ESSAY ABSTRACTS

AUTOANTIBODY PRODUCTION IN SJÖGREN SYNDROME J Kramer, N Holodick, T Vizconde, T Rothstein, The Feinstein Institute for Medical Research, North Shore-LI Jewish Health System, Manhasset, NY, USA

Sjögren syndrome (SS) is an autoimmune disease that sometimes results in significant morbidity; many patients experience xerostomia and xerophthalmia in addition to numerous systemic disease manifestations. Although T cells were initially thought to be the prime drivers of SS, many recent studies detail an important role for B cells as well. At present, it is not known whether B cells derived from glandular tissue have unique characteristics as compared with those from secondary lymphoid organs.

Objective: We tested the hypothesis that B cells from salivary gland tissue have increased proliferative capacity and immunoglobulin secretion. The autoantibody profile and B cell repertoire are distinct in B cells from SS salivary tissue as compared with those from other sites.

Methods: We single-cell-sorted B cells from spleen and submandibular tissue from SS mice, and sequenced immunoglobulin M heavy chain variable regions. We then sort-purified B cells derived from spleen, lymph node, and submandibular tissue of SS mice. B cells were stimulated with lipopolysaccharide and autoantigen arrays, and enzyme-linked immunosorbent spot and proliferation assays were performed.

Results: B cells from salivary tissue of SS mice do not exhibit enhanced proliferation or elevated antibody secretion. Preliminary data suggest differences in repertoire usage may be present in B cells derived from salivary tissue compared with those from spleen. Moreover, autoantigen array data suggest B cells derived from salivary tissue display distinct autoantibody specificities as compared with those from spleen and cervical lymph nodes.

Conclusions: All together, these data suggest antibodies from salivary gland B cells have unique characteristics that likely influence autoantigen binding and contribute to SS disease in a tissue-specific manner.

EVALUATION OF ANGIOGENESIS IN ORAL LICHEN PLANUS: AN IMMUNOHISTOCHEMICAL STUDY WITH CD34 AND ENDOGLIN M Khalili, N Eshghybar, M Asgari, Tehran University of Medical Sciences, Tehran, Iran

Background and objective: Angiogenesis is a major component of neoplastic and chronic inflammatory disorders, but its role in mucocutaneous inflammatory diseases such as oral lichen planus (OLP) has not been established yet. The aim of this study was to determine the angiogenic potential of OLP compared with normal oral mucosa.

Materials and methods: From a group of oral tissue specimens, 15 cases of reticular and 15 cases of erosive oral lichen planus were selected, and 15 samples of normal oral mucosa were used as a control group. Sections (4 μm thick) were cut from paraffin blocks and stained with CD34 and CD105 antibodies. Microvessel counting was performed in areas of highest vascularity (hot spots). Data were analyzed by analysis of variance and post hoc tests. \( P < .05 \) was considered as the limit of significance.

Results: CD34 staining showed a mean microvessel density (MVD) of 6.05 ± 0.86 in normal mucosa, compared with 16.65 ± 3.34 and 31.8 ± 5.39 in reticular and erosive lichen planus, respectively. CD105 staining showed a mean MVD of 1.7 ± 0.77 in normal mucosa and 9.13 ± 1.81 and 19.05 ± 3.02 in reticular and erosive lichen planus, respectively. Intergroup analysis showed significant differences in MVD among the studied groups for both markers (\( P < .001 \)).

Conclusions: Based on our findings, microvessel density was higher in OLP compared with normal oral mucosa, which could be related to a potential angiogenic influence in the pathogenesis and progression of the disease.

MATRIX METALLOPROTEINASE IN ORAL VESICULOEROSIVE DISEASE—ANALYSIS AND THERAPEUTIC MODULATION WITH SUBANTIMICROBIAL DOSE DOXYCYCLINE: A PILOT STUDY T Jhamb, JM Kramer, JE Fantasia, Hofstra North Shore-LI Jewish School of Medicine, New Hyde Park, NY, USA; State University of New York, Buffalo, NY, USA

Matrix metalloproteinases (MMPs) MMP-2 and MMP-9 have been studied in human inflammatory diseases. Oral vesiculoerosive diseases (VEDs) include chronic pathoses such as cicatricial pemphigoid (CP) and lichen planus (LP). Treatment with subantimicrobial-dose doxycycline (SDD) inhibits MMPs and is used in the treatment of other chronic inflammatory processes. MMP-2 and MMP-9 enzyme-linked immunosorbent assays (ELISAs) were performed on sera, saliva, and urine of healthy controls to establish baseline levels.

Objective: We tested the hypothesis that MMP-2 and MMP-9 are increased in sera, saliva, and urine of patients with OLP and CP as compared with healthy subjects. SDD treatment mitigates inflammatory reaction in OLP and CP, resulting in clinical improvement through diminishing MMP expression.

Methods: Sera, saliva, and urine from patients with VEDs were sampled at baseline and at 2 time points following initiation of SDD therapy. Sera, saliva, and urine were also collected from healthy controls. ELISAs were used to compare the levels of MMP-2 and MMP-9 in these fluids from healthy controls (n = 10) and from patients with VEDs before SDD therapy (n = 7). In addition, we used ELISAs to monitor MMP-2 and MMP-9 levels during therapy in patients with VEDs (n = 5).

Results: Preliminary data indicate increased MMP-2 in sera (\( P = .0046 \)) and saliva (\( P = .0121 \)) in patients with VEDs as compared with healthy controls. MMP-9 levels in saliva were elevated but did not achieve statistical significance. In addition, preliminary data show decreased MMP-2 and MMP-9 levels in patients receiving SDD.

Conclusions: MMP-2 levels are increased systemically in patients with VEDs compared with healthy controls. SDD may reduce expression of MMP-2 and MMP-9 in VEDs. SDD may be
an important therapeutic approach to reduce the chronic inflammation characteristic of VEDs by modulation of MMP expression. Additional study subject accrual is ongoing.

HISTOLOGIC LICHENOID FEATURES IN ORAL DYSPLASIA AND SQUAMOUS CELL CARCINOMA
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Histologic features associated with the immune-mediated chronic inflammatory condition oral lichen planus (OLP) have been observed in some premalignant oral lesions, a phenomenon that could increase the risk of erroneous or delayed diagnosis. This study retrospectively examined 352 histologic specimens of oral low-grade (LG) dysplasia, high-grade (HG) dysplasia, and squamous cell carcinoma (SCCA) for 5 histologic characteristics commonly associated with OLP: band-like inflammatory cell infiltrate subjacent to the epithelium (BLI), saw-tooth rete ridge formation (SRR), interface stomatitis (IS), Civatte bodies (CB), and degeneration of the basal layer (DBL). These lichenoid characteristics were evaluated in regard to grade of dysplasia/SCCA, age, gender, and oral cavity subsite. Of the 352 cases, 29% exhibited 3 or more features and met a threshold for overall lichenoid characteristics. BLI was the most common and nonspecific feature noted in almost three-quarters of cases, followed in descending order by IS, DBL, CB, and SRR. Lichenoid features were significantly more frequent in LG lesions than HG lesions. No statistically significant pattern was noted for age or gender. The oral cavity subsite also showed statistically significant differences in lichenoid characteristic frequency, with the buccal mucosa overrepresented and the floor of the mouth underrepresented in relation to the frequency of involvement in SCCA. The study is significant for demonstration of frequent correlation of lichenoid features with certain oral premalignant and malignant lesions. This study also highlights the subjective nature of the assessment of lichenoid features in premalignant and malignant oral lesions, which further complicates accurate and consistent diagnosis.

HPV-ASSOCIATED ORAL EPITHELIAL DYSPLASIA: A DISTINCT HISTOPATHOLOGIC ENTITY S Almazrooa, M Lerman, V Noonan, S-B Woo, Harvard School of Dental Medicine, Boston, MA, USA; Strata Pathology Services (StrataDx), Lexington, MA, USA; Brigham and Women’s Hospital, Boston, MA, USA

Background: The incidence of oropharyngeal and particularly tonsillar squamous cell carcinoma (SCC) has increased, possibly as a result of high-risk human papillomavirus (HPV) infection. Recognition of HPV-SCC in the oropharynx is important because of its more favorable prognosis. In the oral cavity, the association of SCC with HPV is low, and the precursor dysplastic lesion has yet to be well characterized.

Objectives: The aim of this study is to describe the histopathologic features of HPV-associated oral epithelial dysplasia (OED) and to compare them with those of non-HPV-associated OED.

Results: Eight cases were identified in 6 men and 2 women (median age, 65.5 years). Five cases involved the ventrolateral tongue. Bright parakeratin was present in 7 cases, and severe dysplasia was present in all cases. The mean numbers of karyorrhectic and apoptotic cells were 5.9 and 5.3, respectively, at ×600 magnification. All cases expressed p16 in a continuous band that coincided with the presence of high-risk HPV subtypes by in situ hybridization, whereas the probe for low-risk subtypes was negative. All controls exhibited moderate to severe OED; the mean numbers of karyorrhectic and apoptotic cells were 0.6 and 1, respectively. All controls were negative for p16 stain.

Conclusions: HPV-associated OED primarily affects men over the age of 60 and often involves the ventrolateral tongue. It is characterized by marked apoptosis and karyorrhexis, severe epithelial dysplasia, p16 reactivity, and positivity for high-risk HPV subtypes. Recognition and follow-up for malignant transformation may help better characterize the role of HPV in oral SCC development.

INVASIVE FRONT HISTOLOGY OF ORAL SQUAMOUS CELL CARCINOMA CORRELATES WITH OVERALL STAGE AND OVERALL SURVIVAL K Byrd, J Fox, E Bellille, G Wolf, T Danciu, University of Michigan, Ann Arbor, MI, USA

Objective: To study invasive fronts of oral squamous cell carcinoma (OSCC) biopsies, comparing histologic assessments of E-cadherin expression and localization (indicators of epithelial-mesenchymal transformation [EMT]) as well as the Bryne classification with techniques used in prostate cancer (Gleason score) and colorectal cancer (tumor budding).

Methods: A total of 53 biopsies with clinical characteristics were retrieved. Pancytokeratin immunohistochemistry was performed to assess tumor budding and pattern of invasion. The Bryne classification was determined traditionally (“overall”) and at the site with the most pronounced EMT (“worst”). The Gleason score was analyzed as a combination of the Bryne “overall” (>50%) and the Bryne “worst” site (>10%). Tumor budding score and count were obtained at the invasive front. E-cadherin expression and localization were evaluated on the basis of immunohistochemical staining, at both the “overall” and “worst” sites of the invasive front. Chi-square testing was performed with a Monte Carlo estimate.

Results: Median follow-up for overall patient survival was 25 months; 17 patients had died as of the preliminary analysis. There is statistical significance between the Bryne “overall” classification and tumor budding count with overall stage (P = .02). Currently, there is no statistical correlation with Gleason score. Overall loss of membranous E-cadherin is statistically associated with higher stage (P = .005) as well as with a higher tumor budding count (P = .004). Loss of E-cadherin at the “worst” site has borderline significance with survival (P = .049). No association was observed between histologic assessment of the other factors and overall survival, which may be due to the relatively short follow-up period.

Conclusions: Our preliminary study represents a first step in the development of a mathematical risk model for patients with OSCC.

NEUROPIN-1 AND ORAL SQUAMOUS CELL CARCINOMA SS Farahani, K Munger, K Hida, M Gallottini, D Bielenberg, Harvard School of Dental Medicine and Department of Medicine, Harvard Medical School, Boston, MA, USA; Division of Oral Pathobiological Science and Vascular Biology, Hokkaido University Graduate School of Dental Medicine, Sapporo, Japan; Department of Oral Pathology, School of Dentistry, University of São Paulo, São Paulo, Brazil; Department of Surgery, Harvard Medical School and Vascular Biology Program, Karp Family Research Laboratories, Boston Children’s Hospital
Angiogenesis is one of the most important prognostic factors in oral squamous cell carcinoma (SCC). Neuronomins (NRPs) are transmembrane receptors that bind vascular endothelial growth factor (VEGF) and class 3 semaphorins (SEMA3). Upregulation of neuropepmin-1 (NRP1) and its effect on angiogenesis, lymphangiogenesis, and the metastatic process have been shown in some human carcinomas. Western blotting, enzyme-linked immunosorbent assay (ELISA), and immunohistochemistry (IHC) were performed on selected human tongue SCC (HTSCC) cell lines and specimens of HTSCC and dysplasia to evaluate NRp1 or VEGF expression. Selected HTSCC cell lines were injected into nude mice subcutaneously or in the tongue. Resected tumors were evaluated for NRp1 expression, angiogenesis, and lymphangiogenesis by IHC. Normal isolated and calcium treated primary mouse keratinocytes were compared for NRp1 expression. Proliferation, collapse, and migration assays were performed on HTSCC cell lines after adding SEMA3A. HTSCC cell lines and tissue sections showed differential NRp1 expression. Normal mouse tongue expressed NRp1 in the suprabasal epithelium, whereas dysplastic lesions strongly demonstrated NRp1 expression in the basal cell layer. Resected tumors showed NRp1 expression. Primary mouse keratinocytes treated with calcium showed more differentiation, which was correlated with NRp1 expression. SEMA3A treatment did not affect proliferation, but it induced collapse and inhibited migration of HTSCC cell lines.

