiate this entity from hyperplastic gingivitis, Kaposi sarcoma, peripheral ossifying fibroma, and peripheral giant cell granulomas.[7]

Management. Surgical excision with 2-mm peripheral margins, down to the periosteum or causative agent, is the recommended treatment for PG.[4] Lesions should be explored for any surrounding irritants, and the local dentition should be scaled for dental plaque, calculus, foreign bodies, or defective restorations that may cause redundant inflammation and recurrence, which occurs at a rate of 16%.[6] Case reports have shown success with novel therapies for PG, including treatment with the neodymium-doped:yttrium aluminum garnet laser,[8,9] which confers a lower bleeding risk, associated coagulation, and no adverse events. Additional case studies have proposed the use of flash lamp pulsed dye laser,[10] cryosurgery,[11] ethanol injection,[12] and sodium tetradecyl sulfate sclerotherapy (level of evidence, V).[13]

Peripheral ossifying fibroma

Key points

- **Peripheral ossifying fibroma is a reactive proliferation of fibroblasts and odontogenic**

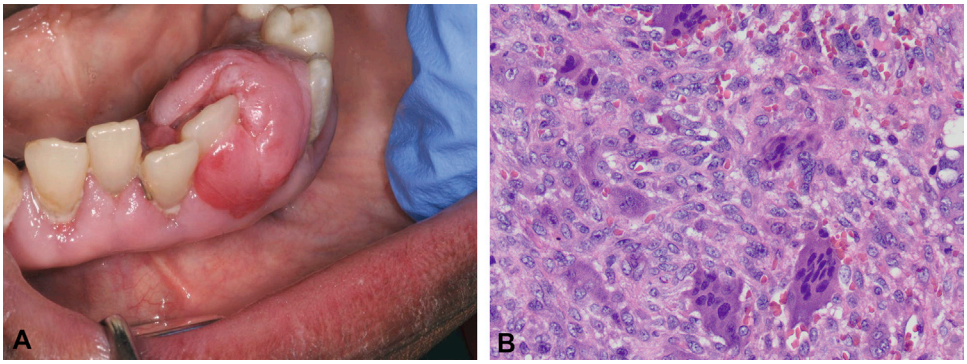

Fig 4. Peripheral giant cell granuloma. **A**, A focally hemorrhagic nodular mass involving mandibular gingiva marginates three-quarters of the lateral incisor tooth. **B**, Multinucleated giant cells set in a matrix of loose reticular collagen and granulation tissue. The granulation consists of dilated vascular channels, endothelial cells, proteinaceous debris, and hemorrhage. (*A*, Courtesy of John McDowell, DDS.)

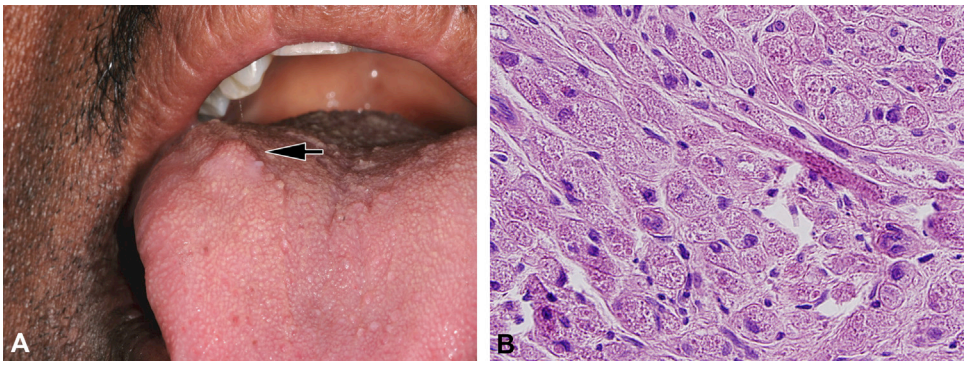

Fig 5. Granular cell tumors. **A**, Nodular freely movable lesion involving the dorsal surface of the tongue. **B**, Nests, cords, and sheets of large cells with deep staining nuclei and granular cytoplasm. These cells are set in a matrix of loose reticular collagen.

epithelial nests within the periodontal ligament

- **Peripheral ossifying fibroma treatment involves complete lesion excision and surgical repair of gingival defects**

Background. Peripheral ossifying fibroma (POF) is a common hyperplastic reactive lesion of the oral cavity from hyperplastic cells in the periodontal ligament. Left untreated, POF can cause significant bone loss and tooth damage. POF is thought to occur as a result of trauma-induced cellular proliferation, with associated reactive dystrophic calcification and bone growth. Approximately 60% of POFs involve the maxillary gingiva, and about 50% of those are in the area of the anterior incisors and canine teeth.[14] Classically, POF has been found to be most prevalent in women 10 to 29 years of age, likely because of a hormonal influence. However, a recent literature review indicates that men develop POF with similar frequency.[15] POF likely has a polygenic origin, but little information regarding specific genetic mutations has been reported.

Clinical features. Pain and local hyperemia are typical symptoms of POF. The lesions are generally <2 cm in diameter but can become as large as 10 cm.[14] Lesion size is not indicative of total growth time, and multiple lesions can occur.[15] Patients with POF typically present with red, localized, swollen gingival mucosa, which can be accompanied by ulceration and tooth movement, depending on lesion size (Fig 3, *A*). Upon histologic examination, POF will contain calcifications and increased endothelial cell proliferation, mature collagen, and streaming fibroblast tissue bands (Fig 3, *B*). The differential diagnosis includes PG, peripheral giant cell granuloma (PGCG), and gingival fibroma.

Management. The criterion standard treatment for POF management is complete local excision that includes a 2-mm surgical margin of healthy tissue and removal of the affected periodontal ligament

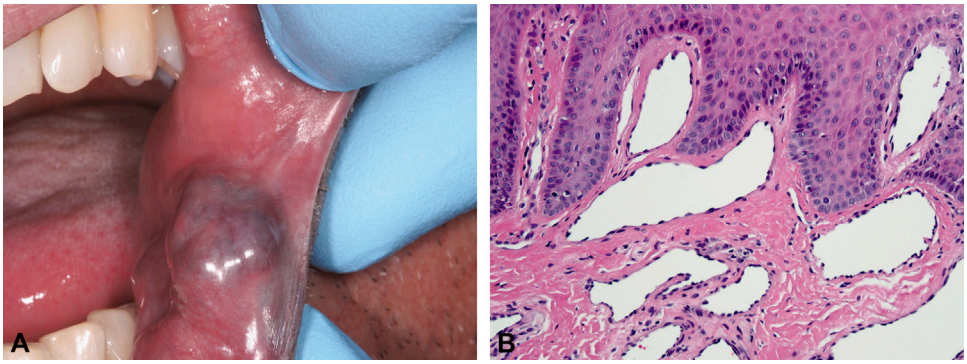

Fig 6. Oral hemangiomas. **A**, Well-circumscribed, purplish nodule on the left buccal mucosa. **B**, A mucosal nodule covered by keratinizing squamous epithelium. The epithelium is supported by loose reticular connective tissue in the lamina propria. Dilated blood channels lined by endothelial cells are seen in the superficial connective tissue. These vascular channels directly abut the overlying basal layer of the epithelium. (*A*, Courtesy of John McDowell, DDS.)

