
EBV AND CD30 POSITIVE MUCOCUTANEOUS ULCERS OF THE ORAL CAVITY, AN UNUSUAL ENTITY: A SERIES OF 3 CASES L Montague, D Cohen, I Bhattacharyya, University of Florida, Gainesville, FL, USA

Introduction: Epstein-Barr virus-positive mucocutaneous ulcer (EBVMCU), related to immunosuppression, has recently been proposed as a distinct clinicopathologic entity by Dojcinov et al. (2010). These lesions are seen in older adults and present as ulcerations of the oropharyngeal mucosa and skin.

Aim: We present a series of 3 cases of oral ulcerations arising in patients with a history of immunosuppression or immunosenescence. We discuss the clinical, histologic and immunohistochemical (IHC) features and compare our findings to reported cases of EBVMCU.

Case 1: A 59-year-old Caucasian male with a history of lymphoma and chemotherapy presented with gingival ulcers in all quadrants of 6 month’s duration.

Case 2: A 41-year-old Caucasian female with a history of methotrexate use presented with a 2-month history of a retromolar region ulcer.

Case 3: An 83-year-old Asian male with no history of immunosuppression presented with an ulcer of the maxillary vestibule of 1-month duration.

Histology: Biopsies of lesions were characterized by a polymorphous inflammatory infiltrate and variable numbers of large atypical B cells and Reed-Sternberg-like cells, which were EBV and CD30 positive and CD3 negative. A similar histomorphology and IHC profile can be seen in the Hodgkin lymphoma-like variant of lymphoproliferative disorders defined by the WHO as “other iatrogenic immunodeficiency-associated lymphoproliferative disorders.” While these Hodgkin-like lesions frequently occur at extranodal sites, there are limited reports of isolated oral ulcerations.

Conclusion: We believe unusual ulcers in adult patients with history of immunosuppression should be evaluated with this entity in mind and when appropriate histologic findings are present, stains for CD30 and EBV should be performed.

ROLE OF HIGH-RISK HUMAN PAPILLOMAVIRUS INFECTION IN ORAL EPITHELIAL DYSPLASIA C McCord, RJ McComb, G Bradley, University of Toronto, Canada

Background: Human papillomavirus (HPV) infection is a causative factor in a subset (70%) of oropharyngeal squamous cell carcinomas. Recent evidence suggests that the prevalence of HPV in oral squamous carcinoma is low (<10%). The relationship between HPV infection and progression from epithelial dysplasia to carcinoma has not been extensively studied.

Objective: To detect high-risk (HR) HPV in oral epithelial dysplasia and correlate with clinicopathologic features.

Methods: 40 consecutive cases of high-grade oral epithelial dysplasia and 37 cases of low-grade dysplasia were examined for p16INK4a (mtm labs, MA) expression by immunohistochemical staining. p16 is a sensitive marker for HR HPV infection. Cases demonstrating strong, diffuse nuclear and cytoplasmic staining in the dysplastic epithelium were considered positive. All p16 positive cases were studied further using in-situ hybridization for HR HPV (Ventana Inform HPV III Family16 Probe). Cases were HPV positive if unequivocal intranuclear hybridization signal was present within lesional epithelium.

Results: HPV 16/18 was detected in 7 of 40 high-grade dysplasias (17.5%), and no low-grade dysplasias. HPV was significantly associated with high-grade dysplasia (p=0.01). Five of 7 (71.4%) HPV-positive dysplasias involved the floor of mouth/ventral tongue. The relationship of HPV infection and anatomical site was statistically significant (p=0.04). Age and sex showed no significant association with HPV infection.

Conclusion: HR HPV is rarely detected in oral epithelial dysplasia, but when present shows significant association with grade of dysplasia and site.

ASSESSMENT OF MATRIX METALLOPROTEINASE LEVELS IN HEALTHY HUMAN CONTROLS: PRELIMINARY DATA RELATED TO DOXYCYCLINE TREATMENT IN PATIENTS WITH VESICULOEROSIVE DISEASES T Jhamb, JM Kramer, JE Fantasia, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA

Oral vesiculoerective diseases (VED) include chronic processes such as cicatricial pemphigoid (CP) and lichen planus (LP). Currently, therapy consists of immunosuppressive agents that demonstrate variable efficacy and cause potentially serious side effects. Enzymes that affect the integrity of collagen and modulate inflammation, such as matrix metalloproteinases (MMPs), may be therapeutic targets in VED. Increased expression of MMP 2 and 9 has been observed in human inflammatory diseases. Upregulation of MMPs has been documented in oral ulcerative disease; although the role of MMPs in the oral VED is poorly understood. Treatment with subantimicrobial dose doxycycline (SDD) inhibits MMPs specifically and is already used for the treatment of other chronic inflammatory processes.

Hypothesis: MMP 2 and 9 are detectable in the sera, saliva, and urine of healthy subjects. Detection and quantification will allow for the assessment of normal levels to be used for comparative purposes.

Methods: ELISAs were used to establish baseline levels of these MMPs in serum, saliva, and urine of healthy controls.

Results: Preliminary data indicate that MMP 9 is detectable in control sera (mean = 707.0 ng/mL ± 220.6) and saliva (mean = 967.8 ng/mL ± 706.6) with lower amounts present in urine (mean = 2.0 ng/mL ± 3.1). MMP 2 was detectable in sera (mean = 164.2 ± 40), but was not in saliva or urine.

Conclusion: These results indicate that ELISAs can be used to evaluate potential differences between MMP 2 and 9 levels in healthy controls. Further studies are underway to investigate whether SDD reduces the expression and activity of MMP 2 and 9 in VED both locally and systemically.
DENTINOAMELOBLASTOMA: A CASE REPORT AND NOSOLOGIC DISCUSSION REGARDING THE ENTITY

D Klingman, H Evans, KJ Penna, JE Fantasia, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY; Nassau University Medical Center, East Meadow, NY, USA

Background: The dentinoameloblastoma (DA) is a rare odontogenic tumor. One case of DA has been reported and is characterized by induction of dentinoid by neoplastic odontogenic epithelium without enamel formation.

Observations: A 44-year-old man presented with an expansile mass of the right anterior mandible. The lesion caused facial asymmetry and effacement of the mandibular vestibule. Panoramic radiograph and computer tomography imaging revealed a large radiodensity of the right anterior mandible causing lingual and marked buccal expansion. There was a radiolucent rim surrounding the radiodense central component. Microscopic examination of the resected specimen revealed hypercellular zones of odontogenic epithelium with focal areas of peripheral palisading consistent with ameloblastic differentiation. This epithelium was intimately associated with an amorphous eosinophilic product consistent with a dentin-like material; dentinal tubules were not observed. The overall histopathology suggested dentinoid induction by tumor cells. Enamel matrix and epithelial ghost cells were not identified, thus excluding other recognized odontogenic tumors. A diagnosis of DA was rendered. Treatment consisted of mandibulectomy without continuity defect and reconstruction with autologous and allogeneic graft, bone morphogenetic protein and titanium mesh.