**Conclusions:** Some HTSCC cell lines and tumors express NRp1, which is correlated with VEGF production, degree of invasiveness of these cell lines, and angiogenesis. Epithelial dysplastic lesions express NRp1, which may correlate with the degree of dysplasia. Calcium may regulate NRp1 expression. SEMA3A treatment may be a potential therapy to inhibit the spread of oral SCC.

**GALANIN RECEPTOR 2 PROMOTES TUMOR ANGIOGENESIS IN HEAD AND NECK CANCER**

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Squamous cell carcinoma of the head and neck (SCCHN) is an aggressive disease with poor patient survival. Galanin receptor 2 (GALR2) is a G-protein coupled receptor (GPCR) that induces aggressive tumor growth. Because GPCRs have multiple effects on tumor progression, we investigated whether GALR2 promotes angiogenesis in SCCHN. To address this impact, we used biochemical and molecular approaches in human SCCHN cells in vitro and in vivo models of human SCCHN. In vivo models included the murine floor-of-mouth syngeneic, orthotopic model of SCCHN and a recently developed model of SCCHN-related angiogenesis using the chick chorioallantoic membrane. GALR2 stimulated angiogenesis by activation of p38 mitogen-activated protein kinase (MAPK) and by enhanced secretion of proangiogenic cytokines, vascular endothelial growth factor (VEGF) and interleukin-6 (IL-6). This occurred via rap1B-p38 MAPK-mediated phosphorylation of tristetraprolin (TTP), an RNA-binding protein that facilitates degradation of cytokine transcripts. Moreover, phosphorylation-mediated inactivation of TTP in SCCHN cells overexpressing GALR2 further increased secretion of IL-6 and VEGF. Given its significant role in promoting tumor progression, GALR2-p38 mediated cytokine secretion may be an excellent target for adjuvant therapy in SCCHN. This study was financially supported by National Institutes of Health/National Institute of Dental and Craniofacial Research grants DE018512 and DE019513 (NJD), DE021293 (CSS), DE021305 (EVT).

**EXPRESSION OF P8 IN HUMAN ORAL SQUAMOUS CELL CARCINOMA**

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**Objective:** This study investigated the expression and potential role of p8, a transcription factor that exhibits paradoxical roles in several human cancers, including human oral squamous cell carcinomas (OSCCs). The mortality rate from oral cancer for the past 4 decades remains over 50%. Because early detection and treatment increase the survival rates of patients, the search for reliable predictors of OSCC progression and prognosis remains relevant.

**Methods and principal findings:** Analysis of the immunohistochemical expression of p8 was carried out on 20 archived surgical specimens of human OSCCs, and expression was correlated with clinical/outcome parameters in a retrospective study. Also, levels of p8 in an OSCC cell line, OSC2, before and after lentiviral-mediated shRNA p8-silencing, as well as the effects of silencing on notable hallmarks of oral carcinogenesis, were assessed by Western blot, reverse transcriptase polymerase chain reaction, and MTT (cell-viability) assay. It was found that p8 was expressed in 85% (17/20) of OSCCs, with levels of expression (means ± standard deviations) exhibiting a significant difference (C2 = 8.352; df = 3; P = .039) for age. Furthermore, the predictive regression models for p8 immunoreactivity versus the degree of histologic differentiation of tumor on hematoxylin and eosin sections was significant (P = .008). The p8-silenced OSC2 cells exhibited altered cell morphology, a decrease of about 53% in cell proliferation (P = .05; n = 3), and a significant downregulation of proteins Ki-67 (about 50%), CEBP (about 50%), and Nrf1 (about 50%).

**Conclusions:** p8 is expressed in a significant number of OSCCs. We found that p8-silencing decreases the viability/proliferative potential of OSC2 cells, suggesting a role for p8 in pathways involving proliferation markers critical for oral cancer progression. The data provide a framework for future studies on p8 mechanistic networks in oral cancer biology.

**APPLICATION OF A BLACK RASPBERRY GEL INDUCES HISTOLOGIC AND CLINICAL REGRESSION OF ORAL INTRAEPITHELIAL NEOPLASIA**

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Therapeutic efficacies of black raspberry (BRB) gel and placebo gels on oral intraepithelial neoplasia (OIN)(0.5 g, 4 times daily for 3 months) were determined by effects on (1) histologic grade; (2) clinical size; (3) loss of heterozygosity (LOH) indices at putative tumor suppressor gene loci associated with OIN progression to oral squamous cell carcinoma; (4) lesional epithelial levels of cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and microvascular densities (MVD); and (5) methylation of p16 promoter regions. Pretreatment OIN biopsies provided a microscopic diagnosis and baseline biomarkers. Metabolic profiling analyses were also conducted. Placement in the BRB gel group (n = 22) and placebo gel group (n = 18) was randomized. Pretreatment parameters (grade, size, LOH indices) were comparable between the BRB and placebo.
cohorts. Trial results have shown (1) that there were no deleterious effects; (2) that BRB gel decreased OIN clinical size (BRB, P = .0019) whereas 17 of 18 placebo gel lesions increased in size (P = .0395; 2-tailed Mann-Whitney U test); (3) that BRB gel reduced OIN histologic grade (BRB, P = .0488; placebo, P = .4961; Wilcoxon matched-pairs signed-rank test); (4) that BRB gel reduced LOH indices at 9p markers (BRB, P = .0156; placebo, P = .9999; Wilcoxon matched-pairs signed-rank test); and (5) that there were comparable 3-month recurrences. Analyses of COX-2, iNOS, and MVD; metabolic profiles (Western blots); LOH analyses at p53 and fragile histidine triad (FHIT) loci; and p16 promoter methylation studies are ongoing. Our results confirm that BRB constituents—and not gel base components—provide the chemopreventive activity and demonstrate clinically relevant efficacy. As many key BRB active constituents are redox-active molecules, we speculate that dysplastic phenotype reduction reflects redox-mediated modulation of gene expression and induction of apoptosis. The comparable recurrence rates imply persistence of altered stem cells and suggest a need for sustained treatment.

ORAL CANCER DETECTION: A COMPARATIVE STUDY IN ARGENTINA H Lanfranchi, M Labrozzi, M Velazco, M Gandolfo, Department of Oral Medicine, School of Dentistry, University Of Buenos Aires, Buenos Aires, Argentina

Although oral cancer is accessible to inspection and diagnosis, due to its location, referral to specialists occurs in advanced stages. Late diagnosis in oral cancer is a universal problem that causes high morbidity and low patient survival. We studied clinical features, histopathologic diagnosis, localization, clinical stage, and survival of oral squamous cell carcinoma (OSCC) in 2 periods: 1992 to 2000 and 2001 to 2009. This work comprised 507 patients diagnosed with OSCC who attended our Oral Medicine Department. Tumor location, clinical and histopathologic diagnosis, clinical staging, and patient follow-up were recorded in a digital database. Statistical analysis was performed using the comparison test of proportions, and prognostic assessment of survival was performed employing the Kaplan-Meier test. Tumor staging corresponding to the 1990-2000 period was 23.6% in early stages and 76.3% in late stages, whereas the 2001-2009 period showed 49.3% in early stages and 50.7% in late stages (P < .001). Tongue localization corresponding to the 1992-2000 period was 26.49% in early stages and 73.48% in late stages, and in the 2001-2009 period it was 64.4% in early stages and 35.61% in late stages (P < .05). The survival rate of OSCC after 60 months was 38% in the first decade and was 64% in the second decade (P < .0004). Results showed a significant increase in the survival rate in the 2001-2009 period. This rise was related to increased survival for OSCCs of the tongue in this last decade. This favorable prognosis would be mainly due to the amount of cancer cases that were diagnosed in early stages because of the implementation of new teaching methods, as well as to the oral cancer prevention programs developed in the last decade in Argentina.

THE CLINICAL APPEARANCE OF ORAL MUCOSAL MALIGNANCIES: REEVALUATION OF COMMON PARADIGMS I Allon, DM Allon, G Gal, Y Anavi, G Chaushu, J Kaplan, Rabin Medical Center, Petach-Tikva and Tel-Aviv University, Tel Aviv, Israel

Objective: To evaluate the clinical appearance and rate of ulceration of oral mucosal malignancies and to investigate the accuracy of clinical provisional diagnoses.

Methods: 10-year retrospective analysis.

Results: A total of 227 oral mucosal malignant tumors were included. Squamous cell carcinoma (SCC) and its variants accounted for the majority (78%) of malignant tumors. The most common clinical presentations were nonulcerated (59.7%) and ulcerated masses (20.4%). Only 11.9% presented as indurated ulcers. The highest ulceration rate of all malignancies was recorded for SCC, with only about half of SCC and its variants ulcerated at presentation. Approximately a third of cases were not suspected for malignancy clinically, reflecting a false negative rate of 31.1%, with lower false negative rates in ulcerated tumors. There was better agreement between clinical and microscopic diagnoses in the SCC group than in other types of malignancy (P < .001).

Conclusions: The majority of oral mucosal cancers were nonulcerated. Nonulcerated mass was by far a more common clinical appearance than were indurated ulcers. Although the study was performed in a training center for oral and maxillofacial surgery, the false-negative rate for clinical diagnosis of malignancy approached a third of all malignancies, with the highest rates in tumors lacking surface ulceration. To improve the reliability of clinical diagnosis of malignancy in oral mucosa, nonulcerated masses should be regarded with a higher level of suspicion, parallel to suspicion levels currently reserved for mucosal ulcers and ulcerated masses.

MACRO- AND MICROSCOPIC OPTICAL IMAGING TOWARD DIAGNOSIS OF ORAL EPITHELIAL DYSPLASIA B Malik, J Jabbour, S Cheng, R Cuenda, J Jo, J Wright, Y Cheng, K Maitland, Texas A&M University, College Station, TX, USA; Texas A&M Health Science Center, Baylor College of Dentistry, Dallas, TX, USA

Clinical guidelines for early detection of oral cancer include a screening examination wherein the clinician visually inspects and palpates the high-risk sites for development of oral cancer. The actual evaluation of risk then usually requires one or more biopsies, the location(s) of which are increasingly critical to identify. Therefore, development of noninvasive clinical tools that can help the clinician identify the most accurate sites of precancerous lesions is of great importance and can potentially increase the diagnostic yield of the overall screening process. To this end, we have developed a multimodal, multiscale imaging system based on macroscopic fluorescence lifetime imaging (FLIM) and high-resolution reflectance confocal microscopy (RCM). In the current study, we used the Syrian hamster cheek pouch 7,12-dimethylbenz[a]anthracene model of carcinogenesis. FLIM provided the biochemical screening by probing the endogenous fluorescence of structural proteins (collagen) and metabolic cofactors (nicotinamide adenine dinucleotide, flavin adenine dinucleotide), and RCM provided information on nuclear morphology and overall tissue architecture. The results show that qualitative differences between normal, precancerous, and cancerous sites were resolved with FLIM/RCM imaging and that the imaging correlated well with the histopathologic evaluation. Although FLIM allowed for distinguishing between normal and cancerous tissue, RCM was still necessary for identifying cellular changes associated with dysplasia. Such a simultaneous assessment of tissue physiology/morphology can help identify the diagnostic state of the oral tissue. This study suggests that FLIM/
RCM imaging can serve as a guiding tool for standard screening methods and provides the groundwork for application of this multiscale imaging modality in a clinical setting.