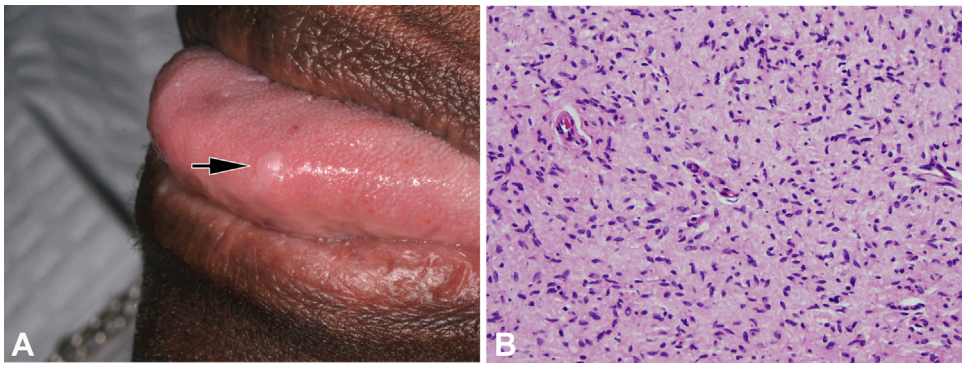

Fig 7. Neurofibroma. **A**, A single, well-circumscribed nodular lesion involving the lateral border of the tongue. **B**, Proliferation of spindle-shaped cells. The spindle cells have elongated basophilic nuclei and minimal eosinophilic cytoplasm. The cells are often arranged in a fascicular pattern as they ramify throughout a connective tissue stroma that is focally myxoid. (*A*, Courtesy of John McDowell, DDS.)

and periosteum, because recurrence rates are reported to range from 16% to 28%.[6,16] POF can affect the nearby dentition, and tooth extraction along with scaling (removal of dental plaque and calculus) and root planing (smoothing of the root surface) should be considered to eliminate recurrence.[16,17]

Peripheral giant cell granuloma

Key points

- **Peripheral giant cell granulomas are reactive lesions of osteoclastic origin**
- **The diagnosis is based on unique histologic presentation of giant cells in a fibrovascular stroma**
- **Excision is the treatment of choice**

Background. PGCGs are reactive oral lesions of the gingiva or mucosa. They are thought to arise from osteoclasts or from the mononuclear phagocyte cells. Lesions are twice as prevalent in females as males. The age of incidence varies between the sexes. The likelihood of being affected is highest for females and males in the fifth and second decades of life, respectively.[18]

Clinical features. The appearance of PGCG can vary greatly. Lesions are typically soft, spongy, and bleed easily.[6] Coloration of the lesion is most frequently red, but lesions may also appear as purple, blue, pink, brown, or white. While they may appear anywhere in the oral cavity, the most common locations are the incisor and canine regions, with a higher likelihood of involving the mandible than the maxilla (Fig 4, *A*). PGCGs range greatly in size, with most lesions being <2 cm in diameter.[19] Significant growth and ulceration relates to repeated trauma to the lesion.[6,18]

PGCGs appear clinically similar to PG and POF.[20] Histologic examination reveals numerous multinucleated giant cells dispersed throughout proliferation of spindle-shaped and ovoid mesenchymal cells. Lesions

Table I. General characteristics and clinical features of tumors of nerve sheath origin

Lesion	Site of occurrence	Appearance	Clinical presentation	Histopathology
Traumatic neuroma	Mental foramen, lower lip, and tongue[33,36,62]	Solitary, nonencapsulated nodules <2 cm in diameter[36]	Pain on palpation, tenderness, and paresthesia[36,59]	Characterized by axons arranged in a disordered, random fashion, as well as by the presence of inflammatory cells and stromal fibrous connective tissue[36]
Schwannoma	Tongue, palate, floor of mouth, buccal mucosa, gingiva; intraosseus in mandible[33,37]	Solitary, encapsulated growths[33,38]	Slow-growing, asymptomatic[33,38]	Spindle-shaped cells arranged in characteristic tissue patterns referred to as Antoni A and Antoni B type tissue[37,38]; Antoni A tissue is characterized by cells with fusiform nuclei, arranged in a palisade distribution around eosinophilic masses known as Verocay bodies[63]; Antoni B is characterized by cells and fibers that have a more random distribution, with the presence of interstitial edema and microcysts[37,63]
Neurofibroma	Tongue, buccal, and labial mucosa, gingiva, palate, salivary glands, and maxilla[33,34,40-42]	Slow-growing, nonencapsulated tumors <2 cm in diameter; solitary or multifocal[41,42]	Nontender to palpation, asymptomatic; plexiform variant associated with NF-1 presents with pain and neurologic defects. (Fig 7, *A*)[41,42]	Spindle-shaped cells with thin, wavy nuclei and an abundance of mast cells within the tumor (Fig 5, *B*)[41,42,64]; PEN shares histologic findings with neurofibroma and schwanomma, and can best be distinguished by immunohistochemical staining[33]
PEN	Masticatory mucosa of palate and gingiva, tongue, and margins of the lips[33,43]	Small, solitary lesions; plexiform, fungating, multinodular, epithelioid, vascular, and myxoid types[33,43]	Superficial lesions are usually painless[33,43]	Epithelial membrane antigen-positive capsule, S100 positive Schwann cells, peripheral nerve axons positive for neurofilament, and a negative glial fibrillary acidic protein immunoreactivity[33,43]

NF1, Neurofibromatosis 1; *PEN*, palisaded encapsulated neuroma.

may exhibit extensive capillary growth (Fig 4, *B*). A stratified squamous epithelial surface will be evident and often ulcerated. Acute and chronic inflammatory cells and hemorrhage can be present,[20] along with hemosiderin.[6] Mineralized tissue is visible in 35% of lesions.[20]

Management. Early diagnosis of PGCG is vital to minimizing the extent of surgical treatment necessary to reduce complications, such as exposed bone, tooth displacement, or bone loss.[19] Radiography can help determine the origin and boundaries of the lesion.[21] PGCG has a more aggressive growth rate in pediatric patients than in adults. Recurrences are common.[18]