Conclusions: The clinical, imaging and histopathological characteristics of DA are described. The DA is classifiable as a mixed odontogenic tumor exhibiting epithelial and mesenchymal components; separate and distinct from odontoameloblastoma, dentinogenic ghost cell tumor, and other odontogenic tumors with a mineralized component.

THE IMPACT (OR LACK THEREOF) OF A THIRD HISTOLOGIC SECTION ON SAMPLING ERROR IN INTRAOPERATIVE EVALUATION OF HEAD AND NECK SPECIMENS

JM Bastaki, BM Purgina, LT Wiehagen, RR Seethala, University of Pittsburgh, PA, USA

Margin status in head and neck (H&N) cancer is a strong predictor of local control and outcome. Intraoperative consultation is useful in obtaining negative margins, but can occasionally show discrepancy with final margin status, typically due to sampling error. The literature suggests that increasing the number of sections per specimen may reduce this form of error. We thus compared the frozen-permanent discrepancy rate resulting from sampling error between 2005–2012 when the standard number of sections was 2 per specimen (2s) and 2012–2011 with a standard of 3 sections per specimen (3s). 96 discrepancies were found in 15,840 H&N frozen section parts (0.61%), of which 65 (67%; 0.42% of total volume) were due to sampling error. Of these sampling discrepancies, 41 (63%; 0.26% of total volume) occurred on margins. Overall error rate was slightly lower in the 3s period (42/8350, 0.50%) than in the 2s period (54/7490, 0.72%) but this difference was not significant (Pearson X²; p=0.08). But somewhat surprisingly, the proportion of sampling errors was actually higher in the 3s period (33/42, 79%) as compared to the 2s period (32/54, 59%) (p=0.04). A larger proportion of these sampling errors (24/33, 73%) were on margins in the 3s period than in the 2s period (17/32, 53%), though this difference was not significant (p=0.10). Our findings suggest that sampling error on frozen sections is not necessarily reduced by increasing the number of sections per part, and that perhaps multiple parameters beyond simply number of sections may contribute to sampling error.

CALCINUS PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE INVOLVING THE TEMPOROMANDIBULAR JOINT

A Ritchie, N Freuen, S Ruggiero, M Schwartz, J Fantasia, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA

Background: Calcium pyrophosphate dehydrate (CPPD) crystal deposition disease is a type of crystal-forming arthritis with deposition of CPPD in the joint tissues. Deposition of CPPD often occurs in the articular tissues of the appendicular skeleton and less commonly the temporomandibular joint (TMJ).

Objective: To describe the clinical, imaging, gross and microscopic features of CPPD of the TMJ.

Observations: A 52-year-old woman presented for evaluation of right-sided pain in the TMJ region. Computerized tomography revealed a lesion arising in the joint space. The differential diagnosis included synovial chondromatosis, pigmented villonodular synovitis, and chondrosarcoma. Surgical exploration confirmed the extent of disease, and tissues were submitted for frozen section. Florid rhomboid to square crystal deposition exhibiting weak birefringence with associated cartilage metaplasia was identified; a presumptive diagnosis of pseudogout was rendered. The TMJ including the glenoid fossa was resected with prosthetic joint reconstruction. Grossly, the surgical specimen revealed multiple small, white, chalky deposits involving all submitted tissues of the TMJ resection. The articular surface of the condyle was deformed. Microscopic features identified on frozen section were noted on the permanent sections, corresponding to the CPPD deposits noted grossly. Chondroid metaplasia was a striking feature with only focal areas of metaplastic bone identified. A focal giant cell and histiocytic reaction was noted in relation to some of the crystal deposits, but was not a prominent feature.

Conclusions: CPPD is a rare crystal deposition arthropathy and can simulate other benign and malignant pathological processes, clinically, radiographically, and microscopically.

AGGRESSIVE YET BENIGN? THE SPECTRUM OF AMELOBLASTOMATOUS TUMORS

L Bowers, D Cohen, I Bhattacharyya, University of Florida, Gainesville, FL, USA

Malignancy is defined by the presence of any one or all of the following: anaplasia, invasion, or metastasis. The ameloblastoma is considered a benign yet aggressive odontogenic neoplasm known to invade and destroy adjacent soft and hard tissue, yet histologically it appears without the hallmarks of malignancy. Histologically benign ameloblastoma is reclassified as malignant when metastasis is detected and high-grade lesions of ameloblastic carcinoma may or may not metastasize. A reclassification scheme is proposed that would involve categorization of ameloblastomas according to histologic features, radiographic appearance, site, and demographic features, with the goal of alerting clinicians as to the potential biologic behavior of the individual ameloblastomatous tumor. Examples of various ameloblastomas, “atypical” ameloblastomas, ameloblastic carcinoma, and metastatic/malignant ameloblastoma will be discussed along with a review of the literature.
ASSSESSMENT OF KI67 AND P53 IN BENIGN VERSUS MALIGNANT AMELOBLASTIC TUMORS

RA Abdelsayed, I Stojanov, I Zakjary, Georgia Health Sciences University, Augusta, GA, USA

Introduction: Ameloblastic tumors are relatively common and represent a continuum of histologic features and biologic behavior. These lesions are classified into histologically benign, conventional ameloblastoma (AB) and malignant (metastasizing) ameloblastoma (MAB), and ameloblastic carcinoma (ABC). Microscopically, the distinction between AB and MAB, in the absence of clinical and radiographic data, is not possible. However, microscopic diagnosis of ABC can be made when there is sufficient cellular atypia, mitosis and tumor necrosis. Nevertheless, the distinction between ABC and the histologically benign lesions may be challenging at times. The intent of this pilot study is to assess the utility of Ki67 and P53 to examine whether they can be reliable in the distinction of these lesions.

Methods and Materials: Three cases of AB, 1 MAB and 2 ABCs were identified. Representative sections from each of the lesions were immunostained using Ki67 and P53. Quantification of positive and negative cells was performed using Biocuant NOVA Prime imaging analysis.

Results: Ki67 stained 3.3-5.0%, while P53 stained 0.9-3.5% of cells in ABs. Ki67 stained 13.8% and P53 stained 2.1% of cells in MAB. However, in ABCs, Ki67 stained 55.5-65.8%, whereas P53 stained 40.7-56.2% of cells. In ABs, positive cells were confined to the peripheral ameloblast-like cells; while in MAB, there were positive central and peripheral cells. In ABCs, positive cells were distributed throughout tumor islands.

Conclusion: Ki67 and P53 intensity and pattern of reaction may be used reliably to distinguish ABC from histologically benign ameloblastic lesions. However, these markers were unreliable in distinguishing AB from MAB, therefore; clinical and radiographic data are needed to make this distinction.