INTRAORAL BASAL CELL CARCINOMA: REPORT OF 2 NEW CASES WITH LITERATURE REVIEW T Woods, D Cohen, NM Islam, I Bhattacharyya, University of Florida, Gainesville, FL, USA

Intraoral basal cell carcinoma (IOBCC) is an extremely rare entity that is often confused with the peripheral ameloblastoma (PA). Basal cell carcinomas are thought to arise from pluripotential basal cells present within surface epithelium and adnexal structures, so theoretically they can arise within the oral cavity. Most of the well-documented cases arise from the gingiva. Many of the early cases reported as IOBCC actually represent PA. We present 2 cases displaying histologic, immunohistochemical, and clinical features characteristic of an IOBCC. The histologic features of IOBCC that help separate it from a PA include prominent retraction artifacts, tumor arising from surface epithelium, scattered mitotic figures and apoptotic cells, presence of mucoid ground substance, and tumor infiltrating widely throughout the connective tissue. Clinically, IOBCCs resemble carcinomas, compared with the benign and innocuous appearance of the PA. IOBCCs typically present as surface ulcerations varying from rodent ulcer to an ulcerated erythroleukoplastic appearance. This contrasts with the classic “bump on the gum” appearance of PAs, with usually intact surface and appearing as small, discrete, sessile, exophytic lesions. In the more recent literature, Del Rosario et al. and Koutlas et al. described IOBCC with positive immunoreactivity of only the neoplastic basal cells for the antiepithelial antibody Ber-EP4, a cell surface glycoprotein. Normal skin or oral epithelium, PA, and squamous cell carcinomas do not stain with Ber-EP4, a very important distinguishing factor separating these entities.

HISTOLOGIC AND IMMUNOHISTOCHEMICAL DIFFERENTIATION BETWEEN GLANDULAR ODONTOGENIC CYSTS AND CYSTS WITH FEATURES OF GLANDULAR ODONTOGENIC CYST L Montague, A Neuman, K Kimbler, NM Islam, D Cohen, I Bhattacharyya, University of Florida, Gainesville, FL, USA

Background: Glandular odontogenic cysts (GOCs) are relatively uncommon, developmentally distinct odontogenic cysts with unusual histopathologic features. Due to the overlap of key microscopic features with other developmental cysts, particularly dentigerous cysts, it is imperative that stringent criteria and specific markers be identified. Immunohistochemistry has been studied to aid differentiation of GOCs from other cysts. Tosios et al., with a very limited sample size, reported increased expression of bcl-2 in GOCs compared with dentigerous cysts.

Objective: To determine whether GOCs can be consistently differentiated from other cysts based on histologic features and to compare bcl-2 expression in GOCs and other cysts with features of GOC.

Methods and materials: We identified 141 cases from 1994 to 2012 coded as GOC or cysts with some features of GOC. Four reviewers categorized these as “GOC” or “non-GOC cyst” using criteria established by Fowler et al. Of these, 15 cases were initially selected and stained for bcl-2.

Results: A total of 23 cases were categorized by all reviewers as GOC. Fifteen cases were agreed to be “non-GOC.” The remaining cases were designated as “equivocal” with significant interobserver disagreement. All stained cases diagnosed as GOC were strongly bcl-2 positive in the basal and suprabasal cell layers. The non-GOC cysts were minimally to focally positive for bcl-2.

Conclusions: True GOCs can be difficult to distinguish histologically from cysts with some features of GOC. Staining for bcl-2 appears to be consistently strong in GOC and therefore may be a useful discriminator when limited clinical information is available and overlapping microscopic features are present.

INTERPRETATION OF SOX2 IMMUNOHISTOCHEMICAL STAIN IN AMELOBLASTIC CARCINOMA: AN EXPANDED COHORT Y Lei, J Jaradat, A Owosho, K Adebiyi, B Neville, S Müller, E Bilodeau, University of Pittsburgh, Pittsburgh, PA, USA; Emory University, Atlanta, GA, USA; Obafemi Awolowo University, Ile, Osun, Nigeria; Medical University of South Carolina, Charleston, SC, USA

SOX2 (sex determining region Y-box 2), originally identified as a pivotal transcription factor for epithelial renewal, is found to be overexpressed in a spectrum of epithelial malignancies. As an odontogenic epithelial-derived cancer, ameloblastic carcinoma (AC) often poses diagnostic challenges, especially in its separation from benign ameloblastoma with atypical cytologic features or unusual clinical course. In our previous publication, we identified SOX2 as a marker for high-grade transformation in ameloblastic neoplasms with only 2 stained AC cases. Here we include an additional 8 AC cases to provide a more comprehensive interpretation. SOX2 marks the basal proliferative zone of epithelium in dentigerous cysts. It is negative in mature epithelium and in ameloblastic neoplasms without high-grade transformation. The diffuse strong nuclear staining pattern has 100% specificity to indicate the presence of high-grade features (7/7), and 70% sensitivity (7/10) in comparison with other benign ameloblastic neoplasms (P = .039). Although previously shown as a promising marker for ameloblastic neoplasms, calretinin is weakly positive in a few cells in 50% (5/10) of AC and 43% (3/7) of benign ameloblastic neoplasms, with little value in highlighting the high-grade change (P = .36). A diffuse nuclear stain pattern of SOX2 is suggestive of a high-grade process in ameloblastic neoplasms. Focal aggregates of cells harboring dense nuclear stain should raise caution for a malignancy arising in ameloblastoma with otherwise classical benign features. This is conceptually consistent with recent studies that show that increased SOX2 expression is associated with a poorer prognosis in oral cancer, sinonasal cancer, and urothelial cancer.

MAMMARY ANALOG SECRETORY CARCINOMA: 20 CASES IN MINOR SALIVARY GLANDS J Wollenberg, S Wetzel, J Kacher, P Freedman, New York Hospital Queens, Flushing, Queens, New York, NY, USA; JKJ Pathology, Spring, TX, USA

Mammary analog secretory carcinoma (MASC) is a newly recognized salivary gland tumor with a unique histologic appearance, immunohistochemical profile, and chromosomal translocation. In the seminal paper, these tumors are described as circumscribed, lobulated masses with microcystic, tubular, and solid structures. To date, 89 cases of MASC have been reported. Of those cases, only 21 were located intraorally. We present an additional 20 cases of MASC involving the minor salivary glands. Microscopically, these tumors are locally infiltrative and composed of mildly pleomorphic cells with abundant eosinophilic
and granular cytoplasm. The majority of the minor salivary gland tumors are arranged in solid, microcystic, and tubular growth patterns. However, 8 of the 20 cases in this series consisted of one or more cysts lined by tumor cells with papillary projections extending into the cyst lumen. These tumors are described as having a papillary cystic morphology. Immunohistochrometry showed these tumors to be positive for proteins S-100, mammaglobin, and vimentin, with variable positivity for GCDFP-15. This is similar to the staining pattern of secretory carcinoma of the breast, which is consistently positive for S-100 and mammaglobin. Although fluorescence in situ hybridization reveals consistent t(12;15), this may not be practical for routine diagnosis in most laboratories. A recent publication suggests the use of histopathologic features along with strong immunohistochemical positivity for S-100 and mammaglobin as diagnostic criteria. These additional cases help to further refine the histologic spectrum of mammary analog secretory carcinoma.

**ISOLATION OF CEMENTUM PROTEIN IN A CEMENTOBLASTOMA**

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In recent years cementum protein (CEMP-1) has been isolated from human cementoblastoma. CEMP-1 is considered as a specific marker of cementoblasts, periodontal progenitor cells, and mineralization processes such as octacalcium phosphate crystal nucleation of hydroxyapatite precursor. Also, CEMP-1 has been observed to induce phenotype differentiation of periodontal ligament cells toward the cementoblastic/osteoblastic and chondroblastic. The aim of this study was to identify the presence of CEMP-1 in a lower right first molar cementoblastoma in a 26-year-old man. An orthopanoramic radiograph showed a well-defined radiopaque lesion in the lower right first molar region. The excisional biopsy showed cementum-like tissue, prominent basophilic reversal lines, and fibrous connective tissue as a capsule. An immunofluorescence study was performed with the use of polyclonal antibody against CEMP-1 at a 1:100 concentration diluted with bovine serum albumin. Subsequently, a secondary goat anti-rabbit antibody labeled with fluorescein isothiocyanate (FITC, Santa Cruz Biotechnology, Inc) in a 1:75 concentration was incubated according to the manufacturer’s instructions and with phosphate-buffered saline (PBS) 1× diluted for 2 hours at room temperature. At the end, 2 more washes with PBS 1× were performed. As a negative control, the same procedure was done but with the absence of the primary antibody. The expression of CEMP-1 was positive in subpopulations of cementoblasts and mineralized tissue. CEMP-1 could help to identify and standardize tumoral lesions like cementoblastoma.

**PAPILLARY CYSTADENOCARCINOMA ARISING IN PAPILLARY CYSTADENOMA OF THE SUBLINGUAL GLAND**

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Papillary cystadenoma (PCA) and its malignant counterpart papillary cystadenocarcinoma (PCAC) are both rare neoplasms in sublingual salivary glands. There is considerable overlap in microscopic characteristics, with PCA being encapsulated whereas PCAC was infiltrative. Atypia, necrosis, or increased mitotic activity may not be present. We report a sublingual tumor in a 78-year-old woman, present for several years and stable in size, presenting gradual growth for 4 months. A multilobulated, nonulcerated, bluish submucosal mass of 4-cm diameter occupied the floor of the mouth. Magnetic resonance imaging identified a well-circumscribed, multicystic mass, located above the mylohyoid and replacing the sublingual gland. Biopsy exhibited multiluminal cystic architecture. The lining epithelium was thin, composed of uniform cuboidal cells creating delicate luminal papillary projections. The cytology was bland, lacking atypia, prominent mitotic activity, or necrosis, and the diagnosis was PCA. During surgery the lesion seemed to present a distinct capsule and separated easily by extracapsular dissection. However, in the most posterior region, firm attachment to the submandibular gland area was observed. The microscopic analysis of the resection specimen showed features identical to those of the biopsy, with a clear capsule in the majority of the periphery, except for the posterior aspect, where a clear infiltrative pattern was observed. The final diagnosis was reversed to PCAC. The history of a long duration with a recent increase in size, the encapsulation of most of the tumor periphery, and the localized front of invasion all suggest transformation from PCA to PCAC. This has never been described before in this particular tumor type, although it is well recognized in long-standing pleomorphic adenoma.

**DENDRITIC CELL NEUROFIBROMA WITH PSEUDOROSETTES: A REPORT OF 5 INTRAORAL CASES**

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Dendritic cell neurofibroma with pseudorosettes (DCNP) is a rare benign peripheral nerve sheath tumor first described in 2001 by Michal et al. Only 25 cases (26 lesions) have been published in the English-language literature, with no intraoral lesions reported to date. DCNP has been reported in adults with no gender predilection; the mean age was 46.5 years (range, 24-73). DCNPs commonly present as well-circumscribed, dome-shaped, firm nodules in the dermis of the trunk (40%), extremities (32%), or the head and neck region (28%). DCNP is characterized by a biphasic population of neural cells with S-100 and CD57 positivity. Type I cells are small and lymphocyte-like with dark nuclei; type II cells are large and neural ganglion-like with pale, vesicular nuclei showing intranuclear pseudoinclusions. Type I cells are generally arranged concentrically around centrally located type II cells, forming pseudorosettes. The tumor cells are negative for neuroendocrine, muscular, and epithelial markers. There is no reported tendency for lesional recurrence or malignant transformation after complete excision. We present a series of 5 cases of DCNP, the first report of intraoral lesions. The lesions presented in 2 men and 3 women, with a mean age of 53.4 years (range, 36-73). Three presented on the buccal mucosa and 2 on the tongue. Each tumor demonstrated all the characteristic features of DCNP. Both cell populations exhibited strong S-100 positivity. Strong CD57 positivity was consistently demonstrated in type II cells and was variable among type I cells. Pathologists should consider DCNP in their differential diagnoses when confronted with unusual neural lesions that do not exhibit classic features of neurofibromas, schwannomas, or other benign peripheral nerve sheath tumors.
TWO CASES OF EWING SARCOMA/PRIMITIVE NEUROECTODERMAL TUMOR WITH INITIAL PRESENTATION IN THE MANDIBLE

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Ewing sarcoma and primitive neuroectodermal tumor (ES/PNET) represent opposite ends of a spectrum of malignant round-cell neoplasms that show variable degrees of neuroectodermal differentiation. Initial presentation of ES/PNET in the oral cavity is exceedingly rare, and involvement of the gnathic or craniofacial region occurs in approximately 1% to 2% of cases. We contribute 2 cases of ES/PNET presenting as enlarging mandibular radio-lucencies from a 5-year-old boy and a 34-year-old man. Although ES/PNET may involve any site, it predominantly affects bone, representing the third most common primary malignancy of bone following osteosarcoma and chondrosarcoma. It is most common in children and young adults, with 80% of cases occurring before 20 years of age. This malignancy has a slight male predilection and affects white people with a much greater frequency than African Americans. The histopathology is variable but typically includes a population of monomorphous, round, blue, undifferentiated cells (ES) or cells with neuroectodermal features (PNET) arranged in sheets or nests. Immunohistochemical analysis shows the majority of cases are positive for proteins CD99 (95%) and FLI-1 (90%), and a minority of cases highlight neuroendocrine markers. A translocation involving EWS on chromosome 22 and FLI-1 on chromosome 11 is seen in 90% of cases. The treatment for ES/PNET is surgery and chemotherapy with or without local radiation therapy. The prognosis of this family of malignant neoplasms is reported to be 65% survival at 5 years. Here, we describe 2 unusual cases with initial presentation in the gnathic bones prompting a diagnosis of ES/PNET.