Surgical excision of the lesion is the primary treatment option (level of evidence, V). Excisions are completed with 2- to 5-mm surgical margins from the periphery. Extra care should be taken to remove the periosteum or periodontal ligament from which a PGCG may have originated. If the lesion and any local irritants are completely removed, a low recurrence rate from 1.4% to 12% has been reported. Lesions that occur near a dental implant have a higher chance of recurrence.[20]

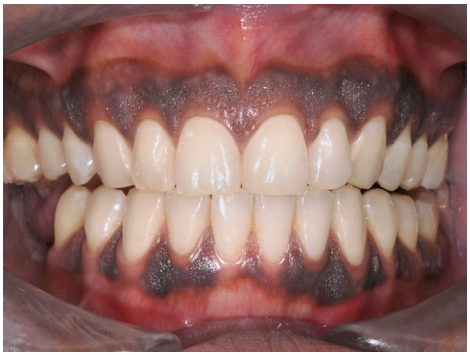

Fig 8. Physiologic hyperpigmentation. Generalized gingival pigmentation, which is normal in this African American patient. (Courtesy of John McDowell, DDS.)

Granular cell tumors

Key points

- **Granular cell tumors are of Schwann cell origin and appear granular histologically because of lysosomes**
- **Granular cell tumors are normally benign, but 1% to 2% of all cases undergo malignant transformation**
- **Treatment is with surgical excision**

Background. Granular cell (GC) tumors are generally benign neural neoplasms. Their granular histologic appearance can be attributed to altered lysosomal vacuoles. These lesions account for 0.5% of all soft tissue tumors.[22] Originating from Schwann cells, they are potentially caused by Wallerian degeneration after axonal trauma.[23] Females are twice as likely to develop the tumors as males. Prevalence is highest in individuals 20 to 40 years of age.[6] Less than 2% of these tumors may become malignant; however, these tend to appear on the lower extremities and those of the head and neck region are exceedingly rare. The reported 5-year disease survival of malignant disease is 62.8%.[22]

Clinical features. Approximately 40% of GC tumors appear in the oral cavity. The tongue is the most common site. The lesions are typically painless and firm to the touch. Coloration may vary and lesions may be yellow, white, or pale in appearance (Fig 5, *A*). In approximately 10% to 15% of patients, >1 lesion will be present. Normally, growth is limited to about 2 cm in diameter, but lesions may grow larger (≤12 cm), especially if they become malignant.[6,24]

Upon histologic examination, the tumor is not encapsulated. The epithelium may appear normal or demonstrate pseudoepitheliomatous hyperplasia. Tumor cells appear polygonal or round with small nuclei, eosinophilic cytoplasm, and cytoplasmic granules. The tumor cells will be arranged in sheets or clusters that are separated by connective tissue and skeletal muscle fibers (Fig 5, *B*).[6,24]

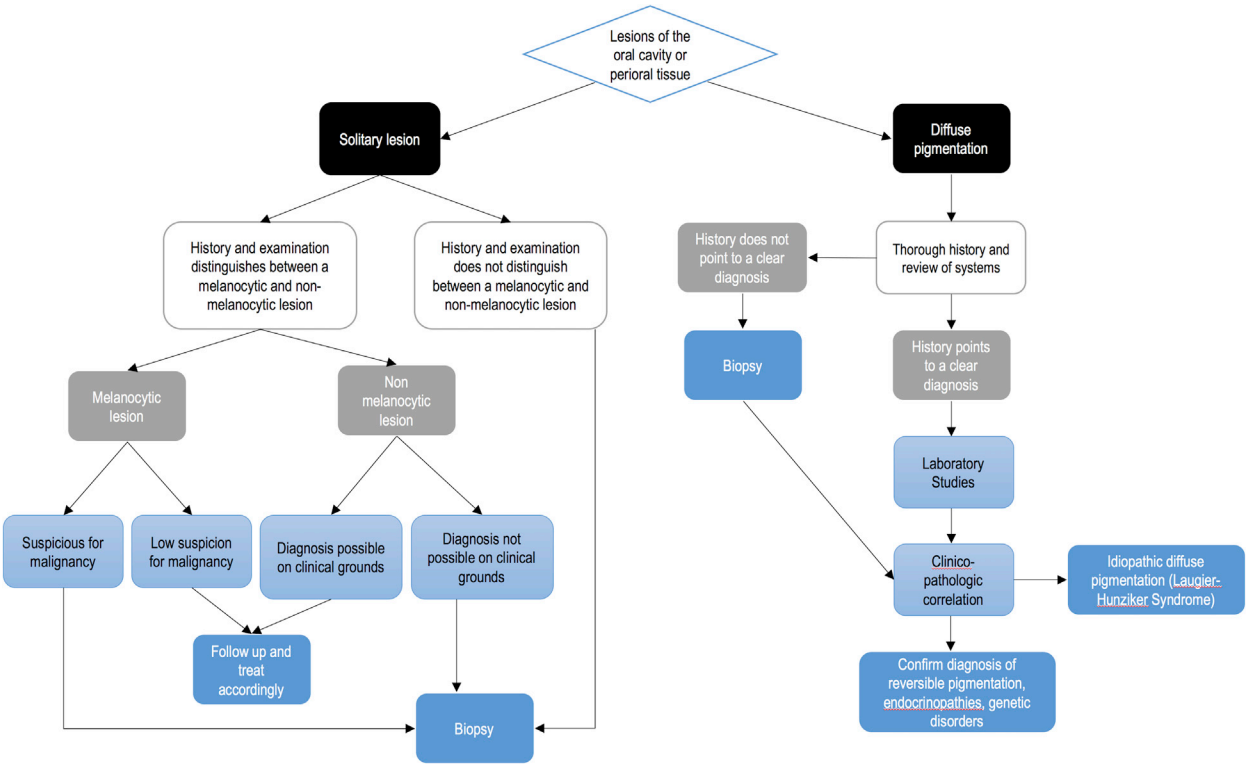

Fig 9. Algorithm for the diagnosis of benign lesions.