DENDRITIC INTERSTITIAL CELLS AND MYOFIBROBLASTS IN THE STROMA OF SELECTED ODONTOGENIC LESIONS: A POSSIBLE CLUE TO CLINICAL BEHAVIOR

M Khalili, Tehran University of Medical Sciences, Iran; A Taheri Borujeni, Ahvaz University of Medical Sciences, Iran

Background and objective: Epithelial-stromal interactions are important in normal development and regeneration and have been shown to influence the growth potential of various tumors. CD34-positive dendritic interstitial cells (DICs) and myofibroblasts are stromal cells that appear to be involved in regulation of tumor growth and invasion. The aim of this study was to evaluate and compare the distribution of these cells in the stroma of ameloblastoma, odontogenic keratocyst (OKC) and dentigerous cyst (DC) of the jaws.

Materials and methods: 20 cases of ameloblastoma, 40 OKCs and 20 dentigerous cysts were selected according to the inclusion and exclusion criteria. 4 μm sections were cut from paraffin blocks and immunohistochemically stained with CD34 and alpha-SMA antibodies. The staining pattern was graded according to cell density and the percentage of stromal cells expressing the respective antigens was categorized as 0, +, + +, and + + + when up to 5%, between 5% and 25%, between 25% and 50%, or more than 50% of stromal cells stained positively. Data were analyzed with Chi-square and Fisher’s exact tests. P<0.05 was considered as the limit of significance.

Findings: The distribution of CD34-positive stromal cells in ameloblastoma was lower than DC and OKC. No significant difference was seen between DC and OKC. The distribution of myofibroblasts in ameloblastoma was significantly higher than DC and OKC. The difference between DC and OKC was not significant.

Conclusion: Based on our findings, CD34-positive dendritic cells and myofibroblasts could be associated with clinical behavior in odontogenic lesions. According to the distribution of these cells in OKC, we could suggest a cystic rather than neoplastic nature for this entity.
**Methods:** 15 cases of HNSCC were retrieved from the Oral and Maxillofacial Pathology Service. Pattern of invasion was assessed using Byrnes’ classification. E-cadherin and Twist1 immunoreactivity were evaluated on staining intensity and distribution. Vimentin immunoreactivity was noted as present or absent. HNSCC cell lines derived from patient tumors were evaluated for EMT markers by Western blotting and immunofluorescence. Invasive activity was assessed by culturing cells atop 3-D type I collagen matrices in cell culture inserts.

**Results:** Aberrant E-cadherin staining was observed at the invasive front in all samples. 46% of tumors demonstrated vimentin positivity and 27% of tumors demonstrated strong nuclear Twist1 expression. Twist1-positive tumors exhibited strong vimentin positivity and loss of membranous E-cadherin staining. There was no correlation between pattern of invasion and immunohistochemical staining of the 3 markers. All tumors aberrantly expressed at least one EMT marker, although high vimentin and Twist expression were not necessarily observed in cases with morphological changes suggestive of EMT. In cells from oral cavity SCC, high Twist1 expression coupled with high vimentin and loss of E-cadherin correlated with collagen-invasive activity in vitro.

**Conclusion:** Preliminary studies identify aberrant expression of EMT markers at the invasive front of HNSCC and suggest that high vimentin expression coupled with high Twist1 expression may play an essential role in tumor invasion.

**PATHOGENESIS OF ORAL LICHEN PLANUS: NEW FINDINGS ON THE CRITICAL ROLE OF TH17, TH0, AND TH2 CELLS IN THE DEVELOPMENT OF EROSiVE AND RETICULAR LESIONS**

G Ficarra, D Tesi, R Biagiotti, L Lombardelli, F Logiodice, O Kullolli, MG Giudici, M-P Piccinni, Reference Center for the Study of Oral Diseases, AUOC Careggi & University of Florence, Italy; Department of Internal Medicine and DENOTHE Center, University of Florence, Italy

The pathogenic role of Th17, an additional subset of CD4+ T helper cells beyond the traditional Th1, Th0, and Th2 cells, was investigated together with Th0, Th1 and Th2 cells in reticular (RL) and erosive lesions (EL) of Oral Lichen Planus (OLP), which is a chronic T-cell mediated inflammatory disease with a T-cell infiltrate preceding epithelial damage. Materials and methods: 14 patients with OLP were studied. Healthy adjacent mucosa (HAM) was also analyzed. Quantitation of mRNA for cytokine and transcription factors in RL, EL and HAM was measured using the Quantigene 2.0 multiplex assay (Panomics, Fremont, CA, USA). IL-17A, IL-17F, IL-23 R, RORC (Th17-type cytokines, receptor and transcription factor) and IFNγ, L-4, IL-5, IL-13, GATA3 (Th0-type cytokine) mRNAs were increased in biopsies of EL, whereas in biopsies of RL of OLP IL-13 and GATA3 (Th2-type molecules) mRNA were increased, when compared to HAM biopsies. IL-17A, TNF-α, GM-CSF, IL-6 (Th17-type cytokines), IFNγ and IL-5 (Th0-type cytokines) levels produced by CD4+ T-cell clones generated from EL were increased compared to IL-17A,TNF-α, GM-CSF,IL-6, IL-5 and IFNγ produced by CD4+ T-cells from HAM. A prevalence of Th17, confirmed by IL-17A, IL-17F and RORC mRNA expression of these T clones, and a prevalence of Th0 CD4+ T clones derived from EL, was shown, when they were compared to Th17 and Th0 CD4+ T cell clones derived from HAM T clones, whereas a prevalence of Th2 and a decrease of Th0 CD4+ T clones from RL, compared to Th2 and Th0 CD4+ T cell clones derived from HAM clones was observed. Moreover, an increase of CD161 expression by IL-17-producing T clones derived from EL compared to IL-17-producing T-cell clones generated from RL was observed. Thus, the critical role of Th17 and Th0 in EL and of Th2 cells in RL of OLP is presented.

**EXPRESSION OF OSTERIX AND PERIOSTIN IN CEMENTO-OSSEOUS DYSPLASIA AS EVIDENCE FOR ITS PDL ORIGIN**

Y Cheng, Y Ren, J Wright, J Feng, TAMHSC-Baylor College of Dentistry, Dallas, TX, USA

The etiology and pathogenesis of cement-osseous dysplasia (COD) are still unclear. Although most pathologists believe that it is of periodontal ligament (PDL) origin, no evidence beyond the histological features and its unique location has been provided to support this theory. Osterix (OSX) is an essential transcription factor that is expressed in osteoprogenitor cells and in cementoblasts. Periostin is a matricellular protein. In the jaw bones, periostin is only expressed in PDL and peristeum. In this study, we investigated the expression patterns of OSX and peristin with immunohistochemistry in various stages of COD. Based on clinical, radiographic and histological findings, 2 cases for each of the early, mid- and late-stage COD were selected. OSX nuclear staining was found in the stromal cells and in cells incorporated in newly formed calcified matrix in the early and mid-stages of COD, but not in the cells in sclerotic calcified masses in late-stage COD. Periostin was found in the stroma but not in the calcified matrix in all stages of COD. The coexpression of OSX and periostin in the COD lesional cells and stroma strongly suggest that COD is of PDL origin.