POSTER ABSTRACTS

ORAL LESIONS AS THE PRESENTING MANIFESTATION OF CROHN DISEASE

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Crohn disease (CD) is an immune-mediated disorder of the gastrointestinal tract; CD and ulcerative colitis comprise the 2 major types of inflammatory bowel disease. The underlying etiology has been attributed to defects in mucosal immunity and the intestinal epithelial barrier in a genetically susceptible host, resulting in an inappropriate inflammatory response to intestinal microbes. The lesions of CD can affect any region of the alimentary tract, as well as extraintestinal sites such as the skin, joints, and eyes. The most common presenting symptoms are periumbilical pain and diarrhea associated with fevers, malaise, and anemia. Oral involvement has been termed oral CD and may manifest as lip swelling, cobblestoned mucosa, mucogingivitis, and linear ulcerations and fissures. Oral lesions may precede gastrointestinal involvement and can serve as early markers of CD. We describe a 6-year-old boy who presented for evaluation of multifocal gingival erythema and swellings. His medical history was unremarkable for gastrointestinal disorders or distress. Histopathologic examination showed multiple well-formed granulomas that were negative for special stains and foreign body material. A diagnosis of granulomatous gingivitis was rendered. The patient and his parents were advised to seek consultation with a pediatric gastroenterologist, and following colonoscopy the boy was diagnosed with early-stage CD. Timely recognition of the oral manifestations of CD is critical, because only a minority of patients will continue to exhibit CD-specific oral lesions at follow-up. This places the dental practitioner in a unique position to detect occult CD in an otherwise asymptomatic patient, which may ultimately lead to early diagnosis and treatment.

DRY MOUTH AND NUTRITION: QUALITY OF LIFE IN PATIENTS WITH SJÖGREN SYNDROME

H Lanfranchi, M Ansola, Department of Oral Medicine, School of Dentistry, University of Buenos Aires, Buenos Aires, Argentina

Sjögren syndrome (SS) is an autoimmune disease that affects the exocrine glands, causing dry mouth. Local moisturizers, immunosuppressants, and antimuscarinic medications are commonly prescribed. However, there are few studies addressing the influence of eating habits caused by dry mouth on the quality of life of patients with this disease. In the present study, we evaluated the nutritional status and eating habits in patients with SS and made adjustments to their diet by adding moisture and soft textures that avoid damaging the oral mucosa. We studied 25 patients with SS through nutritional interviews to inquire about their eating habits. (Patients were diagnosed with SS according to the criteria established by the Sjögren International Clinical Collaborative Alliance [SICCA].) Of these 25, 22 (90%) reported having to limit their food selection because certain foods caused them discomfort. Nutritional status was assessed based on body mass index, laboratory assays, and asking about changes in weight since disease onset. Based on the results, each patient’s diet was modified, focusing on changes in the consistency and moisture of foods. Each patient was given a healthy eating plan and a guide to the selection and preparation of foods for patients with dry mouth, designed by our Nutrition Service, that ensure the inclusion of all necessary nutrients. With this help, 85% of the patients self-reported improvements in their diet and ability to swallow foods and therefore in quality of life. These results show the importance of the creation of a personalized eating plan that is consistent with the patient’s degree of oral dryness and that ensures the nutritional value is maintained. This study was supported by National Institutes of Health contract NOI-DE-32636.

ORAL LESION OF PSEUDOXANTHOMA ELASTICUM

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We report a case of pseudoxanthoma elasticum involving the oral cavity in a 65-year-old woman. Pseudoxanthoma elasticum is a heritable multisystem disorder with cutaneous, ophthalmologic, and cardiovascular manifestations. The disorder is caused by mutations in the ABCC6 gene located on chromosome 16p13.1. A recent study found an association of oral mucosal lesions and cardiovascular disease. Our patient presented with 2 areas of leukoplakia on the soft palate. Both lesions were excised and submitted for histopathologic diagnosis to rule out epithelial dysplasia. One lesion was diagnosed as hyperkeratosis and mild acanthosis, whereas the other was consistent with pseudoxanthoma elasticum.

QUANTITATIVE SCORE OF LANGERHANS CELLS IN LICHEN PLANUS AND AMALGAM LICHENOID REACTION

SMC Grossmann, GR Souto, RA Mesquita, Universidade Federal De Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

We report a case of pseudoxanthoma elasticum involving the oral cavity in a 65-year-old woman. Pseudoxanthoma elasticum is a heritable multisystem disorder with cutaneous, ophthalmologic, and cardiovascular manifestations. The disorder is caused by mutations in the ABCC6 gene located on chromosome 16p13.1. A recent study found an association of oral mucosal lesions and cardiovascular disease. Our patient presented with 2 areas of leukoplakia on the soft palate. Both lesions were excised and submitted for histopathologic diagnosis to rule out epithelial dysplasia. One lesion was diagnosed as hyperkeratosis and mild acanthosis, whereas the other was consistent with pseudoxanthoma elasticum.
Amalgam lichenoid reaction (ALR) presents clinical and histologic features of oral lichen planus (OLP); however, each is a different example of lesion evolution and of evidence of hypersensitivity to amalgam. Langerhans cells (LCs) are cells of the innate immune system and are responsible for initiating adaptive immune response. The aim of this study was to measure the number of LCs in specimens of ALR, OLP, and normal oral mucosa (NOM). LCs were identified by immunohistochemistry for the CD1a protein in 21 samples of OLP, ALR, and NOM in oral epithelium and lamina propria. The inflammatory cells were evaluated in subepithelial region (RS) and in below region of subepithelial region (BRS) for samples of OLP and ALR. Density of LCs (cells/mm³) was determined using the AxioVision 2.4 software (Microsoft and Carl Zeiss Vision GmbH, Göttingen, Germany). Samples were obtained from the files of the Service of Maxillofacial Pathology, School of Dentistry, Universidade Federal de Minas Gerais (1965 to 2010). Significantly higher density was observed for CD1a+ LCs in RS (95.73 cells/mm³) and OLP (87.04 cells/mm³) with the OLP when compared with RS (44.71 cells/mm³), OLP-ALR (42.12 cells/mm³), and OLP-NOM (29.82 cells/mm³). The densities of LCs were correlated with the density of inflammatory cells, and there were strong and positive correlations between oral epithelium cells, RS, BRS, and OLP, when compared with inflammatory infiltrate in OLP (P < .05). A strong positive correlation was also observed in the BRS in ALR (P < .05). Higher densities of inflammatory cells were observed in the OLP and ALR when compared with NOM (P < .05). Our results suggest that different immunomodulatory mechanisms can be associated with the pathogenesis of OLP and ALR. This study was supported by the Brazilian National Council for Scientific and Technological Development (CNPq); the Foundation for Research Support of the State of Minas Gerais (Fapemig); and the Brazilian Coordination for the Improvement of Higher Education Personnel (CAPES).

RECURRENT ALLERGIC CONTACT STOMATITIS PRESENTING AS ORAL BULLAE C Fisher, P Edwards, University of Michigan, Ann Arbor, MI, USA

Objective: To report a case of allergic contact stomatitis, initially presenting clinically as oral bullae.

Background: Allergic contact stomatitis is a delayed-type hypersensitivity reaction (type IV). Its oral manifestations include inflammation followed by erosions, and it can present as bullae, occasionally resembling lesions of pemphigoid or pemphigus. These manifestations usually occur within 24 to 72 hours of contact with the antigen.

Methods: A 25-year-old Asian man presented with a chief complaint of recurring, multiple, nonpainful blisters occurring on the hard palate. The patient reported no lesions anywhere else on the body. A large (>1 cm), fluid-filled bulla was on the left hard palate, and multiple smaller bullae and erosions were seen on the right hard palate. These lesions resolved within 1 week without therapy.

Results: Subsequently, a 4-mm punch biopsy was performed. Frozen sections stained with hematoxylin-eosin demonstrated stratified squamous epithelium with underlying connective tissue containing a mild mixed inflammatory infiltrate. Direct immunofluorescence demonstrated strong fibrin positivity along the Basement Membrane Zone (BMZ) and weak positivity for C3 and immunoglobulin M (IgM) along the BMZ; it was negative for IgG and IgA. A complete blood cell count with differential and serology for antinuclear antibodies and double-stranded DNA were unremarkable.

Conclusions: The patient later revealed that the bullae only occurred after he consumed large quantities of alcoholic beverages. Based on the clinical history and presentation, a diagnosis of allergic contact stomatitis was made.

OROFACIAL LESIONS IN INFANTS MANAGED BY NASOALVEOLAR MOLDING APPLIANCES B Taylor, B Acharya, C Flaitz, University of Texas School of Dentistry at Houston, Houston, TX, USA

Objective: This retrospective clinical study documented common orofacial lesions in infants with cleft lip and palate (CL/P), who were managed using a nasoalveolar molding appliance (NAMA).

Methods: Following approval by the institutional review board, the authors studied a convenience sample of infants referred for presurgical treatment of CL/P with NAMA between 2006 and 2011 at a pediatric dental residency clinic. Dental records and photographs were evaluated, including demographics, medical history, cleft type, orofacial lesions, and treatment complications. Data were analyzed using descriptive statistics, t test, and χ² test with significance at P < .05.

Results: Records of 141 infants were evaluated, including 101 (71.6%) with unilateral (U) CL/P and 40 (28.3%) with bilateral (B) CL/P; 56% were boys and 44% were girls. Ethnicity included 23% white, 10% black, 58% Hispanic, 5% Asian, and 4% other. Mean age at initial examination was 48 days, and mean length of treatment was 80 days. Documented oral lesions were sucking callus (70%), palatal keratosis (29%), candidiasis (22.5%), neonatal palatal and gingival cyst (28%), traumatic ulcer (21%), sucking ulcer (6%), neonatal tooth (6%), eruption cyst (1.4%), neonatal alveolar lymphangioma (0.7%), and pyogenic granuloma (0.7%). In total, 77% of infants had >1 oral lesion. Facial lesions included milia/acne (64%), contact tape irritation (63%), nevus simplex (33%), seborrheic dermatitis (27%), impetigo (0.7%), abrasion (0.7%), and eczema (0.7%), with 77% of infants having facial lesions. Except for palatal keratosis (P = .03), there was no significant difference in orofacial lesions based on cleft type.

Conclusions: Orofacial lesions, including NAMA complications, are common in infants with CL/P undergoing NAMA therapy, but the majority are not associated with the type of cleft.

INTRAVASCULAR FASCIITIS INVOLVING THE UPPER LIP J O’Donnell, Jr., T Rosenberg, L Kahn, R Kelsch, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA

Background: Intravascular fasciitis is a rare variant of nodular fasciitis involving arteries or veins, typically in an extremity. However, approximately 10% of published cases involve the head and neck.

Observation: We report a case of a 46-year-old woman with an upper lip submucosal mass. The lesion was noted following minor trauma to the lip and was present for several months. At the time of evaluation, neither ulceration nor paresthesias was appreciated. An excisional biopsy was performed. Histopathologic evaluation revealed a proliferative spindle cell lesion with readily identifiable mitoses. The lesion was multinodular, with individual nodules occluding the lumina of medium-sized vessels. Immunohistochemical analysis demonstrated positive staining of lesional spindle cells for smooth muscle actin and positive...
staining of the accompanying prominent endothelial cell pop-
ulation by CD34. Intense positivity of smooth muscle markers
highlighted the surrounding vessel wall. Based on these fea-
tures, a definitive diagnosis of intravascular fasciitis was rendered.

