Oral Disease, Part 2

by Helena Pasieka, MD

	CLINICAL	PATHOLOGY	TREATMENT	ASSOCIATIONS
SALIVARY GLAND DISEASES				
Mucocele	Painless submucosal swelling. Color ranges from clear/blue/colorless depending on depth of lesion. Lower labial mucosa most common, but can occur anywhere where there are minor salivary glands.	Collection of mucus surrounded by macrophages and granulation tissue. Look for the inflamed minor salivary gland as a clue.	Superficial mucoceles often resolve w/o intervention by spontaneous rupture. However, most require surgical excision.	
Cheilitis glandularis	Ranges from slight hypertrophy of lower lip to nodular enlargement with eversion. Most commonly in adult men.	Localized dense accumulations of inflammatory cells within and around the mucous glands in a background of actinic chelitis.	Vermilionectomy of the lower lip, with or without cosmetic debulking is the standard of care. Injections of corticosteroids can provide symptomatic relief..	
Sjögren's syndrome	Slow onset of variable degrees of eye and oral dryness. Increased dental carries and difficulty wearing dentures. Increased candidiasis.	Salivary glands with focal aggregates of >50 lymphocytes adjacent to normal-appearing acini. In the parotid gland characteristic epimyoepithelial islands are seen.	Symptomatic care and management of the associated complications. Salivary stimulation (sugarless gum, hard candies, pilocarpine) or artificial saliva.	
Salivary gland tumors	Submucosal, painless, rubbery firm swelling often noted on the posterior hard palate or anterior soft palate.	Varies depending on the specific type of salivary tumor.	Benign salivary gland tumors are conservatively excised. Malignant tumors are more extensively removed +/- radiotherapy as adjunct.	
HEMATOLOGIC/ONCOLOGIC DISEASE				
Chemotherapy-induced mucositis	Multiple oval or irregularly shaped ulcers, usually on the gingivae, lateral tongue, or buccal mucosa. Usually appear 4-7 days after chemotherapy administered.	Lichenoid mucositis.	Usually resolves in 2-3 weeks cessation of chemotherapy. Palifermin (keratinocyte growth factor) may reduce severity for those on high-dose chemotherapy. Meticulous oral hygiene and symptom management.	
Leukemia	Many oral manifestations, most commonly bruising or hemorrhage related to thrombocytopenia. Also, pallor of anemia, increased viral, fungal and bacterial infections related to leukopenia. Diffuse, firm, non-tender gingival enlargement can be caused by infiltration of the gingival connective tissue by leukemic cells.	Infiltration of leukemic cells into gingival connective tissue (most commonly with monocytic or myelomonocytic leukemias).	Multi-agent chemotherapy and peripheral blood stem cell or bone marrow transplantation are most commonly used to treat acute leukemia.	
Lymphoma	Slow growing, painless, soft or rubbery, with purplish swelling. Most commonly on the palate and the buccal vestibule. Overlying telangiectasia sometimes seen. Ulceration possible, mimicking SCC.	Infiltration of atypical lymphocytes, usually of B-cell type.	Chemotherapy and/or monoclonal antibodies (e.g. rituximab).	HIV, other iImmunosuppression, older age.
Melanoma	Most commonly on hard palate, maxillary attached gingiva. Has same features as cutaneous melanoma.	Proliferation in epithelium and infiltration of the connective tissue by atypical melanocytes, with or without melanin production. Can use Melan-A or S100 to stain.	Wide surgical excision with (-) margins. Sentinel lymph node biopsy for prognostication. Minimal radial growth phase on mucosa, so they differ from cutaneous melanomas in that they present in the vertical growth phase. Chemotherapy and XRT of little utility. Worse prognosis than cutaneous lesions, w/5year survival rate of ~15%, and median from dx of < 2 years.	