**DOC2B PROMOTER METHYLATION IN ORAL CANCER TISSUES**

R Radhakrishnan, K Satyamoorthy, S Prasad, S Bhat, Manipal College of Dental Sciences, Manipal University, Manipal, India

The development of oral squamous cell carcinoma (OSCC) is a result of multiple molecular events triggered by various risk factors resulting in alteration in DNA methylation machinery, suggesting a role for epigenetic modification. In this study, we screened for differential methylation in human oral cancer DNA and compared it with its matched normal control using methylation sensitive arbitrarily primed polymerase chain reaction (MSAP-PCR) assay. Several CpG rich fragments which were differentially methylated were identified, cloned and sequenced. The sequence identified in the promoter region of DOC2B gene spanning –376 to +36bp, methylated in oral cancer tissues as confirmed by methylation sensitive dimethyl sulphoxide polymerase chain reaction (MS-DSMO-PCR) was further validated by bsulfite genome sequencing (BGS). DOC2B promoter and other differentially methylated sequences characterized in our series may serve as diagnostic markers in human oral cancer.

**ANEUPLOIDY IN ORAL LICHEN PLANUS IS A CONSISTENT PHENOMENON IN HIGH-RISK PATIENTS**

A Hirshberg, N Yarom, T Shani, I Kaplan, L Trakhtenbrot, Tel-Aviv University Tel-Aviv, Israel; Rabin Medical Centre, Beilinson Campus, Petah-Tiqwa, Israel; Cancer Research Center, The Chaim Sheba Medical Center, Israel

Oral lichen planus (OLP) carries an increased risk for malignant transformation. In a previous study we analyzed oral brush samples obtained from 57 patients with OLP. The samples
were simultaneously analyzed for morphology and fluorescent in-situ hybridization (FISH) using chromosomes 2 and 8 centromeric probes. Aneuploid cells (ACs) were found in 16 patients (28.1%); in 10 (17.5%) over 5% of the cells were aneuploid. The aim of the present study was to show if the ploidy state of the patients persists over time. In 33 patients a second brush sample was obtained in a mean follow-up time of 43 months following the first analysis. 13 out of 16 patients with over 1% ACs detected in the first sample had over 1% ACs also in the second sample. ACs were detected in 2 patients in whom the first sample was negative. In 15 patients, ACs were not found in both samples. The ploidy state of OLP is relatively consistent over time and can therefore be used as a reliable tool that can discriminate a subgroup of high-risk patients that require close follow-up for early detection of oral cancer.

COMPARISON OF CD44 EXPRESSION IN INTRAORAL SALIVARY DUCTAL PAPILLOMAS AND ORAL PAPIL-LARY SQUAMOUS CELL CARCINOMA S Fitzpatrick, L Montague, D Cohen, I Bhattacharyya, University of Florida, Gainesville, FL, USA

CD44 is a transmembrane adhesion molecule that is reported to be useful in the differentiation of benign and malignant papillary lesions. Previous studies have shown positive staining of CD44 in sinonasal papillomas and breast intraductal papillomas with loss of expression in invasive carcinoma allowing distinction between these similar-appearing lesions. In addition, oral mucosal lesions have also demonstrated loss of CD44 in invasive carcinoma when compared to normal epithelium, hyperplasia, or oral squamous papillomas. To the best of our knowledge, no prior studies have compared variations in CD44 expression in salivary ductal papillomas when compared to oral papillary squamous cell carcinomas. In this study, 18 cases of intraoral minor salivary gland ductal papillomas and 19 cases of oral papillary squamous cell carcinomas were evaluated for expression of CD44. Within the ductal papilloma group, 6% showed absent staining to CD44, 33% weak staining, 60% moderate staining, and 0% strong staining with 76% diffusely expressing the stain and 24% focally expressing it. The papillary squamous cell carcinoma group showed 0% absent staining to CD44, 0% weak staining, 26% moderate staining, and 74% strong staining with 100% in a diffuse pattern. In conclusion, comparison of CD44 staining patterns between salivary ductal papillomas and oral papillary squamous cell carcinomas failed to exhibit reactivity as reported in previous studies performed on nasal and breast neoplasms. We hypothesize that the strong reactivity of CD44 in papillary squamous cell carcinoma noted in our study is probably attributable to the high level of differentiation that these lesions typically exhibit when compared to the papillary nasal carcinomas and papillary carcinomas of the breast.

SUPERFICILY INVASIVE SQUAMOUS CELL CARCI-NOMA OF THE ORAL CAVITY C Haberland, C Sasaki, B Judson, R Virk, M Prasad, Yale-New Haven Hospital, CT, USA

Superficially invasive or microinvasive squamous cell carcinoma (SISCC) is a poorly defined entity in the oral cavity. The purpose of this study is to describe the clinical and histopathologic features of this lesion. We defined SISCC of the oral cavity as a horizontally spreading squamous cell carcinoma that develops from a carcinoma in situ or severe dysplasia with focal and/or superficial invasion of less than 2 mm and no deeper than the lamina propria. Twelve cases met these criteria. Clinically, there was an equal sex distribution (6 male, 6 female) and the average age was 53 years old (range, 33–84 years). The most common location was the lateral tongue (n=8), followed by floor of mouth (n=2) and soft palate (n=2). Histopathologically, the average depth of invasion from the tumor surface to deepest point of invasion was 1.16 mm and measured from the nearest basement membrane to the deepest point of invasion was 0.53 mm. In 7 of the cases the tumor cells invaded <50% of the lamina propria. A moderate to severe lichenoid band-like lymphocytic response to the tumor was noted in 7 of the cases. Intracellular keratinization in tumor cells was observed in all cases, but keratin pearls were seen in only 4. Only 2 cases were found to have a papillary surface. The nuclear grade was found to be severe (grade 3) in 8 cases. All cases were treated with surgical resection and only 4 cases received a modified radical neck dissection, but no metastasis were found. Follow-up ranged from 1–18 years and there were frequent positive margins at surgery, and multiple recurrences, but no regional or distant metastasis. In summary, we describe SISCC of the oral cavity as a flat, minimally invasive, intensely immunogenic carcinoma with high-grade nuclei that are indolent but horizontally aggressive.