Table II. Characteristics of diffuse/bilateral benign pigmentations of oral mucosa

Disease	Clinical features	Pathophysiology
Peutz–Jeghers syndrome	Autosomal dominant syndrome; growth of hamartomatous polyps in the gastrointestinal system with increased risk for gastrointestinal carcinomas; hyperpigmented macules on the oral mucosa, most often distributed on the lip or periorally[53]	Increased melanin within the basal layer of the epidermis of the oral epithelium
Addison disease	Brown patches seen diffusely on the gingiva, buccal mucosa, palate and, tongue[53]; in conjunction with systemic symptoms, such as weakness, hypotension, and nausea/vomiting[53]	Increased production of ACTH that increases the production of MSH[53]
Heavy metals	Most common example is lead poisoning[54]; typically presents as a blue-black line along the gingival margin, called the Burtonian line[54]; discoloration is proportional to the amount of inflammation[52]; pigmentation will regress with treatment of the underlying cause[52]	Elevated serum levels of metals, such as lead, bismuth, mercury, silver, arsenic, and gold
Drug-induced pigmentation	Hyperpigmented patches most often are found on the palate and gingiva[54]	Drug or metabolite deposition in the oral epithelium and lamina propria[53]; enhanced melanin deposition or postinflammatory changes secondary to the offending agent[51]
Postinflammatory	Particularly seen in lichen planus[57]; multiple diffuse brown-black pigmented macules located near areas of reticular or erosive lichenification[57]	Deposition of melanin in the basal layer of the epithelium or in connective tissue[57]
Smoker's melanosis	Diffuse brown macular discoloration of the oral mucosa, and tend to be more visible and intense in the anterior mandibular labial mucosa[56]	Increased number of melanocytes and increased melanocytic activity because of smoking[56]

ACTH, Adrenocorticotropic hormone; *MSH*, melanocyte-stimulating hormone.

Table III. Genodermatoses with oral cavity manifestations[70]

Genodermatosis	Mode of inheritance	Description of oral cavity lesion
Follicular keratosis (Darier disease)	Autosomal dominant	White papules on oral mucosa
Tuberous sclerosis	Autosomal dominant	Hemangiomas and gingival fibrous papules
Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu)	Autosomal dominant	Telangiectasias of oral and vermillion mucosa; hemorrhagic ulcers on gingival and oral mucosa
Lipoid proteinosis (Urbach–Wiethe disease)	Autosomal recessive	Cobblestone-appearing lesions in the oral mucosa
Gardner syndrome (FAP variant)	Autosomal dominant	Mandibular osteomas; dentigerous cysts
Peutz–Jeghers syndrome	Autosomal dominant	Mucosal hyperpigmentation, commonly found on the lip or periorally
Cowden syndrome	Autosomal dominant	Oral papillomas with a cobblestone pattern of the gingival, lip, buccal, and labial mucosa
Multiple endocrine neoplasia type 2B (MEN IIB)	Autosomal dominant	Mucosal neuromas on tongue and lips, can manifest on palatal, gingival, and buccal mucosa
Dystrophic epidermolysis bullosa	Autosomal dominant and recessive	Vesiculobullous lesions of the oral mucosa
Pachyonychia congenita	Autosomal dominant	Oral leukoplakia on buccal mucosa and tongue
White sponge nevus (of Cannon, hereditary mucosal leukokeratosis)	Autosomal dominant	Thick, spongy, white plaques on the gingival, labial, and buccal mucosa
Hereditary benign intraepithelial dyskeratosis	Autosomal dominant	White plaques on oral mucosa

Adapted from Wilder et al.[70]

Table IV. Characteristics of focal benign pigmentation of oral mucosa

Lesion	Clinical features	Dermoscopy findings	Pathophysiology
Ephelides	Also known as freckles; tan to brown macules seen often on sun-exposed skin, including the vermillion border of the lips[56]; darken with exposure to ultraviolet light[56]; consider Peutz–Jeghers or Addison disease when numerous ephelides either orally or periorally	Light brown, intertwined pigment network[65]; "moth-eaten" borders[66]	Actinic radiation-induced melanin production[56]
Labial melanotic macule	Small, typically <1 cm, well-circumscribed brown, black, blue, or gray macules on the vermillion border of the lips[55]; females more affected than males[55] (Fig 10)	May include ≥1 of the following patterns[67]: • Structureless, which is also commonly seen in malignant lesions • Parallel, including hyphal and fish-scale variants • Reticular • Dotted or globular	Increased amount of melanin in the basal layer of the epidermis causing hyperpigmentation of basal keratinocytes, increased number of melanophages, absence of rete peg elongation, and normal number of melanocytes[55]
Amalgam tattoo	Most common type of oral pigmentation[56]; also known as focal argyrosis; typically in an abraded areas of the mucosa[56]; often radio-opaque on radiographs[68]	Structureless, homogenous, grainy, bluish pattern[69]	Deposition of dental amalgam restorative material into the oral mucosa during dental treatment[53]; amalgam releases mercury, then silver, and silver sulfide corrosion causes tissue pigmentation[56]; amalgam deposition in connective tissue can be seen microscopically (Fig 11, *B*)
Oral melanoacanthoma	Brown/black well-circumscribed macules or papules[61]; may rapidly increase in size from a few millimeters to a few centimeters[61]; must be differentiated from Peutz–Jeghers and Addison pigmentation; may regress independently after a biopsy procedure[61]	Starburst pattern with symmetric pigmented streaks along the lesion's periphery[69]	Result of a proliferation of both keratinocytes and melanocytes[61]; most often a reaction to mastication or trauma[61]; dendritic melanocytes diffusely within the epithelium[61]; immunoreactive to histochemical marker S100[61]
Melanocytic nevi	Congenital or acquired; well-defined macules (Fig 12, *A*); classified as junctional, intradermal, or intramucosal, and their color varies depending on the location of the nevus cells[56]; superficial nevi appear darker brown, whereas intramucosal nevi are lighter in color[53]	Structurally homogeneous with broad or conspicuous pigment network and streaking	Accumulation of nevus cells in the epithelium or connective tissue[56]

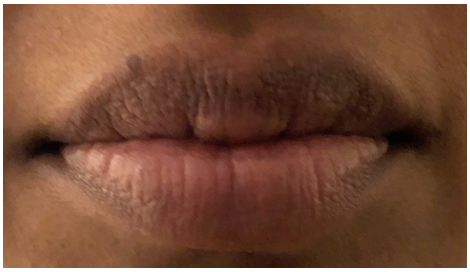

Fig 10. Labial melanocytic macules. Single, well-circumscribed, homogenous brown macules on the vermillion border.