Conclusions: Intravascular fasciitis has been infrequently
reported in the oral cavity. The lesional cellularity and brisk
mitotic activity, as seen in the family of pseudosarcomatous
myofibroblastic proliferations, could lead to a misdiagnosis of
sarcoma. Recognition of the typical histologic features of intra-
vascular fasciitis is important for the practicing oral pathologist.

DETECTION OF HUMAN HERPESVIRUS TYPE 8 IN
ORAL BIOPSIES OF KAPOSI SARCOMA BY IMMUNO-
HISTOCHEMISTRY AND POLYMERASE CHAIN REAC-
TION J Seo, P Tobouti, N Sugaya, S Sousa, University of
São Paulo, São Paulo, Brazil

Kaposi sarcoma (KS) is a multifocal vascular tumor that
occurs most commonly in patients who have immunosuppression
caused by HIV. KS-associated herpesvirus, also called human
herpesvirus 8 (HHV8), has been identified as the causative agent.
KS growth involves the upregulation of many key HHV8 gene
products, such as the latency-associated nuclear antigen (LANA-1
or LNA-1). Frequently, the oral cavity may be the initial site of
KS, and the discovery there of KS is often also the first clinical
indication of HIV infection in previously undiagnosed individ-
uals. Due to the great variability of morphologic aspects, it may
be necessary to assess the positivity to HHV8 in order to differ-
entiate KS from other vascular lesions. In our biopsy service, the
main problem can be the small size of most biopsies, which
sometimes creates difficulties in the detection of HHV8. Thus, in
the present study we aimed to compare immunohistochemistry
(IHC) and polymerase chain reaction (PCR) techniques to detect
HHV8 in oral biopsies of supposed KS. Sixteen cases diagnosed
in the last 5 years were retrieved from the files of the Oral
Pathology Department at the University of São Paulo. The
biopsies measured an average of 2.5 mm in diameter. For IHC,
the material was submitted to the streptavidin-biotin method, and
the antibody used was anti-HHV8-LNA (Novocastra, Leica
Biosystems). For PCR, DNA from the lesions was isolated using
the phenol-chloroform extraction protocol. Primers were obtained
from the National Center for Biotechnology Information Gen-
Bank databases. Real-time PCR was performed on DNA using
Jumpstart SYBR green mastermix (Sigma-Aldrich) on a thermo-
cycler (Applied Biosystems 7500 Real-Time PCR System). Fifteen
samples, which were HHV8-IHC positive, were positive
for HHV8-DNA detection.

Conclusions: IHC was found to be as sensitive and reliable
as real-time PCR even in small biopsies, being a cheaper and
faster method.

ECHINOCOCCUS OF THE TONGUE: A CASE REPORT
AND REVIEW OF THE LITERATURE S Wetzel, K Murtagh,
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Flushing, Queens, New York, NY, USA

Echinococcosis is a zoonosis caused by a canine tapeworm.
Although dogs are the definitive host where eggs from the organism
are ingested. Infection results in formation of a hydatid cyst.
Echinococcal infections are endemic to the Middle East, Europe,
and parts of Africa. However, there is an increase in cases arising
outside of these regions. The most common sites for hydatid cyst
formation are the liver and lungs. Only 1% to 2% of cases are
seen in the head and neck region. The current case is that of an
African man that presented with an enlarged tongue. Imaging
studies revealed a cystic lesion involving the deep musculature.
Histologic examination of the excision specimen showed an
echinococcal organism residing within the hydatid cyst. This case
represents an unusual anatomic location for this occurrence, as
well as an uncommon geographic location. For these reasons,
a parasitic infection did not enter into the differential diagnosis.
Failure to recognize this condition can lead to complications
during the excision process. These risks include anaphylaxis and
secondary infection from removal of the cyst. This case represents
the significance of proper recognition and treatment for this
condition.

NK/T CELL LYMPHOMA, NASAL TYPE J Doscher, M
Johnson, Yale—New Haven Hospital, New Haven, CT, USA

NK/T cell lymphoma of the nasal type is an aggressive
lymphoma commonly presenting as a destructive process of the
facial midline, often demonstrating clinical and histologic features
of necrosis and angioinvasion. It was initially categorized as an
angiocentric lymphoma in the Revised European-American
Lymphoma (REAL) classification. It has been recategorized as
extranodal NK/T cell lymphoma in the World Health Organiza-
tion classification of lymphoid neoplasms. Historically these
tumors were considered part of “midline lethal granuloma.” This
entity frequently arises in extranodal regions, especially the nasal
or paranasal sinuses. Other extranodal sites include the palate,
trachea, skin, and gastrointestinal tract. In most instances,
Epstein-Barr virus (EBV) genomes are detectable in the tumor
cells, and immunohistochemistry detects CD56 positivity. The
pathologic diagnosis of nasal-type NK/T cell lymphoma is based
on expression of cytoplasmic CD3 and CD56 and positivity for
EBV in situ hybridization. If EBV in situ hybridization is nega-
tive, the immunophenotype studies should demonstrate cyto-
plasmic CD3 expression and positive cytotoxic molecules such as
TIA-1. Nasal-type NK/T cell lymphoma is known to be one of the
most aggressive lymphomas, so it is imperative to offer an
appropriately aggressive treatment at an early stage of disease.
We present the clinical and therapeutic treatment course and
outcome of a 60-year-old white man diagnosed with NK/T cell
lymphoma. This includes a clinicopathologic review, approaches
to diagnosis, and surgical and prosthetic treatment strategies for
patient optimization throughout oncologic therapies.

CD30-POSITIVE IMMUNOBLASTIC PROLIFERATIONS
OF THE ORAL CAVITY: IS ATYPICAL HISTIOCYTIC
GRANULOMA RELATED? R Eversole, A Dovigi, Oral
Pathology Diagnostic Services, San Diego, CA, USA

Background: CD30 (Ki-1) is a surface differentiation
protein that is demonstrable in 1% of bone marrow cells and is
a member of the tumor necrosis superfamily 8. This glycoprotein
is expressed on Reed-Sternberg immunoblasts in Hodgkin
lymphoma and other lymphoblastic lesions of the skin and
internal organ sites. CD30-positive lymphoproliferative diseases
are rare in the oral cavity and may be seen in conjunction with
systemic and cutaneous counterparts.

Material and methods: Archived formalin-fixed sections
from 67 cases of oral CD30-positive lymphoproliferative lesions
with large cell lymphoblasts were analyzed for lymphoid markers.
Cytologically, the large cell nuclei varied from Sternberg to
cerebriform to pronate. Stromal infiltrates varied within these
lesions, including small lymphocytes, commaforn lymphocytes,
plasma cells, neutrophils, and eosinophils. Follow-up data were obtained.

Results: CD30-positive cells were encountered in 2 lesions with benign outcomes: traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) and atypical lymphoblastic (histiocytic) granuloma (ALG). Cases with malignant behavior included solitary mucosal and systemic large anaplastic CD30-positive T cell lymphoma.

Conclusions: Mucosal CD30-positive lymphoproliferative lesions can be classified in a way similar to that used for cutaneous lesions, with TUGSE and ALG behavior being similar to that of cutaneous lymphomatoid papulosis.

UNUSUAL ATYPICAL EPITHELIAL PROLIFERATION OF UNKNOWN BIOLOGIC BEHAVIOR IN A 5-YEAR-OLD BOY R Gopalakrishnan, G Velasco-Peña, MD Rohrer, IG Coulas, University of Minnesota, Minneapolis, MN, USA; Private Practice, St Cloud, MN, USA

A 5-year-old boy presented clinically with a subgingival suprabony fistula with the mandibular anterior central incisors. There was no obvious clinical intraosseous involvement. The oral mucosal epithelium did not reveal any clinical changes suggestive of a process originating from the surface. Histopathologic evaluation revealed soft tissue fragments that were surfaced or lined by hyperkeratinizing and acanthotic stratified squamous epithelium exhibiting cytologic variations that include irregular rete pegs, loss of polarity, individual cell keratinization, increased nuclear/cytoplasmic ratio, and prominent nucleoli. Areas of prominent endophytic epithelial proliferation comprising cords and islands that showed cytologic atypia were also present. The differential diagnosis was between a well-differentiated squamous cell carcinoma and an atypical epithelial proliferation of uncertain biologic behavior. Review of the literature revealed a similar lesion reported by Elzay and O’Keefe (Oral Surg Oral Med Oral Pathol 1979;47:436) who also discussed the unusual presentation of their case and the inability to completely exclude well-differentiated squamous cell carcinoma. External consultation with 3 senior oral pathologists resulted in the diagnoses of atypical epithelial proliferation (2 pathologists) and squamous cell carcinoma (1 pathologist), further underscoring the difficulty in obtaining a definitive diagnosis. No additional treatment was performed, and the patient remained lesion-free in a 10-month follow-up.

SUSTAINED OVEREXPRESSION OF INSULIN-LIKE GROWTH FACTOR II mRNA–BINDING PROTEIN 3 IN ORAL EPITHELIAL DYSPLASIA: A POTENTIAL PROGNOSTIC BIOMARKER OF IMPENDING INVASION G Mainville, C Allen, L Ayers, J Hagen, M Tong, D Kellough, S Mallory, Ohio State University, Columbus, OH, USA

Identification of an invasion-predictive biomarker that identifies oral epithelial dysplasia (OED) lesions with a high transformation potential could have clinical implications by helping to target chemoprevention. Insulin-like growth factor II mRNA–binding protein 3 (IMP3), which is a recently identified oncoprotein essential for mRNA binding, trafficking, and stabilization, is overexpressed in many cancers, including oral squamous cell carcinoma (OSCC). Clinical studies have shown that IMP3 expression in biopsies correlates with the presence of carcinoma in excised cervical epithelium. The objective of this case-control retrospective pilot study was to determine whether or not patterns of IMP3 expression are associated with OED progression to OSCC. Immunohistochemically stained archival tissues (2 groups, age- and site-matched, ≥4 biopsies followed for ≥4 years, transformed [n = 5] and nontransformed [n = 4] to OSCC) were analyzed by light microscopy and with TissueStudio 3.5 image analysis software (Definiens, Munich, Germany). Statistics confirmed comparable initial clinical and histologic features between the transformed and nontransformed groups. Microscopic evaluation revealed greater distribution of moderate to intense IMP3 staining in OED lesions that transformed. Image-analyzed samples revealed that intense IMP3 staining increased over time in those OED lesions that transformed to OSCC (Pearson r; P = .002; all patients combined). In contrast, no such association was noted in nontransformed OED lesions (P = .105). Pearson r values (intense IMP3 expression over time) for each individual patient were: transformed group, 0.82, 0.37, 0.99*, 0.92, and 0.72* (*P = .015); nontransformed group, 0.11, 0.53, −0.70, and 0.57. These data, which show increasing levels of intense IMP3 expression in progressive OED lesions, suggest that high sustained levels of intracellular IMP3 contribute to development of an invasive phenotype.

REPRODUCIBILITY OF THE BRANDWEIN VS BRYNE PREDICTIVE HISTOLOGIC RISK SCORE MODELS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA: A PILOT STUDY N Ramer, A Curran, E Sabo, E Childers, L Solomon, V Murrah, J Wu, Mount Sinai Medical Center, New York, NY, USA; University of North Carolina, Chapel Hill, NC, USA; Howard University, Washington, DC, USA; Rambam Medical Center, Haifa, Israel; Tufts University, Boston, MA, USA

Background: Histologic risk models (HRMs) are validated outcome predictors for head and neck squamous cell carcinoma (HNSCC). We attempted to determine the reproducibility of the Brandwein and Bryne HRMs in HNSCC resection specimens.

Methods: Two de-identified coded slides from 10 HNSCCs were selected for review by 6 oral pathologists. A detailed scoring guide for both HRMs was provided. Brandwein criteria include perineural invasion, lymphocytic infiltrate, and the worst pattern of invasion at the interface, vs the Bryne criteria of histologic variability, host response, degree of keratinization, POI, and pleomorphism. Total scores for each HRM were calculated for each OMP. The Cohen kappa weighted coefficient was calculated for evaluating the agreement between the Bryne and Brandwein scoring methods. Consistency (reliability) between pathologists and intraclass coefficients of correlation were computed separately for each scoring method.

Results: Six OMPs completed the study. The weighted Kappa coefficient of agreement was calculated using the online QuickCalcs kappa calculator. Agreement between the 2 scoring methods was R = 0.216. The intraclass coefficients of correlation for assessing the consistency of tumor grading among the pathologists were computed using the Medcalc software. Both methods showed a very good inter-rater consistency, with the Bryne score showing a slightly lower intraclass coefficient of correlation (R = 0.92; 95% CI, 0.80-0.98) than the Brandwein score (R = 0.93; 95% CI, 0.83-0.98).