SINONASAL RENAL CELL CARCINOMA-LIKE ADENO-CARCINOMA K Magliocca, Z Patel, J DelGaudio, S Budnick, S Muller, Emory University, Atlanta, GA, USA

The sinonasal renal cell carcinoma-like adenocarcinoma (SRCLA) is a recently characterized malignancy. A review of the English language literature reveals only 4 previously reported cases of SRCLA. We present 2 additional cases, the first presenting with chronic nasal obstruction and epistaxis in a 51-year-old male, and the second presenting as recurrent epistaxis in a 38-year-old male. Microscopically, the neoplasms were characterized by back-to-back ductal structures composed of cuboidal cells with clear cell morphology. Cytologically, mild nuclear and cellular atypia were identified but abnormal mitoses were absent. A highly vascular stroma with delicate fibrous septae was identified between aggregates of neoplastic glandular epithelium. Immunohistochemically, both tumors stained positively for vimentin, CK-7 and S100. Neither tumor marked with RCC. PAX-2 was positive in the first case, but negative in the second case. The microscopic differential diagnosis, including metastatic renal cell clear cell carcinoma, clear cell neoplasms, squamous cell carcinoma with clear cell change, and ectopic pituitary adenoma, will be highlighted. Pre-operative tumor embolization followed by wide local excision with close clinical follow-up appears to be the treatment of choice; however, these recommendations are limited by the rarity of the neoplasm and a relatively short follow-up period of the available case material.

MAMMARY ANALOGUE SECRETORY CARCINOMA OF LABIAL SALIVARY GLANDS F Kralovich, J Stewart, Oregon Health & Science University, Portland, OR, USA

Mammary analogue secretory carcinoma of salivary glands (MASC) is a recently described distinctive salivary gland neoplasm. Similar to rare secretory carcinomas of the breast, MASCs have microscopic features resembling both acinic cell carcinoma and low-grade cystadenocarcinoma of salivary glands with a lobulated growth pattern demonstrating cystic and microcystic spaces filled with eosinophilic secretory material. The tumor cells
generally stain weakly for periodic acid-Schiff with diastase and are positive for S100 protein and strongly positive for vimentin. Also, like their counterpart in the breast, these tumors are characterized by a t(12;15) (p13;q25) ETV6-NTRK3 translocation. In the past year we have encountered 2 such tumors in the upper and lower lips, both of which had relatively weak periodic acid-Schiff staining with diastase and were positive for vimentin and S100. Fluorescence in situ hybridization (FISH) was performed on both tumors with the ETV6 break-apart probe showing disruption of ETV6 (12p13). Microscopic criteria as well as the clinical significance for the diagnosis of MASC will be discussed.

RETROSPECTIVE DIAGNOSIS OF NUT MIDLINE CARCINOMA I. Solomon, K Magliocca, S Muller, Emory University, Atlanta, GA, USA

Background: NUT midline carcinomas (NMC) are aggressive tumors arising primarily in the head, neck and mediastinum in young individuals. NMC exhibits a chromosomal translocation resulting in overexpression of nuclear protein in testis (NUT), previously only detected by FISH. An extensive survey for NMC in a series of poorly differentiated carcinomas of the upper aerodigestive tract has not been previously reported.

Design: The EUH pathology database from 2003–2012 was queried using the search terms: undifferentiated, carcinoma (Ca), poorly differentiated, nasopharyngeal, thymic, sinonasal, mediastinal; tumors for which another primary site was identified were excluded. Diagnosis of NMC was based on strong diffuse nuclear immunohistochemical (IHC) staining with rabbit monoclonal antibody NUT (C52B1) (Cell Signaling Technology, Inc., Danvers, MA, USA).

Results: 47 cases with material available for testing included 18 poorly differentiated Cas, 6 non-keratinizing Cas, 4 undifferentiated Cas, 5 sinonasal undifferentiated Cas (SNUC), 2 sarcomatoid Cas, 3 thymic Cas, 2 poorly differentiated non-small cell Cas, 2 high grade adenocarcinomas, 2 intermediate grade mucoidermod Cas, and 1 each: epithelial malignancy, pituitary Cas, poorly differentiated basaloid Ca. Average patient age was 54.9 years (range:16–82), with 19 women and 28 men. A single case of NUT translocation was detected in a 26-year-old man with a left nasal and maxillary sinus tumor diagnosed as poorly differentiated Ca with neuroendocrine features and focal squamous differentiation.

Conclusions: In this series a NUT translocation was detected in 5.6% of poorly differentiated Ca cases of the head & neck and establishes a basis for the inclusion of NUT monoclonal antibody in diagnostic IHC panels.

THE FREQUENCY OF BENIGN AND MALIGNANT TUMORS IN ULCERATED VERSUS NONULCERATED EXOPHYTIC LESIONS OF ORAL MUCOSA I. Allon, DM Allon, G Chaushu, I Kaplan, Goldschleger School of Dental Medicine, Tel-Aviv University, Israel Rabin Medical Center, Tel-Aviv, Israel

Objectives: To investigate the spectrum of pathologies in ulcerated versus non-ulcerated exophytic lesions of oral mucosa.


Results: The analysis included 713 biopsies. There was a wide age range, 9.6% of patients < 20 years, 29.1% 20 to 50 years, and 61.4% >50, with a female predominance (44.9% male, 55.9% female), p = 0.02. 91.5% of lesions were non ulcerated, 8.5% ulcerated. 69.6% of all lesions were reactive, 21.3% benign tumors, 7.8% malignant tumors, and 1.3% premalignant. A significant difference in the distribution of lesions was seen between the ulcerated and non-ulcerated groups: in the ulcerated group 48.3% were reactive, 15% benign tumors and 35% malignant, in the nonulcerated 70.4% were reactive, 21.9% benign and 5.2% malignant tumors, p< 0.0001. An age-related increase in the frequency of malignant tumors was noted, from 3.0% in the below 20 age group to 11.1% in the over 50 group, while the frequency of benign tumors was almost constant 23.9%–22.9%, respectively, p< 0.0001.

Conclusions: Approximately 1/3 of the exophytic lesions were neoplastic. The chances of an ulcerated mass to represent a malignancy are significantly higher than a non-ulcerated one, especially in patients over 50. Nevertheless, 5.2% of the non-ulcerated lesions harbor a malignancy, which may be missed if only surface ulceration is considered a disturbing clinical sign. These results strongly support the importance of removing and submitting for microscopic analysis all exophytic lesions of the oral mucosa, regardless of surface ulceration.

SURROGATE MARKERS: THE DIF ALTERNATIVE FOR FORMALIN FIXED/PARAFFIN EMBEDDED SPECIMENS R Eversole, Oral Pathology Diagnostic Services, San Diego, CA, USA

Background: Coupled with routine histopathologic assessment, direct immunofluorescence (DIF) provides confirmatory diagnostic findings for immunopathologic desquamative diseases of skin and mucosa. The DIF antibody markers do not recognize the appropriate epitopic targets on formalin fixed tissues. DIF requires special transport media fixation, frozen sections, frequent repeat biopsy and a fluorescence microscope. This communication describes surrogate immunomarkers that can be employed on formalin fixed current and archived specimens.