Management. For benign tumors, the current accepted treatment is surgical excision with 5-mm margins from any palpable lesion. The recurrence rate for GC tumors is about 7%. Recurrent tumors tend to be newly developed ones rather than tumors originating from previous lesions (level of evidence, V).[6] Currently, no effective treatment for those exceedingly rare metastatic GC tumors exists. In a case study, 1 patient responded to treatment with pazopanib, a tyrosine kinase receptor inhibitor (level of evidence, V).[25]

Oral hemangiomas

Key points

- **Oral hemangiomas are common benign neoplasms that typically self-involute**
- **Management is primarily observation; however, surgery may be performed for debulking**

Background. Oral hemangiomas are common, benign neoplasms that are most frequently seen in infants and children. Hemangiomas are 3 times more prevalent in females than males. Risk factors for infantile hemangiomas include prematurity and low birth weight. The etiology is currently unknown; however, an association exists between the neoplasm and higher than normal concentrations of CD105, vascular endothelial growth factor A, and cyclooxygenase-2.[26]

Clinical features. The head and neck region is the most commonly affected site for hemangiomas, accounting for 60% of cases.[27] Hemangiomas characteristically appear as bright red papules or nodules of variable size (Fig 6, *A*). Tumors start with a rapid proliferation phase, which lasts 6 to 8 months. Histopathologically, this phase is characterized by endothelial hyperplasia and the formation of a multilaminated basement membrane (Fig 6, *B*).[27] Most lesions reach 80% of their maximum size by 3 to 5 months. The proliferation phase is followed by a slower involuting phase. Histopathologic characteristics of this phase include fibrosis, fat deposition, and regression of the lesion.[27]

Management. Most hemangiomas self-involute without intervention. Approximately 10% to 20% of patients require treatment.[28] Treatment options include cautery, cryotherapy, laser therapy, radiotherapy, sclerotherapy, and surgery.[29] Sclerotherapy and laser therapy are the most common choices. Sclerosing agents have a high response rate, are less expensive, and are easily accessible.[30] The documented use of 3% sodium tetradecyl sulfate injected peripherally then centrally has been shown to be efficacious (level of evidence, IV).[30] Sclerotherapy may result in skin and soft tissue injury (tissue irritation and thrombosis) in 12% to 30% of patients and nonpermanent neuropathy in 10% of patients.[31,32] Laser therapy has been shown to be an effective treatment option and includes yellow light lasers (578-585 nm; level of evidence, V) and neodymium-doped:yttrium aluminum garnet laser (level of evidence, IV).[32] Potential adverse effects include tissue sloughing and scarring.[31,32]

Tumors of nerve sheath origin: Neurofibroma and neuroma

Key points

- **Benign peripheral nerve sheath tumors of the oral cavity include traumatic neuroma, neurofibroma, schwannoma, and palisaded encapsulated neuroma**
- **Lesions are usually benign but may be associated with other disorders and may carry a risk of malignant transformation**
- **The diagnosis of lesions is histologic, and treatment involves surgical excision**

Background. Neurogenic tumors of the oral cavity are rare, with oral peripheral nerve sheath tumors representing only 0.2% of all oral cavity lesions.[33,34] These tumors are generally benign, but their presence can be indicative of other disorders and some lesions carry a risk of malignant transformation. Tumors can be reactive, occurring in response to nerve injury, or they may have true neoplastic origin.

Clinical features. Benign peripheral nerve sheath tumors in the oral cavity include traumatic neuroma, neurofibroma, schwannoma or neurilemmoma, and palisaded encapsulated neuroma or solitary circumscribed neuroma.[34] Traumatic neuroma is a nonneoplastic process, occurring in response to nerve damage and consisting of proliferating Schwann cells and axons histopathologically.[35,36]

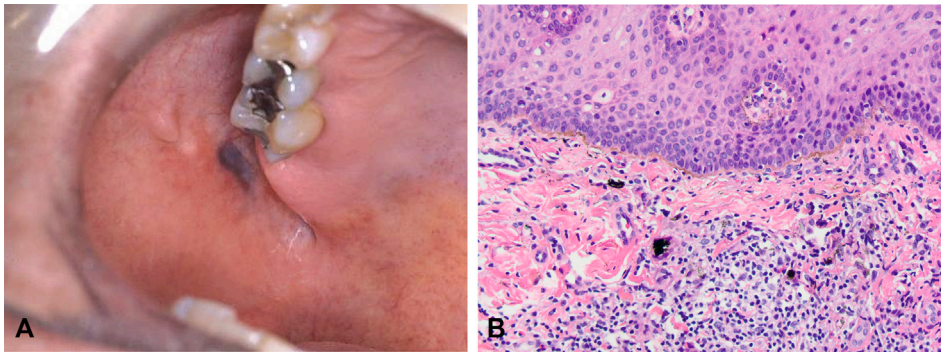

Fig 11. Amalgam tattoo. **A**, A well-circumscribed, deeply pigmented lesion on the buccal mucosa. Note the proximity to amalgam fillings. **B**, The ellipse is covered by keratinizing squamous epithelium, supported by collagen containing a diffuse chronic inflammatory infiltrate. Entrapped within the infiltrate is pigmented foreign material, consistent with amalgam that is occasionally surrounded by multinucleated giant cells and histiocytes. (*A*, Courtesy of John McDowell, DDS.)

Schwannomas are neoplastic lesions that originate from Schwann cells. They are rarely found within the oral cavity and represent 0.04% of all intraoral lesions.[33,37] Tumors are reported most frequently in the third and fourth decades of life, and the incidence of malignant transformation is reported to range from 8% to 13.9%.[38]

Neurofibromas are the most common peripheral nerve sheath tumor, with reported frequencies of 20.8% and 32% among all intraoral peripheral nerve sheath tumors (Fig 7, *A*).[33,39] The risk of malignant transformation of a solitary neurofibroma is low but higher when associated with neurofibromatosis 1 (NF1).[40,41] Individuals with NF1 have a 2% to 6% risk of tumor malignancy.[42] The plexiform variant of neurofibroma is considered pathognomonic for NF1 and, when associated with NF1, can present with pain, neurologic defects, and a higher risk of malignant transformation.[42]

Because of the clinical similarities in appearance of these tumors to other neoplasms, a diagnosis requires obtaining a biopsy specimen and histopathologic assessment (Table I).[33,35]

Management. Surgical excision is the recommended treatment for most peripheral nerve sheath tumors. Recurrence after resection in cases of schwannoma and palisaded encapsulated neuroma is rare.[37,38,43] Recurrence after surgical excision of neurofibroma is low; however, larger lesions, which are generally associated with NF1, have a higher risk of recurrence (level of evidence, IIIA).[42] In younger patients, the presence of a solitary neurofibroma may be indicative of NF1, and therefore the referral of patients for genetic testing who are <20 years of age and who present with a recurrence of a solitary neurofibroma is recommended.[43]

Physiologic hyperpigmentation

Key points

- **Physiologic hyperpigmentation is characterized by diffuse symmetrical pigmentation of the oral mucosa**
- **Diagnosis is made clinically, and no treatment is necessary**

Background. Physiologic hyperpigmentation (PH) is characterized by a diffuse symmetrical pigmentation of the oral mucosa,[44] most commonly the gingiva. The amount of mucosal keratinization, vascularization, and the size and melanization of oral melanosomes, as well as the quality of underlying submucosal tissues, are known influencing factors on the degree of pigmentation.[45] PH is far more common in individuals with darker skin, and it affects males and females equally. Prevalence varies with the studied population.[46]