Conclusions: In this pilot study, we compared the reproducibility of the Brandwein and Bryne histologic risk scores for HNSCC among oral pathologists. A larger study with more cases and additional scorer training is needed to determine if agreement can be sustained or improved.
OLFACTORY CARCINOMA: A REPORT OF A RARE ENTITY  T. ALAli, K Abushara, J Bastaki, Otorhinolaryngology—Head and Neck Surgery Department and Department of Pathology, Zain and Sabah Hospitals and Kuwait Cancer Control Center, Hawally, Kuwait

Olfactory neuroblastoma is a rare neoplasm that arises from the olfactory membrane in the sinonasal tract. Recently, some cases have been shown to possess a divergent differentiation from a ganglioneuroblastoma to carcinoma, adenocarcinoma, or even sarcoma. Herein, we report a rare case of olfactory neuroblastoma with a divergent carcinomatous differentiation in a 49-year-old Kuwaiti man. The patient presented with a 1-year history of nasal obstruction, pressure on the left eye, epiphora, and anosmia. He had a history of head trauma and craniotomy for cerebrospinal fluid leak in the 1990s. Endoscopic examination revealed a large bulky mass originating from the skull base and occupying the left nasal cavity, protruding posteriorly into the nasopharynx. Computed tomography and magnetic resonance imaging studies showed a mass with a well-defined pedicle originating from the skull base with a bony defect. With high suspicion for a meningioma or any other neural component, a neoplastic process could not be completely excluded, the mass was excised endoscopically. The histologic section of the mass revealed a clear, round blue cell tumor with a lobular growth pattern in an edematous and somewhat vascular stroma. Pleomorphism, mitotic figures, and pseudodrosettes were also present in the tumor. Immunohistochemical stains were performed, and the tumor was positive for synaptophysin and chromogranin. S-100 highlighted the sustentacular cells. Of note, AE1/AE3 cytokeratin was diffusely positive. With a dual phenotype of olfactory neuroblastoma and a carcinoma, this tumor is best described as olfactory carcinoma.

BIOLOGIC CONSEQUENCES OF INCISIONAL BIOPSY ON THE PRIMARY TUMOR  M. Donoghue, M Selvamani, KP Mohan, PS Basandi, A Ramakrishna, M Joshi, KSN Siva, Bharani College of Dental Sciences, Davangere, Karnataka, India

Background: Incisional biopsy (IB) is the most effective means of diagnosing and grading tumors. The proliferative phase lasting 6 to 7 days postbiopsy has been established. In tumors, the subsequent healing response can be lacking. Thus, IB can be expected to have some biologic consequences for the primary tumor.

Objectives: To evaluate the changes in tumor biology post-IB by comparing the IB and surgical resection (SR) tumor specimens.

Methods: SR specimens of squamous cell carcinoma (SCC) and their IB specimens (N = 60) with a gap of 6 days or more were retrieved from the archives. Sections stained with hematoxylin-eosin were evaluated for mean vascular density (MVD), number of mitoses per 10 high-power fields (HPFs), atypical mitosis, and the type, intensity, and distribution of inflammatory cells. Sections were also prepared for estimation of the mitotic index using Ki-67 staining.

Results: Partial results from analysis of sections stained with hematoxylin-eosin showed statistically insignificant rise of MVD in SR in comparison with IB samples (0.106 ± 0.163 and 0.089 ± 0.145, respectively). The number of mitoses per 10 HPFs was reduced in the SR in comparison with IB samples (4.20 ± 3.6 and 4.43 ± 3.7, respectively). The number of specimens showing normal mitosis was slightly reduced, and the number of specimens with abnormal mitosis slightly increased, in the SR samples. Among the inflammatory cells, eosinophils showed a significant (P = .05; P < .05) rise in the SR samples. The distribution, nature, and severity of the inflammatory response were not significantly altered. Mitotic index is pending completion.

Conclusions: This preliminary study suggests that there are some biologic consequences of IB for the primary tumor. Larger studies are needed to quantify these consequences and determine their effects in terms of tumor behavior.

ORAL BIOPSY AS A BEHAVIOR MODIFICATION AGENT IN TOBACCO/ALCOHOL CESSEATION  T. Peters, C Phillips, V Murrah, University of North Carolina, Chapel Hill, NC, USA

Tobacco is the predominant etiologic factor for oral cancer (OC). Prognosis for OC has essentially remained unchanged for many years. Moreover, field cancerization increases risk for second primaries. Strategies to decrease etiologic factors are critical. Biopsy results may act as a behavioral change agent. Our objective was to determine whether biopsy diagnoses are associated with risk factor cessation. Studies were sent to subjects identified in the University of North Carolina Oral Pathology database with a diagnosis of hyperkeratosis, dysplasia, or carcinoma. Data obtained included demographics, risk factor use, and any change in use since biopsy. A total of 1632 questionnaires yielded a 38% response rate. Results from the Fisher exact test showed a higher quit rate for both cigarettes and alcohol in those with carcinoma versus those with hyperkeratosis (P < .01). The same was true for cigarette use in those with dysplasia versus hyperkeratosis (P < .03). Subjects with dysplasia or carcinoma were 2.78 times more likely to quit or reduce cigarette use versus those with hyperkeratosis (95% CI, 1.38-5.59). Significantly higher cigarette quit rates were seen in men with carcinoma versus those with hyperkeratosis (P < .01); this was not true for women. The results convey important implications for patient education. Biopsied patients with premalignant or malignant diagnoses are likely to discontinue etiologic habits; however, there is a need to educate patients with benign diagnoses, because our study indicates that they are more likely to continue their habits. These patients may have a false sense of reassurance, which is not supported by current carcinogenesis statistics. The lack of premalignant or malignant diagnosis today is no guarantee for the future. Surgeons can play a role in preventing OC by emphasizing strategies for tobacco/alcohol cessation for all patients whom they biopsy.

ORAL SQUAMOUS PAPILLOMA, MULTIPLY RECURRENT, IN A PATIENT WITH PSORIASIS RECEIVING THE TUMOR NECROSIS FACTOR ALPHA ANTAGONIST ADALIMUMAB  A. Ritchie, T Jhamb, N Odingo, J Fantasia, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA; State University of New York, Stony Brook, NY, USA

Background: Tumor necrosis factor alpha (TNFα) is a cytokine secreted by macrophages that regulates various biologic processes including cell proliferation, differentiation, apoptosis, lipid metabolism, and coagulation. Increased TNFα has been implicated in autoimmune diseases, insulin resistance, and cancer. TNFα antagonists are known to cause reactivation of many bacterial and viral infections. Adalimumab is a monoclonal antibody that neutralizes TNFα activity and induces complement-mediated cell lysis of mononuclear cells expressing TNFα.
Objective: To describe TNFα antagonists and their role in reactivation of low-risk human papillomavirus in the oral cavity.

Observation: A 50-year-old man presented initially with a squamous papilloma of the midline mandibular gingiva that recurred 3 times after the initial excision. The medical history revealed treatment for psoriasis with adalimumab, subsequent to the first excision. Potential causes for persistence or recurrence of the squamous papilloma include incomplete excision, viral re-infection, viral reactivation in an immunocompetent or immuno-suppressed patient, and TNFα antagonist–associated human papillomavirus infection.

Conclusions: TNFα antagonist medications can reactivate latent viral infections or increase susceptibility. Reporting of similar cases is encouraged to further establish a link between TNFα antagonist drug use and various oral pathologies including infection, inflammation, and neoplasia.

NEUROEPITHELIAL STRUCTURES ASSOCIATED WITH THE SUBEPITHELIAL NERVE PLEXUS OF TASTE BUDS: A FORTUITOUS FINDING RESEMBLING THE JUXTAORAL ORGAN OF CHIEVITZ CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Numerous embryologic epithelial remnants have been described in the oral region, and when they are intimately associated with peripheral nerves, they may pose a diagnostic pitfall for pathologists. The literature contains well-documented cases in which the juxtaoral organ of Chievitz (JOC) was identified in a surgical specimen removed because of an oral malignancy and correct recognition of this anatomic structure potentially avoided unnecessary treatment. To the best of our knowledge, this is the first report of such a case in which a neuroepithelial structure similar to, if not morphologically identical to, that of the JOC was found in the posterior lateral border of the tongue in close association with the subepithelial nerve plexus of taste buds.

Methods: We performed review and interpretation of the English-language literature pertaining to the juxtaoral organ of Chievitz (JOC) and embryologic epithelial remnants of the oral region.

Results: Embryologic epithelial remnants are normally found in the soft tissues and jaws of the oral and paraoral regions. These remnants have been found in close association with peripheral nerves.

Conclusions: Proper recognition of these anatomic structures is crucial to prevent misdiagnosis of squamous cell carcinoma or perineural invasion.

PLEXIFORM ENCAPSULATED NEUROMA: ANALYSIS OF CASES WITH SPECIAL EMPHASIS ON THE PLEXIFORM VARIANT

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Background: Palisaded encapsulated neuroma/solitary circumscribed neuroma (PEN) is a benign neural lesion that occurs on skin or mucosa. The plexiform variant and some examples of multilobular PEN may be confused with other plexiform neural lesions, such as plexiform neurofibroma (PNF), plexiform neurilemmoma (PNL), and mucosal neuromas of multiple endocrine neoplasia type 2B (MEN-2B).

Objectives: To perform a clinicopathologic analysis of cases of PEN, and to determine if morphology and immunohistochemistry (IHC) can be used to accurately differentiate plexiform PEN from other plexiform neural lesions.

Materials and methods: Cases of PEN, PNF, PNL, and MEN-2B from University of Kentucky College of Dentistry files were reviewed. IHC was performed on selected cases with proteins S-100, NFP, EMA, GFAP, and CD34. Examples of neurofibroma, neurilemmoma, and traumatic neuroma were used as IHC controls.

Results: Of 50 cases of PEN, 31 occurred in males and 19 were found in females. A wide age range was noted (12-86 years; mean, 29.5 years), yet half of the lesions occurred in the fifth and sixth decades. The lip was the most common site (18), followed by hard palate/gingiva (17), head/neck skin (6), soft palate (4), tongue (3), and buccal mucosa/vestibule (2). PEN cases consistently exhibited fascicular arrangements of Schwann cells and axons. Artificial clefiting was identified in 41 cases. Myxoid change was never prominent and was focally identified in only 4 cases; 36 cases appeared lobular, 12 cases were multilobular, and 2 were plexiform. All tested cases of PEN were diffusely positive for S-100 protein, whereas more modest reactivity was found in PNL cases. MEN-2Bs displayed a thick, EMA-positive perineurium, showed variable numbers of axons and collagen fibers, and were positive for GFAP.

Conclusions: IHC analysis with S-100, NFP, EMA, and GFAP, along with careful attention to morphologic features, should allow accurate diagnosis of plexiform PEN. Correlation with clinical appearance and family history also is recommended, especially in problematic cases.

ECTOMESENCHYMAL CHONDROMYXOID TUMOR: A SERIES OF 5 CASES

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Ectomesenchymal chondromyxoid tumors (ECTs) are rare, benign, intraoral mesenchymal soft tissue tumors, with only 44 cases reported in the English-language literature. We herein report our experience with 5 ECTs and review the immunohistochemical and clinicopathologic features of this rare entity. The mean age of patients was 42 years (range, 7-53 years), with no gender predilection. All tumors were located on the dorsal tongue. The pathologic differential diagnosis of the ECT was myoepithelioma, nerve sheath myxoma, and cellular neurothekeoma. Histologically, all tumors exhibited a lobular proliferation of ovoid to round cells with cellular pleomorphism, a net-like growth pattern, and slit-like cystic spaces, with at least a focally myxoid background (5/5, 100%). Fine calcifications and multinucleated giant cells were noted in 2 cases (2/5, 40%). Immunohistochemically, the tumors were positive for S-100 (5/5, 100%), mostly positive for glial fibrillary acidic protein (GFAP) (4/5, 80%), and focally to diffusely positive for SMA (4/5, 80%), with rare P63 expression (2/5, 40%). The extracellular myxoid material was positive for glial fibrillary acidic protein (GFAP) (4/5, 80%), and focally to diffusely positive for SMA (4/5, 80%), with rare P63 expression (2/5, 40%). The extracellular myxoid material was positive for glial fibrillary acidic protein (GFAP) (4/5, 80%), and focally to diffusely positive for SMA (4/5, 80%), with rare P63 expression (2/5, 40%).
for mucicarmine (2/2, 100%). Calponin and AE1/AE3 were consistently negative (4/4, 100%, and 3/3, 100%, respectively). Some cases exhibited rare positivity for CD57 (2/5, 66%) and CD68 (1/2, 50%) and focal positivity for CAM 5.2 (1/5, 20%).