Material and Methods: 15 archived fixed cases each of pemphigus vulgaris (PV), mucous membrane pemphigoid (MMP), erosive lichen planus (ELP) and varying numbers of rare oral bullous diseases were assessed by standard immunoperoxidase methodology using 3 primary antibodies reactive with epitopes on 1) Keratinocyte pericellular membrane bound Ig (AB001); 2) Lamina lucida basement membrane bound complement (AB002); and 3) Basement membrane bound fibrin products (AB003). These antibodies were selected after screening a variety of immunomarkers for reactivity.

Results: 14 of 15 cases of PV, 15 of 15 cases of MMP, and 13 of 15 cases of ELP mirrored results seen with DIF (i.e.: AB001, pericellular and AB002 pericellular positivity for PV, AB002 basement membrane positivity for MMP and AB003 basement membrane positivity for fibrin products).

Conclusion: Selected immunomarkers directed to autoantibodies that are in vivo bound to host antigens in formalin fixed/paraffin embedded lesional specimens can replicate patterns seen with direct immunofluorescence.

REACTIVE EXOSTOSIS: CLINICOPATHOLOGY OF 27 LESIONS; COMPARISON WITH TORI AND BUCAL EXOSTOSIS J Bouquot, G Welch, P Suarez, S Zarghouni, University of Texas, Houston, TX, USA

Background: Reactive cortical lesions can have a rapid onset and alarmingly active histopathology, as opposed to the much more common, histologically more mature and less alarming tori and buccal exostoses. Maxillofacial reactive exostosis
(RE) is not rare, we believe, but is virtually unreported except for the very specialized variant, subpontic osseous hyperplasia.

**Objective:** To clinicopathologically characterize, for the first time, a series of RE lesions.

**Methods:** 27 cases and 32 controls (tori and buccal exostoses) were derived from 2 surgical pathology services.

**Results:** Average subject age at diagnosis was 38 years (range: 27–51), compared to 52 years for controls (range: 38–69). Lesions were located on the non-midline hard palate (n = 13), facial surfaces of the posterior mandible (n = 6) or maxilla (n = 3) and beneath pontics (n = 4); 1 occurred on the lingual surface of the ramus. Lesions averaged 11 mm in diameter (range: 4–28 mm). Mild pain/tenderness was associated with 6 lesions; overlying mucosa was not erythematous or ulcerated. Average duration was 9.3 months. Local trauma or inflammation, e.g. adjacent to dental fistulae, was considered causative in 14 cases and in the 4 subpontic lesions; all other lesions had no obvious cause. All cases showed large areas of new bone formation, primarily woven and immature lamellar bone. All cases showed active osteoblasts and fatty marrow was seldom seen.

**Conclusion:** The clinicopathology of RE differs considerably from tori and buccal exostoses. RE apparently remains histologically immature for months, perhaps years.

**PITFALLS IN FORENSIC ODONTOLOGY: REVIEW WITH ORIGINAL RESEARCH ON GENDER IDENTIFICATION GENES**

R George, Melaka Manipal Medical College, Melaka, Malaysia

The reliability of forensic evidence lies in its accuracy; even though the conventional methods of investigation in forensic odontology are much refined, the investigator must be aware of the pitfalls in each of these methods. The limitations and possible errors that can commonly occur during forensic dental investigations are reviewed in this paper, along with original study done on genes of forensic gender identification. Gender of 37 subjects was identified accurately by detection of SRY gene with real time PCR, using exfoliated epithelial cell adhered on acrylic dentures as the source of DNA, as an alternate to the commonly used Amelogenin gene to get unambiguous results. Regardless of the technologies used for gender identification, the result may be erroneous in certain conditions. This paper highlights the pitfalls of forensic investigation and precautions that an investigator should be aware while collecting evidence and conducting forensic dental investigations.

**THE HEAD, NECK AND SYSTEMIC MANIFESTATIONS OF LEVAMISOLE-CONTAMINATED COCAINE USE**

K Magliocca, N Coker, D Parker, S Parker, C Mitchell, A Church, Emory University, Atlanta, GA; University of Florida, Gainesville, FL, USA

Levamisole is a drug which was once utilized in the management of autoimmune diseases such as Behcet’s disease and rheumatoid arthritis. In 2000, this immunomodulating agent was removed from the market as a result of adverse cutaneous and hematologic effects in humans. The drug is still available as a veterinary anti-helminthic and has been detected in cocaine within the United States. A common clinical finding resulting from the use of levamisole-tainted cocaine includes purpura of the earlobe and helix, but retiform purpura has been reported on the trunk and extremities with some frequency. Importantly, hematologic abnormalities such as a granulocytosis is not uncommon. Some individuals develop oral ulcers, possibly as a consequence of neutropenia. The clinical differential diagnosis depends on the extent of the physical and laboratory findings, but may include lupus erythematosus, anti-phospholipid antibody syndrome, erythema multiforme, Wegener’s granulomatosis and even meningococcal vasculitis. This presentation documents the available clinical, laboratory and histopathologic findings of 2 new patients, aged 43 and 63 years, suspected of consuming levamisole-contaminated cocaine. The clinical, histopathological and laboratory findings will be discussed, in addition to the approach to the diagnostic work-up designed to exclude other differential diagnostic entities.

**IMMUNOHISTOCHEMICAL CORRELATION OF MMP-2 AND TIMP-2 IN LEUKOPLAKIA WITH DYSPLASIA**

R Radhakrishnan, D Bajracharya, B Shrestha, Asha Kamath, Manipal College of Dental Sciences, Manipal University, Manipal, India

Aims: To study the expression of matrix metalloproteinase (MMP-2) and tissue inhibitors of matrixmetalloproteinase-2 (TIMP-2) in oral leukoplakias with epithelial dysplasia in various histological grades and correlate the association between these proteolytic enzymes.

Materials and Methods: A retrospective immunohistochemical study was carried out on 30 clinically and histologically proven cases of leukoplakia with dysplasia and 10 cases of normal buccal mucosa using antiMMP-2 and antiTIMP-2 monoclonal antibodies.

Results: Mann Whitney U test, for comparing the expression of both MMP-2 and TIMP-2 in normal mucosa with dysplasia was highly significant (P < 0.001). Kruskal Wallis test to compare the median score of MMP-2 and TIMP-2 in different grades of dysplasia showed statistical significance (P <0.001) and a Spearman’s correlation between MMP-2 and TIMP-2 through different grades of dysplasia and cells observed showed positive correlation.