Clinical features. PH presents as a diffuse form of homogenous brown pigmentation (Fig 8), and commonly involves the attached gingiva, followed by the buccal mucosa, labial mucosa, tongue, and palate.[46] PH can present in infancy and is thought to increase or darken with puberty. Similar to skin melanocytes, the amount of melanin produced in oral melanocytes is influenced by genetic background, and pigmentation intensity may be influenced by physical, chemical, and hormonal factors.[47]

A diagnosis of PH is established clinically upon exclusion of other diffuse disorders of hyperpigmentation, including smoker's melanosis, Addison disease, hemochromatosis, drug-induced, and focal pigmentations, such as amalgam tattoo, oral melanotic macule, oral melanoma, and postinflammatory hyperpigmentation. Tissue histology will show increased melanin in the basal layer and the upper

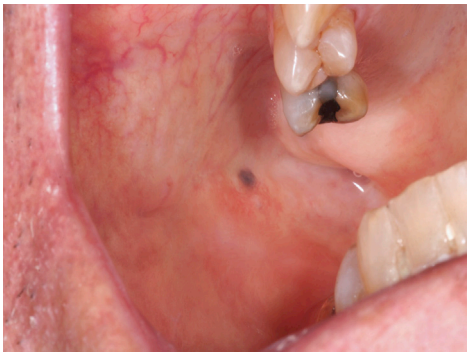

Fig 12. Oral melanocytic nevi. A single, well-circumscribed, lightly pigmented to tan macule on buccal mucosa. (Courtesy of John McDowell, DDS.)

lamina propria, with melanin incontinence and increased melanophages. These features are shared with smoker's melanosis and oral melanotic macules.[48]

Management. A thorough examination of oral mucosal surfaces is required to differentiate PH from other abnormal pigmentation disorders, especially in the setting of recent onset of hyperpigmentation. No treatment is required; however, the use of cryotherapy[49] and erbium:yttrium aluminium garnet laser can be effective means of management, if required (level of evidence, V).[50]

Benign pigmented lesion and mimickers

Key points

- **Benign pigmented lesions may have intrinsic or extrinsic etiologies**
- **Oral pigmentation may be localized or represent a component of systemic illness**
- **Appropriate clinical evaluation requires a thorough patient history and physical examination, and a biopsy specimen should be obtained for indeterminate lesions**

Background. Oral pigmented lesions are relatively common, and they may be physiologic or pathologic in character.[51] They can be classified in several ways, including melanocytic versus nonmelanocytic lesions, intrinsic versus extrinsic pigmentation, or focal versus diffuse pigmentation (Fig 9). Intraoral pigmentation can have a large diagnostic schema, ranging from a localized reactive process to manifestations of a more concerning systemic illness.[52] Appropriate clinical evaluation requires a detailed history, a detailed physical examination, and potentially further assessment after obtaining a biopsy specimen.[45]

Clinical features. Diffuse/bilateral pigmentation features of benign pigmented lesions and mimickers are shown in Table II.

Peutz–Jeghers syndrome. Peutz–Jeghers syndrome is an autosomal dominant syndrome that is characterized by diffuse hyperpigmented macules on the lips or periorally. Other genodermatoses with oral manifestations can be found in Table III.[53]

Addison disease. Individuals with primary adrenal insufficiency may present with brown patches involving the oral mucosa because of the increased production of adrenocorticotropic hormone.[53]

Heavy metals. Oral mucosal pigmentation can be caused by elevated serum levels of metals, such as lead. Pigmentation typically presents as a blue-black line along the gingival margin, called the Burtonian line.

Drug-induced. Drug or metabolite deposition in the oral epithelium and lamina propria may cause pigmented lesions. Lesions tend to be most often are found on the palate and gingiva.[51]

Postinflammatory. Pigmented lesions can occur because of acute or chronic inflammatory changes.[54]

Smoker's melanosis. Characterized by diffuse brown macular discoloration of the oral mucosa, smoker's melanosis most often involves the anterior mandibular labial mucosa.[53]

Focal pigmentation features are shown in Table IV.

Ephelides. Ephelides are common tan to brown macules seen often on sun-exposed skin as a result of radiation-induced melanin production.[53]

Labial melanocytic macules. Labial melanocytic macules are small, uniformly pigmented macules often seen on the lower lip of young adult females (Fig 10).[55] These lesions were previously classified as lentigos.[56]

Amalgam tattoo. Amalgam tattoos are blue-black macules caused by deposition of dental amalgam restorative material into the oral mucosa during dental treatment (Fig 11).[53]

Oral melanoacanthoma. Oral melanoacanthomas appear as brown/black well-circumscribed macules or papules as a reaction to mastication or trauma.[57]

Oral melanocytic nevi. Oral melanocytic nevi are well-defined macules or papules (Fig 12) caused by an accumulation of nevus cells in the epithelium or connective tissue.[58]

Management. The diagnosis and management of oral mucosal lesions may be challenging for the clinician. Often, clinical history and examination may be sufficient to appropriately identify a lesion. However, more extensive investigation may be needed in uncertain cases in order to reach a definitive diagnosis. Dermoscopy is a possible noninvasive approach that can be used to assess suspicious lesions, and common features distinguishing isolated lesions are seen in

Table IV.[59] Reflectance confocal microscopy is another noninvasive modality with the potential to distinguish between malignant and nonmalignant lesions, but this technology is limited by the paucity of established guidelines.[60] The gold standard for diagnosis of oral mucosal lesions is obtaining an oral biopsy specimen.[61] Biopsy specimens have particular utility for focal lesions, and a biopsy specimen should always be obtained from lesions that are suspicious for melanoma and rapidly growing lesions.[45] For diffuse lesions, biopsy specimens have less utility and may have nonspecific findings. In these instances, a review of systems with laboratory studies may be needed to establish a diagnosis.[61]

In conclusion, the diagnosis of oral mucosal lesions is an essential component to clinical practice. Oral lesions are relatively common entities, but clinicians may find it challenging to differentiate benign from malignant lesions. Causes of oral mucosal tumors and other lesions range from extrinsic factors, reactive processes, systemic disease, and neoplastic progression. Clinical suspicion with a thorough patient history and appropriate examination may be able to elicit a compelling diagnosis. However, for many tumors and oral pigmentations involving the mucosa, obtaining a biopsy specimen may be of diagnostic utility.[1,61]