**EVALUATION OF ANGIogenesis IN CENTRAL AND PERIPHERAL GIANT CELL GRANULOMAS OF THE JAWS AND ORAL CAVITY**

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**Background and objective:** Peripheral giant cell granuloma (PGCG) and central giant cell granuloma (CGCG) are 2 pathologic lesions with similar histopathologic features. PGCG is a reactive lesion, whereas controversies exist regarding the true nature of CGCG (reactive vs neoplasm). The aim of this study was to evaluate the angiogenic potential of these lesions using CD105 immunostaining and microvessel density (MVD) count.

**Materials and methods:** In this descriptive study, 30 cases from each lesion were selected and 4-μm sections were stained with CD105 antibody. MVD was evaluated by counting vessels in areas of highest vascularity (hot spots) using light microscopy at 400 magnification. Data were analyzed by 2-way analysis of variance, Pearson correlation coefficient, paired *t* test, and *t* test with *P* < .05 as the limit of significance.

**Results:** All cases in both groups showed immunoreactivity with anti-CD105 antibody. MVD was not significantly different between CGCG and PGCG groups (*P* = .390). Similar findings were observed comparing peripheral supportive stroma and central mass in the PGCG group (*P* = .402). In the CGCG group, no significant relation existed between MVD and clinical signs (or symptoms) (*P* = .317) or cortical perforation (*P* = .434).

**Conclusions:** Based on our findings, there was no difference between PGCG and CGCG regarding microvessel density and angiogenesis, which could suggest a similar pathogenesis for these lesions.

**CASE REPORT: METASTATIC LUNG CARCINOMA PRESENTING AS VASCULAR SWELLING OF THE MAXILLARY GINGIVA**

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We report the case of an 80-year-old woman who presented with a 2-week history of a bulky and vascular-appearing swelling of the maxillary gingiva, which involved the facial and palatal gingiva of teeth 2 and 3. The swelling was in close approximation to implants that were supporting a fixed partial denture. There was no history of pain. Our differential diagnosis included reactive lesions (pyogenic granuloma, peripheral ossifying fibroma, and inflammatory fibrous hyperplasia), hemangioma, and malignant neoplasm (due to extension of the lesion to the facial and palatal gingiva). The lesion was biopsied, and hematoxylin-eosin stained sections revealed a soft tissue specimen composed of a nodular mass of mucosa. The surface was lined by stratified squamous epithelium and appeared cytologically bland. Within the underlying lamina propria, a proliferating malignant epithelial neoplasm was seen, which involved the margins. The proliferating epithelium exhibited a somewhat nest-like growth pattern. The nuclei were very large, with a vesicular pattern and large, prominent, pink nucleoli. Mitotic activity was extraordinarily brisk, and atypical mitotic spindles were easily identified. The proliferating neoplasm was highly infiltrative, and evidence of ductal differentiation was observed in the deepest portions. Our impression was metastatic neoplasm suggestive of lung carcinoma. Immunohistochemical staining with thyroid transcription factor-1 was performed to confirm the diagnosis, which was subsequently reconfirmed clinically.

**THE INCREASED P16 AND CYCLIN D1 EXPRESSION IN RECURRENCE OF SALIVARY GLAND PLEOMORPHIC ADENOMA**

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Pleomorphic adenoma (PA) is the most common salivary gland tumor. Although it is classified as a benign tumor, its incidence of recurrence after initial surgical treatment is significant and varies largely, owing to differences in surgical technique. Furthermore, recurrent pleomorphic adenoma (RPA) has been associated with an increased risk of malignant transformation. However, few studies were found on RPA, its biologic behavior, and its risk factors. Recently, cell cycle markers have been receiving increasing attention, with regard to their importance in the biologic behavior of tumors. The aim of the present study was to investigate the participation of the cell cycle markers p16, cyclin D1, and retinoblastoma (Rb) in PA, RPA, and RPA with malignant transformation (RPAT). Altogether, 24 cases of PA, 21 cases of RPA, and 2 cases of RPAT were studied. The immunohistochemical reactions to p16, cyclin D1, and Rb were evaluated. Expression scores were assigned according to the percentage of positive nuclear tumor cells, from 0 to 3 (0, less than 10%; 1, 10% to 25%; 2, 25% to 50%; 3, staining of more than 50% of cells). The Mann-Whitney test was used to compare different tumor groups. The majority of the PA cases showed negative or weak p16 and cyclin D1 expression, whereas in the majority of the RPA cases, as well as in the 2 RPAT cases, strong expression of these proteins was demonstrated. Regarding Rb, all groups (PA, RPA, and RPAT) were shown to be negative or to have weak expression. In conclusion, this study may suggest that the p16, cyclin D1, and Rb pathways were not affected in PA, whereas in RPA and RPAT, the p16 and cyclin D1 pathways were altered, indicating that those proteins are probably important in the development of recurrence of pleomorphic adenoma and malignant transformation.

**POLYMORPHOUS LOW-GRADE ADENOCARCINOMA OF THE UPPER LIP WITH METACHRONOUS MYOEPITHELIOMA OF THE BUCCAL MUCOSA CASE REPORT AND LITERATURE REVIEW OF SYNCHRONOUS AND METACHRONOUS MINOR SALIVARY GLAND TUMORS**

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Examples of synchronous and metachronous minor salivary gland tumors (MSGTs) are uncommon. We report a patient who initially presented with polymorphous low-grade adenocarcinoma (PLGA) and subsequently with myoepithelioma (MYO). A 91-year-old white woman presented in 2009 with a 1-cm, firm, nontender, well-circumscribed nodule of the left side of the upper lip extending to the anterior buccal mucosa. Excisional biopsy revealed PLGA. Although the margins were positive, further treatment was not recommended due to the patient’s age. In 2011, the patient returned with a 1.5-cm asymptomatic mass of
the left buccal vestibule. Excision of the lesion revealed a circumscribed proliferation of ductal and plasmacytoid cells arranged in spherical or whorl-like islands and immersed in a mucinous stroma, consistent with MYO. The PLGA recurred 3 years after initial diagnosis. Excision was again associated with positive margins, and again no further treatment was recommended. A few months later, at a scheduled follow-up appointment, she presented with a painless nodule of the left upper lip, consistent with recurrent PLGA. One month later, she died of unrelated causes. We also present a review of the literature regarding MSGTs.

FAMILIAL CHERUBISM WITH ODONTOGENIC TUMOROUS PROLIFERATIONS 1 Koutras, Y Ha, E Reichenberger, D Primley, R Gopalakrishnan, University of Minnesota, Minneapolis, MN, USA; University of Connecticut; Private Practice in Oral Surgery, St Cloud, MN, USA

Cherubism is a rare autosomal dominant condition affecting the jaws that maps to chromosome 4p16, with mutations identified in the gene encoding c-Abl-binding protein SH3BP2. The lesions of cherubism have been well characterized radiographically and histopathologically. Generally, lesions are multilocular and expansile and feature vascular fibrous tissue in association with multinucleated giant cells. Herein, we describe a family with cherubism, 2 members of which, in addition to giant cell lesions, presented with odontogenic tumors: one, the son and proband, at age 25, with central odontogenic fibroma-like features; the other, his mother, at age 57, with primary intraosseous odontogenic carcinoma and areas of benign fibro-osseous lesion. In both patients, the lesions occurred in the mandible and presented with focal enlargement that is unusual for cherubism. The son underwent incisional biopsy and did not have additional treatment. His mother underwent extensive mandibulectomy due to widespread tumor. The son has 2 affected children; a third child is at age 5 and has not yet shown any features of the disease. Mutation analysis of affected members of the family resulted in the identification of heterozygous mutation in SH3BP2 with c.1244G\rightarrowC (p.Arg415Pro). To the best of our knowledge, association of cherubism with odontogenic lesions has not been reported in the literature. This association further supports the theory linking cherubism with disturbed odontogenesis.

COMBINED ODONTOGENIC TUMORS: A REPORT OF 3 CASES A Neuman, I Bhattacharyya, D Cohen, C Dunlap, University of Florida, Gainesville, FL

Combined odontogenic tumors have rarely been reported in the literature. We present 3 new cases exhibiting distinctly separate histologic features, including ameloblastoma with ameloblastic fibro-odontoma (AFO), ameloblastoma with odontogenic keratocyst (OKC), and calcifying odontogenic cyst (COC) with ameloblastic fibroma (AF). We review the histopathology of these unusual lesions and discuss relevant literature. A search of archival material of the University of Florida’s Biopsy Service revealed only 3 such lesions among the 72 171 specimens submitted from 2004 to 2012. The location, radiographic and clinical findings, and histology of these lesions are presented. Lin et al., Seim et al., and others believe that hybrid odontogenic lesions are not a result of collision between 2 distinct entities but rather are due to the pluripotentiality of the odontogenic epithelium, with both lesions likely developing from a common epithelial source. In addition, although we have in our archives a combined adenomatoid odontogenic tumor (AOT) with calcifying epithelial odontogenic tumor (CEOT), we did not include this lesion, because many authors believe that CEOT-like areas often occur in AOTs and therefore the combined AOT-CEOT should be considered a variant of AOT. A review of the English-language literature revealed examples of “hybrid” odontogenic lesions, including 6 cases of COC with AF and a few other rare combinations. Brannon noted 2 OKCs with ameloblastomatous change. To the best of our knowledge, no case of concurrent AFO with ameloblastoma has been reported. Treatment of these lesions is typically based on appropriate treatment for the more aggressive component.

MULTIFOCAL CALCIFYING EPITHELIAL ODONTOGENIC TUMOR: A CASE REPORT AND REVIEW OF THE LITERATURE A Chi, J Pike, Medical University of South Carolina, Charleston, SC, USA; Private Practice, Hagerstown, MD, USA

The development of multifocal calcifying epithelial odontogenic tumors (CEOTs) is most unusual, with only 5 cases reported thus far in the English-language literature. Here we present an additional case. A 24-year-old woman complained of wisdom tooth pain, and radiographic evaluation showed 2 lesions. The first was associated with the crown of an impacted mandibular third molar and appeared as a radiolucency with radiopaque flecks. The second appeared as a small radiolucency along the mesiolateral aspect of a mandibular second premolar. Among the present case and the 5 previously reported cases, there are 15 total lesions (4 extraosseous, 11 intraosseous). All patients except one had synchronous lesions. The average age was 42 years (range, 24-55 years). The lesions were located in the posterior mandible (n = 6), posterior maxilla (n = 5), anterior maxilla (n = 2), and anterior mandible (n = 2). Clinical findings included swelling (n = 2), pain (n = 1), and tooth displacement (n = 3). Most of the intraosseous lesions presented as well-defined, mixed radiolucent/radiopaque lesions, although 4 were entirely radiolucent. Most cases exhibited typical histopathologic features of CEOT, except for one that exhibited foci of squamous odontogenic tumor. The preferred treatment was conservative enucleation, with recurrent lesions typically managed by curettage or removal of a rim of normal tissue. Follow-up information was provided for 5 patients. One had an intraosseous lesion recur twice, at 7 and 17 years after initial presentation; another patient had 2 peripheral lesions that recurred after 1 year. In all cases, these multifocal tumors appear to represent isolated findings, with no known syndromic association or familial tendency.

NON-CALCIFYING LANGERHANS CELL–ASSOCIATED EPITHELIAL ODONTOGENIC TUMOR S Ganatra, H Castro, B Toporowski, F Hohn, E Peters, University of Alberta, Edmonton, Alberta, Canada; University of Saskatchewan, Saskatoon, Saskatchewan, Canada

The calcifying epithelial odontogenic tumor (CEOT) is a benign, locally aggressive lesion, representing less than 1% of all odontogenic tumors. Most cases are intraosseous, with a predilection for the posterior mandible, and a lesion is often associated with an impacted tooth. Characteristic microscopic features include sheets and cords of variably pleomorphic, polygonal epithelial cells with accumulations of eosinophilic amyloid-like material and spherical laminated calcifications. Alternate tumor presentations have been described, which include
EWSR1-ATF1 gene fusions have been recurrently described in sarcomas, and several different gene partners have been involvement of EWSR1—most frequently involved gene in translocations. C Sreekantaiah, A Rosenberg, J Fantasia, Hofstra North

Lack of calcification.