Conclusion: Our results suggest that both MMP-2 and TIMP-2 have an important role in the progression of normal oral epithelium to dysplasia in the process of oral carcinogenesis. Concomitant increase in the expression of both MMP-2 and TIMP-2 suggested that the activation of MMP-2 is dependent on TIMP-2 acting as a cofactor. Changes in TIMP-2 levels are considered important because they directly affect the level of MMP-2 activity.

**WHOLE SLIDE IMAGING SYSTEM TO PROMOTE EDUCATION & RESEARCH IN THE AMERICAN ACADEMY OF ORAL & MAXILLOFACIAL PATHOLOGY**

A Kulkarni, Y Rawal, CR Handorf, University of Tennessee Health Science Center, Memphis, TN, USA

Whole slide imaging systems emulate the pan and zoom of microscopes. Additionally, they confer the accessibility and versatility common to digital images. Digital microscopy is gaining momentum and is proving to be an efficient parallel to routine microscopy. It allows for remote multiple access, viewing mul-
tiple slides on the same screen, on-screen annotations, image analysis, remote consultation, image capture, etc. A basic setup requires a slide scanner with robotic functionality including scanning at step up magnifications, software to manipulate and compress images, storage solutions to archive images and firewall protected servers to facilitate safe access to remote users. When used for educational purposes, this technology eliminates the need for physical glass slides. In addition to savings in processing and staining chemicals, the benefits are noticeable when the biopsied tissue is limited in quantity. Long-term storage of data is also easily facilitated. Digitization of slides opens up new channels for multi user collaboration and research.

STUDY TO EVALUATE THE EFFICACY OF COMMUNICATION TRAINING IN ACCENT MODIFICATION FOR INTERNATIONAL HEALTH CARE PROFESSIONALS

NM Islam, PK Khurana, Indiana University School of Dentistry, Indianapolis, IN, USA

Objective: The increasingly diverse nature of health care in the United States demands a critical need for clear, accurate, and appropriate communication in the scientific and medical setting to ensure patient safety. While International Medical Graduates (IMGs) bring all their knowledge and expertise, their pronunciation and intonation patterns often become a barrier in their ability to be understood. This breakdown in communication can affect physician-patient or physician-staff understanding and hence patient care. To address these communications problems an American English for Internationals course was developed to train non-native English-speaking medical professionals.

Methods: The participants were IMGs and researchers. Instructors specialized in teaching accent reduction and clinical skills evaluation direction were recruited for the training and research program. The course included 8-12 weekly classes of 90-120 minutes duration. Our study assessed the efficacy of the program and included a pre and post course self-evaluation by the participants, an audio-tape assessment and a videotape assessment by 2 independent observers from the Clinical Skills Evaluation Center.

Results: Of the 80 enrolled, analysis of first 48 participants completing the program showed improved ability to clearly understand and pronounce words distinctly, stress words or syllables accurately and use body language/facial expressions appropriately. The results suggest that programs directed at improving the communication skills of non-native English speakers can be successful through appropriate and focused training.

Conclusion: The American English program for International medical graduates significantly improves verbal and body language communication skills.

SCLEROSING RHABDOMYOSARCOMA OF THE PTERYGO-MAXILLARY FOSSA: CASE REPORT AND REVIEW OF THE LITERATURE

J Robinson, M Richardson, B Neville, T Day, A Chi, Medical University of South Carolina, Charleston, SC, USA

Sclerosing rhabdomyosarcoma (SRMS) is an unusual rhabdomyosarcoma variant characterized by prominent hyalinizing matrix and often pseudovascular growth pattern. Here we report a case arising in a 40-year-old male. The tumor was centered in the pterygomaxillary fossa with extension into the lateral skull base, infratemporal fossa, masticator space, lateral pterygoid plate, buccal soft tissue, and mandible. Fine needle aspiration yielded a preliminary diagnosis of high-grade pleomorphic undifferentiated sarcoma, for which he received neoadjuvant chemotherapy with subsequent surgical resection. Microscopic examination showed a malignant spindle cell neoplasm with focal rhabdomyoblastic differentiation and a prominent osteoid-like, hyaline stroma. The tumor cells were diffusely positive for desmin and myogenin. Fluorescence in situ hybridization was negative for translocations involving the FOXO1a, EWSR1 and SS18 loci. 16 months status post primary resection, the patient is alive with multiple lung and bony metastases. Among the 26 cases of SRMS reported thus far (including the present case), there is a broad age range (3–79 years), with an average age at presentation of 36 years. The male-to-female ratio is 1:1.

COMPARISON OF BLOOD AND LYMPHATIC MICROVESSEL DENSITY BETWEEN PLEOMORPHIC ADENOMA AND BASAL CELL ADENOMA

AB Soares, TR de Oliveira, A Altemani, NS de Araujo, VC de Araujo, Department of Oral Pathology, Sao Leopoldo Mandic Institute and Research Center, Campinas, SP, Brazil

Background: Pleomorphic adenoma (PA) is the most common tumor of the salivary gland while basal cell adenoma (BCA), also benign, is an uncommon epithelial neoplasm. PA and BCA are classified as adenomas, composed of luminal and abluminal cells. Blood and lymphatic vessels have received increasing attention, especially in the field of neoplastic vascularization, mostly regarding tumor growth, invasion and metastases. The aim of this study was to compare the tumor blood and lymphatic vascular density of PA and BCA.

Methods: Blood and lymphatic vessels of 11 cases of PA and 11 cases of BCA were analyzed by immunohistochemical technique using the antibodies for CD34, CD105, D2-40.

Results: Comparing PA and BCA, the latter presented higher blood and lymphatic vascular density, demonstrated by significant higher expression of CD105 and D2-40.

Conclusion: This study showed that in spite of PA and BCA being considered part of the same spectrum of differentiation; these tumors are different in blood and lymphatic vascularization. Furthermore, this study suggests that the BCA, a benign tumor, can trigger the angiogenic switch.