REFERENCES

1. Allon I, Kaplan I, Gal G, Chaushu G, Allon DM. The clinical characteristics of benign oral mucosal tumors. *Med Oral Patol Oral Cir Bucal*. 2014;19:e438-e443.
2. Bruch J, Treister NS. *Normal anatomy. Clinical Oral Medicine and Pathology*. Boston, MA: Springer; 2017.
3. Squier CA, Kremer MJ. Biology of oral mucosa and esophagus. *J Natl Cancer Inst Monogr*. 2001:7-15.
4. Jafarzadeh H, Sanatkhani M, Mohtasham N. Oral pyogenic granuloma: a review. *J Oral Sci*. 2006;48:167-175.
5. Mortazavi H, Safi Y, Baharvand M, Rahmani S, Jafari S. Peripheral exophytic oral lesions: a clinical decision tree. *Int J Dent*. 2017;2017:9193831.
6. Marx RE, Stern D. *Oral and Maxillofacial Pathology: A Rationale for Diagnosis and Treatment*. 2nd ed. Hanover Park, IL: Quintessence Publishing Co, Inc; 2012.
7. Greer R, Marx R, Said S, Prok L. *Pediatric Head and Neck Pathology*. Cambridge, United Kingdom: Cambridge University Press; 2017:77-99.
8. White JM, Chaudhry SI, Kudler JJ, Sekandari N, Schoelch ML, Silverman S Jr. Nd:YAG and CO2 laser therapy of oral mucosal lesions. *J Clin Laser Med Surg*. 1998;16:299-304.
9. Powell JL, Bailey CL, Coopland AT, Otis CN, Frank JL, Meyer I. Nd:YAG laser excision of a giant gingival pyogenic granuloma of pregnancy. *Lasers Surg Med*. 1994;14:178-183.
10. Meffert JJ, Cagna DR, Meffert RM. Treatment of oral granulation tissue with the flashlamp pulsed dye laser. *Dermatol Surg*. 1998;24:845-848.
11. Ishida CE, Ramos-e-Silva M. Cryosurgery in oral lesions. *Int J Dermatol*. 1998;37:283-285.
12. Ichimiya M, Yoshikawa Y, Hamamoto Y, Muto M. Successful treatment of pyogenic granuloma with injection of absolute ethanol. *J Dermatol*. 2004;31:342-344.
13. Moon SE, Hwang EJ, Cho KH. Treatment of pyogenic granuloma by sodium tetradecyl sulfate sclerotherapy. *Arch Dermatol*. 2005;141:644-646.
14. Mishra AK, Bhusari P, Kanteshwari K. Peripheral cemento-ossifying fibroma—a case report. *Int J Dent Hyg*. 2011;9:234-237.
15. Franco-Barrera MJ, Zavala-Cerna MG, Fernandez-Tamayo R, Vivanco-Perez I, Fernandez-Tamayo NM, Torres-Bugarin O. An update on peripheral ossifying fibroma: case report and literature review. *Oral Maxillofac Surg*. 2016;20:1-7.
16. Gonzalez-Serrano J, Lopez-Pintor RM, Sanz-Sanchez I, et al. Surgical treatment of a peripheral ossifying fibroma and reconstruction with a porcine collagen matrix: a case report. *Int J Periodontics Restorative Dent*. 2017;37:443-449.
17. Walters JD, Will JK, Hatfield RD, Cacchillo DA, Raabe DA. Excision and repair of the peripheral ossifying fibroma: a report of 3 cases. *J Periodontol*. 2001;72:939-944.
18. Nekouei A, Eshghi A, Jafarnejadi P, Enshaei Z. A review and report of peripheral giant cell granuloma in a 4-year-old child. *Case Rep Dent*. 2016;2016:7536304.
19. Flaitz CM. Peripheral giant cell granuloma: a potentially aggressive lesion in children. *Pediatr Dent*. 2000;22:232-233.
20. Lester SR, Cordell KG, Rosebush MS, Palaiologou AA, Maney P. Peripheral giant cell granulomas: a series of 279 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2014;118:475-482.
21. Sahingur SE, Cohen RE, Aguirre A. Esthetic management of peripheral giant cell granuloma. *J Periodontol*. 2004;75:487-492.
22. Mirza FN, Tuggle CT, Zogg CK, Mirza HN, Narayan D. Epidemiology of malignant cutaneous granular cell tumors: a US population-based cohort analysis using the Surveillance, Epidemiology, and End Results (SEER) database. *J Am Acad Dermatol*. 2018;78:490-497.e1.
23. Musha A, Ogawa M, Yokoo S. Granular cell tumors of the tongue: fibroma or schwannoma. *Head Face Med*. 2018;14:1.
24. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. *Am J Surg Pathol*. 1998;22:779-794.
25. Wei L, Liu S, Conroy J, et al. Whole-genome sequencing of a malignant granular cell tumor with metabolic response to pazopanib. *Cold Spring Harb Mol Case Stud*. 2015;1:a000380.
26. Matsumoto N, Tsuchiya M, Nomoto S, et al. CD105 expression in oral capillary hemangiomas and cavernous hemangiomas. *J Oral Sci*. 2015;57:45-53.
27. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. *Plast Reconstr Surg*. 1982;69:412-422.
28. Leaute-Labreze C, Hoeger P, Mazereeuw-Hautier J, et al. A randomized, controlled trial of oral propranolol in infantile hemangioma. *N Engl J Med*. 2015;372:735-746.
29. Buckmiller LM, Richter GT, Suen JY. Diagnosis and management of hemangiomas and vascular malformations of the head and neck. *Oral Dis*. 2010;16:405-418.
30. Agarwal S. Treatment of oral hemangioma with 3% sodium tetradecyl sulfate: study of 20 cases. *Indian J Otolaryngol Head Neck Surg*. 2012;64:205-207.