CELLULAR ATYPICAL CALCIFYING EPITHELIAL ODONTOGENIC GHOST CELL TUMOR: A REPORT OF AN UNUSUAL CASE J Wollenberg, M Markoff, P Freedman, New York Hospital Queens, Flushing, Queens, New York, NY, USA; Private Practice, Randolph, NY, USA

Calcifying epithelial odontogenic ghost cell tumor (dentino- genic ghost cell tumor) is a locally invasive, solid neoplasm once believed to be the solid variant of calcifying odontogenic cyst. In some cases, the tumor may cause bony expansion or displacement of teeth, but it is usually asymptomatic and discovered during routine radiographic examination. Radiographically, it presents as a well-defined or poorly defined radiolucency with variable amounts of radiopaque calcification. Histologically, the calcifying epithelial odontogenic ghost cell tumor is composed of infiltrating sheets and islands of odontogenic epithelium in a mature connective tissue stroma. A characteristic feature is the transformation of epithelial cells to ghost cells, some of which undergo calcification. Calcifying epithelial odontogenic ghost cell tumor has a high recurrence rate following enucleation. Therefore, resection with an adequate disease-free margin is recommended. The current case is that of a 91-year-old woman who was referred to an oral surgeon in 2010 by her general dentist for evaluation of a radiolucency in the area of tooth 22. At that time, a biopsy was performed and diagnosed as cellular atypical calcifying epithelial odontogenic ghost cell tumor. Due to multiple comorbidities, the patient decided against undergoing any further treatment. Over the next 2 years, imaging studies showed progressive destruction of the mandible. For the first time, the natural course of a calcifying epithelial odontogenic ghost cell tumor has been documented through serial radiographic studies without any surgical treatment.

EWSR1 REARRANGEMENT IN CLEAR CELL ODONTOGENIC CARCINOMA: REPORT OF A CASE A Yancoskie, C Sreekantaiah, A Rosenberg, J Fantasia, Hofstra North Shore-LIJ School of Medicine, Hempstead, NY, USA

Background: The Ewing sarcoma breakpoint region 1 (EWSR1) is the most frequently involved gene in translocations in sarcomas, and several different gene partners have been documented. The translocations resulting in EWSR1-CREB1 and EWSR1-ATF1 gene fusions have been recurrently described in several neoplasms that are histopathologically and behaviorally different and include angiomatoid fibrous histiocytoma, clear cell sarcoma, hyalinizing clear cell carcinoma of salivary gland, and, more recently, soft tissue myxopithelioma and clear cell odontogenic carcinoma (CCOC).

Objective: To evaluate a case of CCOC for EWSR1 rearrangement.

Observation: A 59-year-old woman presented with paraplegia of the left lower limb and a radiolucency in the left body of the mandible. Upon biopsy, a diagnosis of CCOC was rendered, and treatment consisted of segmental mandibulectomy. Formalin-fixed paraffin-embedded tumor tissue was evaluated using fluorescence in situ hybridization (FISH) for the presence of EWSR1 rearrangement with the EWSR1 dual color break-apart probe.

Results: FISH analysis of this CCOC demonstrated EWSR1 rearrangement in > 20% of cells.

GLANDULAR ODONTOGENIC CYST: REPORT OF A SERIES OF 24 CASES JC Whitt, BF Barker, TM Gibson, CL Dunlap, University of Missouri Kansas City, Kansas City, MO, USA

The glandular odontogenic cyst (GOC) is an uncommon odontogenic cyst that exhibits a high rate of recurrence when conservatively excised. A recent report of a large series of GOCs indicated a recurrence rate of 50%. Since its original description as sialo-odontogenic cyst in 1987, over 150 cases have been reported in the English-language literature. We report a series of 24 cases of GOC arising in patients ranging in age from 29 to 79 years, with an average age at surgery of 50 years. Of these lesions, 75% arose in the mandible, with 42% (10/24) located in the anterior mandible. Overall, 63% (15/24) of the lesions were located in the anterior portion of the jaws. There was a strong male (2:1) gender predilection. Twenty-one percent (5/24) of the lesions were located in the dentigerous position. The remainder presented as radiolucencies associated with the roots of teeth, ranging in size from 2.0 to 6.0 cm. The recurrence rate of lesions in this series, based on information available in surgical pathology reports, was 21%, with 2 lesions recurring 3 or more times over a 10-year follow-up period. A variety of microscopic features have been identified in GOC, including cobblestoned surface eosinophilic cells, microcysts, apocrine snouting, clear cells, variable thickness epithelial lining, papillary tufting, mucous goblet cells, plaque-like thickenings, epithelial spheres, cilia, and multiple compartmentation. These cases exhibited many, but rarely all of, these histologic features. The differential diagnosis of GOC includes lateral periodontal cyst, botryoid odontogenic cyst, odontogenic cyst with mucous metaplasia, surgical ciliated cyst, and low-grade intraosseous mucoepidermoid carcinoma.

DENTINOAMELOBLASTOMA, A RARE ODONTOGENIC TUMOR: REPORT OF 2 CASES WITH A REVIEW OF THE LITERATURE M Alqahtani, DM Cohen, MN Islam, I Bhattacharyya, University of Florida, Gainesville, FL, USA

Dentinoameloblastoma (DA) is a rare odontogenic tumor characterized by classic ameloblastoma-like areas with unusual induction of dentinoid by the neoplastic odontogenic epithelium without any evidence of enamel matrix or tooth formation. We present 2 cases of DA presenting as expansile radiolucent lesions of the maxilla. Microscopic examination of the biopsy samples revealed proliferative ameloblastoma-like areas along
with numerous foci of eosinophilic partially calcified dentinoid material. The term DA has been in use since it was first defined by the World Health Organization in 1970 and has been frequently confused with ameloblastic odontoma/odontomeloblastoma. In DA, no enamel matrix is seen, but the presence of dentinoid is consistently noted, with occasional cases also exhibiting cementum-like material. Moreover, in our 2 cases the tumor presented with numerous gland-like structures with dentinoid material and in focal areas bore strong resemblance to an adenomatoid odontogenic tumor (AOT). We identified only 6 additional cases of unequivocal DA in the literature, which have also been termed by some authors as adenoid ameloblastoma with dentinoid. Most cases previously reported as DA did not meet the histologic criteria laid down by the World Health Organization. The dentinoid material seen in DA is believed to be an induction effect of the proliferative ameloblastic epithelium on the mesenchymal tissue. Notably, these lesions exhibit aggressive biologic behavior comparable with that of conventional ameloblastoma, thereby warranting similar treatment. Importantly, the combination of a calcified product so unusual in ameloblastomas, glandular AOT-like (adenoid) areas, and maxillary location may lead to a misdiagnosis of AOT if limited clinical information and only a small biopsy sample are available.

**DENTINOMA: A REPORT OF 2 CASES**

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Dentinoma is a rare odontogenic tumor. Four histologic variants have been reported: immature dentinoma (containing tubular dentine, dysplastic dentine, or dentinoid and odontogenic epithelium), mature dentinoma (immature dentinoma without epithelium), ameloblastic fibrodentinoma (ameloblastic fibroma-like tumors with tubular dentine or dentinoid), and adenomatoid dentinoma. We present 2 cases of dentinoma. The first patient was an 8-year-old boy with an ill-defined radiolucent lesion overlying unerupted teeth 13 and 14. The lesion was curetted. Histopathologically, the biopsy contained abundant hyalinized, eosinophilic material in a vaguely lobular configuration, with entrapped islands of benign odontogenic epithelium as well as stellate and spindled cells. The odontogenic epithelium was present in small and large islands and in strands. Two years later, there was a persistent radiolucency at the site, and this area was re-curetted. This showed typical deposits of dentinoid with entrapped odontogenic epithelium and stellate and spindled cells. Tubular dentine, enamel matrix, and ghost cells were not identified in either specimen. The second patient was a 12-year-old girl with a well-defined radiolucency in the mandible associated with the crown of an unerupted left second molar. The histopathology was identical to that of the re-curetted lesion from case 1. The nature of dentinoid is still poorly understood; it is likely a product from an abnormal epithelial-mesenchymal interaction of tooth development. Ameloblastic fibrodentinoma and dentinogenic ghost cell tumor are found in the category of “odontogenic epithelium with odontogenic ectomesenchyme” under the World Health Organization classification. The category under which dentinoma belongs is still controversial.

**MULTIPLE ORTHOKERATINIZED ODONTOGENIC KERATOCYSTS IN A 23-YEAR-OLD MAN**

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A 23-year-old Hispanic man presented with 4 radiolucent lesions around the impacted third molars in all 4 quadrants. A biopsy was performed for 3 of the lesions around teeth 1, 17, and 32, and the diagnoses were orthokeratinized odontogenic kerato-cysts (orthoOKC) for all three. The cystic lesion around tooth 16 was marsupialized. To the best of our knowledge, a case of multiple orthoOKCs has never been reported in the literature. As loss of heterozygosity of the PTCH gene has recently been reported in some sporadic orthoOKC cases, a patient with multiple orthoOKCs raises the possibility of having nevoid basal cell carcinoma syndrome. Frontal bossing, multiple skin cysts, and pigmented lesions were found clinically on this patient. Other family members also showed some of these clinical features. The investigation of the clinical and radiographic features of nevoid basal cell carcinoma syndrome is still ongoing. A genetic test for PTCH gene sequencing was suggested, but it has not been performed to date.

**PERIPHERAL CALCIFYING CYSTIC ODONTOGENIC TUMOR (SOLID TYPE): 2 CASES AND REVIEW OF THE LITERATURE**

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The World Health Organization 2005 classification has classified calcifying cystic odontogenic tumor (CCOT) and dentinogenic ghost cell tumor (DGCT) as mixed odontogenic tumors with or without hard tissue formation. Both these lesions occur as an intraosseous or extraosseous process at any age. CCOT occurs in either gender, in the canine-incisor area, whereas DGCT is more common in males in the canine-molar area. Most of the intraosseous lesions of CCOT and DGCT are described as well-defined unicocular radiolucencies, whereas extraosseous lesions may show sauceration. The histopathology of these lesions shows ghost cells, odontogenic epithelial island similar to ameloblastoma, epithelial cells transforming into ghost cells with focal areas of calcification, and dentinoid. Review of the archives of the oral biopsy service at the University of Nebraska Medical Center College of Dentistry revealed 2 lesions in the gingiva presenting as gingival nodules. The first patient was a 32-year-old woman with a firm, asymptomatic nodule in the anterior maxilla, whereas the second was a 67-year-old man with an ulcerated firm nodule in the mandibular premolar area. Histologically, features of odontogenic epithelium similar to ameloblastoma, ghost cells, areas of calcification, and dentinoid were noted. These lesions were reported as CCOT (solid type). The literature reports similarities between CCOT and DGCT, resulting in confusion regarding nomenclature, treatment, and prognosis. It appears that these lesions could be combined as DGCT with or without cystic transformation. These cases are presented to clarify the nomenclature and to suggest a reclassification of these lesions.

**LOBODONTIA: REPORT OF A FAMILY WITH A RARE INHERITED DENTAL ANOMALY**

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Lobodontia is a very rare, autosomal dominant dental dysmorphology that may involve some or all of the teeth. Microdontia, hypodontia, shovel-shaped incisors, conical premolars and
canines with accentuated cusps, multituberculate molars with single conical roots, and dens invaginatus have been described in association with this condition. These changes were suggested to have some similarity to the canid (lupine) dentition, resulting in designation of the condition as “lobodontia.” Three teenage sisters were referred to Dental Faculty Practice for evaluation of their teeth. Their father was edentulous due to the removal of his “abnormal” teeth in his teenage years. Intraoral examination of the 2 younger girls showed multiple retained deciduous canine and molar teeth, hypodontia, and multituberculate molars with pronounced, elongated cusps, resulting in “rosette-like” occlusal surfaces. Radiographs revealed multiple impacted canine and premolar teeth with pointed cusps. Although most of the anterior dentition of the oldest sibling was well-formed and complete, her multituberculate molars had marked occlusal attrition. The molar teeth each had a single root and a single large pulp chamber. Based on the clinical and radiographic findings, as well as the family history, the diagnosis of lobodontia was made. The hereditary nature of this condition was discussed with the family, and continued management with the pediatric dentist was recommended. The findings in our patients were similar to those described in the handful of previous reports of lobodontia.