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Oral Disease, Part 2 (continued)

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	CLINICAL	PATHOLOGY	TREATMENT	ASSOCIATIONS
MANIFESTATIONS OF SYSTEMIC DISEASE				
Amyloidosis	Firm macroglossia, often with scalloped edge. Xerostomia or dysgeusia can be seen before the onset of tongue enlargement.	Homogeneous eosinophilic accumulation. (+) congo red stain.		
Pernicious anemia	Gradual onset of smooth, 'beefy-red' tongue, w/ill-defined areas of erythema which can coalesce into diffuse dorsal tongue involvement causing a smooth, beefy-red appearance.	Absence of filiform papillae.	Vitamin B12 injections provide rapid improvement.	
Crohn's disease	Linear fissures +/- ulcers of the vestibule or "cobblestone" ulcers of the buccal mucosa. Sometimes scarring. Can also have cheilitis granulomatosa both clinically and histologically.	Non-necrotizing granulomatous inflammation.	Respond to therapy for bowel lesions. Topical or intralesional corticosteroids also effective.	
Pyostomatitis vegetans	"Snail track" arrangement of multiple tiny, creamy-yellow pustules set against a bright erythematous background. Fragile pustules lead to shallow erosions and ulcerations. Labial, gingival and buccal mucosa are most commonly involved; tongue is usually spared.	Intra- or subepithelial microabscesses containing eosinophils and neutrophils.	Management of the underlying GI disease often results in improvement of oral lesions.	Inflammatory bowel disease.
HIV				
Kaposi's sarcoma	Multiple violaceous macules, plaques, or nodules. Most commonly on palate, but can be anywhere in mouth.	Infiltration of the dermis w/slit-like vascular spaces, and dilated vessels. Many extravasated RBCs and proliferating spindle cells seen.	May improve or resolve with improved immune status (i.e., initiation of HAART).	
Oral hairy leukoplakia	White, shaggy, corrugated protrusions on lateral tongue. Cannot be dislodged with tongue depressor.	Irregular keratin projections, parakeratosis, acanthosis, and groups of pale epithelial cells.	Antiretroviral therapy may lead to regression.	Epstein-Barr virus in HIV. Predictor of rapid decline and progression to AIDS.
Candidiasis	Thick white or cream-colored deposits on tongue or posterior oropharynx with "cottage cheese-like" appearance. Can be dislodged with tongue depressor. Also can have fissuring at the corners of the mouth.	Pseudohyphae and budding yeast sometimes seen in H&E. More easily seen with PAS or GMS stain.	Improvement of immune status. Anti-candidal treatment, such as clotrimazole troches or PO fluconazole.	
HSV	Grouped vesicles on erythematous base, becoming ulcerated. Can coalesce into larger lesions. Look for scalloped border.	Epidermal necrosis and ballooning degeneration. Infected cells are multinucleated w/glassy nuclear contents, marginalized nuclear chromatin, and nuclear molding.	Suppressive therapy with antiviral medications. Severely immunosuppressed may need IV acyclovir.	
CMV	Ulcerations anywhere in mouth. Appear like aphthae, may be slightly larger.	Vascular dilation with large cytomegalic endothelial cells. "Owls eye" appearance due to halo around intranuclear inclusion bodies.	Antiviral drugs (ganciclovir and valganciclovir).	Development on mucosal surface usually a sign of disseminated disease.
SYNDROME ASSOCIATIONS				
Odontogenic keratocysts of the jaw	Often incidentally noted radiolucent or mixed radiolucent/radiopaque lesions of the mandible. Asymptomatic; rarely mild facial swelling and discomfort.	Lining of stratified squamous epithelium with basal layer of the epithelium exhibiting palisaded cuboidal to columnar cells. The luminal surface often with a corrugated morphology and parakeratosis.	Opinions differ and range from wide local excision to marsupialization to curettage.	Nevoid basal cell carcinoma syndrome w/mutations in *PTCH (*Hedgehog signaling pathway).
Multiple osteomas of the jaw	Asymptomatic facial deformity.	Same as typical solitary osteomas.	Surgical removal, screening for malignancy.	Often the earliest marker of Garner syndrome occurring >80% around puberty.
Multiple endocrine neoplasia syndrome type 2B	Multiple mucosal neuromas involving lips and tongue are often the first dermatologic manifestation.	"Plexiform neuromas" of hyperplastic bundles of nerves surrounded by a thickened perineurium.	Screening for malignancy: Medullary thyroid carcinoma with pheochromocytoma in 50% of cases, and digestive neurofibromatosis.	

Sources:
1. Bolognia JL, Jorizzo JL, Rapini RP eds. Dermatology. 2nd ed. Mosby; 2007.
2. Rapini R. Practical Dermatopathology. Mosby; 2005.

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