31. Buckmiller LM. Update on hemangiomas and vascular malformations. *Curr Opin Otolaryngol Head Neck Surg*. 2004;12:476-487.
32. Yang HY, Zheng LW, Yang HJ, Luo J, Li SC, Zwahlen RA. Long-pulsed Nd: YAG laser treatment in vascular lesions of the oral cavity. *J Craniofac Surg*. 2009;20:1214-1217.
33. Alotaibi O, Al Sheddi M. Neurogenic tumors and tumor-like lesions of the oral and maxillofacial region: a clinicopathological study. *Saudi Dent J*. 2016;28:76-79.
34. Salla JT, Johann AC, Garcia BG, Aguiar MC, Mesquita RA. Retrospective analysis of oral peripheral nerve sheath tumors in Brazilians. *Braz Oral Res*. 2009;23:43-48.
35. Chrysomali E, Papanicolaou SI, Dekker NP, Regezi JA. Benign neural tumors of the oral cavity: a comparative immunohistochemical study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997;84:381-390.
36. Eguchi T, Ishida R, Ara H, Hamada Y, Kanai I. A diffuse traumatic neuroma in the palate: a case report. *J Med Case Rep*. 2016;10:116.
37. Sanchis JM, Navarro CM, Bagan JV, et al. Intraoral schwannomas: presentation of a series of 12 cases. *J Clin Exp Dent*. 2013;5:e192-e196.
38. Rathore AS, Srivastava D, Narwal N, Shetty DC. Neurilemmoma of retromolar region in the oral cavity. *Case Rep Dent*. 2015;2015:320830.
39. Jones AV, Franklin CD. An analysis of oral and maxillofacial pathology found in adults over a 30-year period. *J Oral Pathol Med*. 2006;35:392-401.
40. Lykke E, Noergaard T, Rasmussen ER. Lingual neurofibroma causing dysaesthesia of the tongue. *BMJ Case Rep*. 2013;2013.
41. Angiero F, Ferrante F, Ottonello A, Maltagliati A, Crippa R. Neurofibromas of the oral cavity: clinical aspects, treatment, and outcome. *Photomed Laser Surg*. 2016;34:56-60.
42. Marocchio LS, Oliveira DT, Pereira MC, Soares CT, Fleury RN. Sporadic and multiple neurofibromas in the head and neck region: a retrospective study of 33 years. *Clin Oral Investig*. 2007;11:165-169.
43. Koutlas IG, Scheithauer BW. Palisaded encapsulated (''solitary circumscribed'') neuroma of the oral cavity: a review of 55 cases. *Head Neck Pathol*. 2010;4:15-26.
44. Lambertini M, Patrizi A, Fanti PA, et al. Oral melanoma and other pigmentations: when to biopsy? *J Eur Acad Dermatol Venereol*. 2018;32:209-214.
45. Meleti M, Vescovi P, Mooi WJ, van der Waal I. Pigmented lesions of the oral mucosa and perioral tissues: a flow-chart for the diagnosis and some recommendations for the management. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105:606-616.
46. Hassona Y, Sawair F, Al-Karadsheh O, Scully C. Prevalence and clinical features of pigmented oral lesions. *Int J Dermatol*. 2016;55:1005-1013.
47. Eisen D. Disorders of pigmentation in the oral cavity. *Clin Dermatol*. 2000;18:579-587.
48. Feller L, Masilana A, Khammissa RA, Altini M, Jadwat Y, Lemmer J. Melanin: the biophysiology of oral melanocytes and physiological oral pigmentation. *Head Face Med*. 2014;10:8.
49. Talebi M, Farmanbar N, Abolfazli S, Sarraf Shirazi A. Management of physiological hyperpigmentation of oral mucosa by cryosurgical treatment: a case report. *J Dent Res Dent Clin Dent Prospects*. 2012;6:148-151.
50. Ishikawa I, Sasaki KM, Aoki A, Watanabe H. Effects of Er:YAG laser on periodontal therapy. *J Int Acad Periodontol*. 2003;5:23-28.
51. Glick M, ed. *Burket's Oral Medicine*. Shelton, CT: People's Medical Publishing House—USA; 2015.
52. Sreeja C, Ramakrishnan K, Vijayalakshmi D, Devi M, Aesha I, Vijayabanu B. Oral pigmentation: a review. *J Pharm Bioallied Sci*. 2015;7(suppl 2):S403-S408.
53. Kauzman A, Pavone M, Blanas N, Bradley G. Pigmented lesions of the oral cavity: review, differential diagnosis, and case presentations. *J Can Dent Assoc*. 2004;70:682-683.
54. Gondak RO, da Silva-Jorge R, Jorge J, Lopes MA, Vargas PA. Oral pigmented lesions: clinicopathologic features and review of the literature. *Med Oral Patol Oral Cir Bucal*. 2012;17:e919-e924.
55. Pais S, Hegde SK, Bhat SS. Oral melanotic macule--a case report. *J Indian Soc Pedod Prev Dent*. 2004;22:73-75.
56. Tuthill RJ. Weedon's Skin Pathology. *Am J Surg Pathol*. 2011;35:159.
57. Lakshminarayanan V, Ranganathan K. Oral melanoacanthoma: a case report and review of the literature. *J Med Case Rep*. 2009;3:11.
58. Ferreira L, Jham B, Assi R, Readinger A, Kessler HP. Oral melanocytic nevi: a clinicopathologic study of 100 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;120:358-367.
59. Gaeta GM, Satriano RA, Baroni A. Oral pigmented lesions. *Clin Dermatol*. 2002;20:286-288.
60. Lucchese A, Gentile E, Romano A, Maio C, Laino L, Serpico R. The potential role of in vivo reflectance confocal microscopy for evaluating oral cavity lesions: a systematic review. *J Oral Pathol Med*. 2016;45:723-729.
61. Alawi F. Pigmented lesions of the oral cavity: an update. *Dent Clin North Am*. 2013;57:699-710.
62. Kallal RH, Ritto FG, Almeida LE, Crofton DJ, Thomas GP. Traumatic neuroma following sagittal split osteotomy of the mandible. *Int J Oral Maxillofac Surg*. 2007;36:453-454.
63. Parhar S, Singh HP, Nayyar A, Manchanda AS. Intra-oral schwannoma—a case report. *J Clin Diagn Res*. 2014;8:264-265.
64. Campos MS, Fontes A, Marocchio LS, Nunes FD, de Sousa SC. Clinicopathologic and immunohistochemical features of oral neurofibroma. *Acta Odontol Scand*. 2012;70:577-582.
65. Isik B, Gurel MS, Erdemir AT, Kesmezacar O. Development of skin aging scale by using dermoscopy. *Skin Res Technol*. 2013;19:69-74.
66. Ghias A, Shaheen E, Asghar A, Ahmad TJ. Patterns of dermoscopy in common pigmented skin lesions. *J Pak Assoc Dermatol*. 2018;27:346-352.
67. Mordoh A, Casas G, Horacio C, et al. Dermoscopic evaluation improves clinical diagnosis of oral melanotic macules: a study in 50 patients with oral pigmented lesions. *Am J Oral Med*. 2018;4:1-9.
68. Tarakji B, Umair A, Prasad D, Alsakran Altamimi M. Diagnosis of oral pigmentations and malignant transformations. *Singapore Dent J*. 2014;35C:39-46.
69. Rossiello L, Zalaudek I, Ferrara G, Docimo G, Giorgio CM, Argenziano G. Melanoacanthoma simulating pigmented spitz nevus: an unusual dermoscopy pitfall. *Dermatol Surg*. 2006;32:735-737.
70. Wilder EG, Frieder J, Sulhan S, et al. Spectrum of orocutaneous disease associations: genodermatoses and inflammatory conditions. *J Am Acad Dermatol*. 2017;77:809-830.