PREVALENCE OF HUMAN PAPILLOMAVIRUS IN CLINICALLY UNREMARKABLE ORAL MUCOSA IN AN ADULT POPULATION USING DIGENE HYBRID CAPTURE 2TM PLATFORM

J Doscher, J Kramer, K Thai, D Gao, F Ye, D Zhang, J Wu, J Fantasia, Hospital of St. Raphael, New Haven, CT; The Feinstein Institute for Medical Research, Manhasset, NY; Mount Sinai School of Medicine, New York, NY; Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA

Background: Human papillomavirus (HPV) is widespread in the adult population. Prevalence of HPV in clinically unremarkable oral mucosa is unknown. The objective of this study was to determine the prevalence of HPV in clinically unremarkable oral mucosa in a representative urban-based adult population.
The carcinogenic effects of high-risk human papillomavirus (HPV) on cervical epithelium are well documented. These studies have prompted routine screening tests, such as Papanicolaou (PAP) smears, for detection of dysplasia and carcinoma of the uterine cervix. Furthermore, identification of high-risk HPV is a prognostic indicator for progression to dysplasia and carcinoma. HPV infection also contributes to oropharyngeal carcinoma (OPC), as high-risk HPV is identified in an increasing number of individuals with OPC. However, the prevalence of HPV in the oral cavity proper is poorly characterized. Specific aim: To identify the prevalence of high- and low-risk HPV in clinically unremarkable oral mucosa in an adult population. Methods: 100 adults (age range = 18–70 years, median age = 37 years, mean age = 40 years, M/F = 47/53) were screened using a DNA collection device designed for uterine cervical screening. Collection consisted of a combined cytology sample from buccal mucosa, floor of mouth, and palate, avoiding oropharyngeal mucosa. Low-risk (5 types) and high-risk (13 types) HPV was detected using a Digene Hybrid Capture 2TM platform. DNA adequacy for all samples was confirmed, and sufficient cell collection was verified using a ThinPrep1® cytology preparation. Results: Two of the 100 samples tested positive for high-risk HPV in the oral cavity (males, ages 25 and 30). One of these individuals was also positive for low-risk HPV (male, age 25). Conclusion: This study indicates a small percentage of the study sample (2%) is positive for high-risk HPV in the oral cavity, using the methodology described. The therapeutic implications of these findings are currently unknown.

**DIAGNOSIS OF NON-HODGKIN LYMPHOMA OCCURRING IN THE ORAL CAVITY PROPER: A 10 YEAR SINGLE INSTITUTION EXPERIENCE**

E Ko, E Philpone, A Yoon, B Alobeid, D Zegarelli, Columbia University, New York, NY, USA

Despite being the second most common neoplasm of the head and neck, occurrence of lymphoma within the oral cavity is relatively rare, accounting for approximately 3.5% of oral malignancies. We present a review of biopsy specimens from the oral cavity proper which were diagnosed as non-Hodgkin lymphoma by the hematopathology and oral pathology services at Columbia University Medical Center over the past decade. Our search identified 27 patients (13 males and 14 females) with diagnoses of non-Hodgkin lymphoma occurring within the oral cavity proper. Mean age at time of biopsy was 65.4 years. Location of the lesions included tongue (n=5), gingiva (n=4), palate (n=4), vestibule (n=4), buccal mucosa (n=3), maxillary bone (n=3), mandibular bone (n=3), and floor of mouth (n=1). Based on the 2012 WHO classification, the most to least frequent rendered diagnoses were: diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, extranodal marginal zone B-cell lymphoma of mucosal associated lymphoid tissue (MALT), plasmablastic lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and mantle cell lymphoma.

**PIGMENTED (HEMOSIDEROTIC) GRANULAR CELL AMELOBLASTOMA: A CASE REPORT AND REVIEW OF THE LITERATURE**

J Wollenberg, A Grandhi, P Pruden, R Reich, P Freedman, New York Hospital Queens, NY, USA

Thalassemia is a heterogenous group of inherited disorders of hemoglobin synthesis. Thalassemia patients demonstrate secondary hemochromatosis due to a multitude of factors, which include ineffective erythropoiesis with increased breakdown of red blood cells, repeated blood transfusions, or increased absorption of iron from the gastrointestinal tract. Hemochromatosis is characterized by deposition of excess iron in the form of ferritin and hemosiderin in the parenchymal tissues. In the literature, oral manifestations of hemochromatosis included rapid periodontal destruction leading to tooth mobility, blue-grey mucosal pigmentation and deposition in salivary glands leading to xerostomia. Ameloblastoma is a benign, locally aggressive odontogenic epithelial tumor. Histologically, ameloblastomas can demonstrate variable patterns including, but not limited to, follicular, plexiform, and granular cell. Many case reports have been cited in the literature exhibiting melanin pigmentation in odontogenic lesions. The current case is that of a 72-year-old male with a medical history of Thalassemia trait, anemia and previous blood transfusions. The patient’s family history is significant for brother dying as a child of Thalassemia. The patient presented to the oral surgeon’s office with a 2 cm radiolucency in the anterior mandible. Histopathologic examination of the biopsy specimen demonstrated features of a granular cell ameloblastoma with extensive intracytoplasmic pigmentation of the granular cells. Iron stain confirmed the presence of hemosiderin. In view of the patient’s history, the presence of hemosiderin represented the first known manifestation of hemochromatosis secondary to Thalassemia trait.

**COMPARISON OF CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS BETWEEN IV AND PO BISPHOSPHONATE USERS IN ACTINOMYCES-ASSOCIATED OSTEONECROSIS OF THE JAWS**

K Anavi-Lev, Y Anavi, G Chaushul, I Kaplan, The Hebrew University Hadassah School of Dental Medicine, Jerusalem; Rabin Medical Center, Petah Tiqa & Tel-Aviv University, Israel

The study was a 10-year retrospective analysis of archived cases with ONJ. Actinomycoses colonies were identified using H&E, Gram and PAS stains. Only colonies with adjacent tissue reaction were analyzed. Actinomycoses density was calculated by dividing the total number of colonies by tissue surface, actinomycoses relative surface was calculated by dividing total bacterial colony surface by tissue surface.

**Results:** A total of 52 patients were included, 37 (71.1%) in IV and 15 (28.9%) in PO group. The average BP treatment period was 28 months for IV and 58 for PO BP. Actinomycoses relative surface was significantly increased in the PO group, with no significant differences in actinomycoses density. Duration of antibiotic treatment and time for healing exhibited no significant differences between groups. The incidence of diabetes mellitus was significantly increased in PO (60%) vs. IV (22%) groups, both were high compared to 10% expected incidence in Israeli elderly population. Corticosteroid intake was recorded in 25% of patients, with no significant differences between groups.

**Conclusions:** Actinomycoses colonization is common in both IV and PO BP. It may play an important role in disease evolution and duration but without significant differences between PO and IV groups. Both corticosteroid treatment and diabetes mellitus in BP treated patients are co-factors in the development of ONJ.

**CARCINOMA CUNICULATUM: A POTENTIALLY UNDIAGNOSED ENTITY IN THE ABSENCE OF CLINICAL CORRELATION**

R Padilla, V Murrah, UNC School of Dentistry, Chapel Hill, NC, USA
Carcinoma cuniculatum (CC) is a rare variant of squamous cell carcinoma described by Aird in 1954 in the sole of the foot. Multiple other cases have been described in other anatomic locations since then. However, less than 30 cases of CC of the upper aerodigestive tract have been reported. The most common locations within the mouth are the alveolar mucosa/gingiva, and hard palate. Clinically the lesions present as indurated erythro-leukoplakias with a cobblestone-like surface. Histologically the neoplasm is characterized by a predominantly endophytic proliferation of keratinocytes with minimal atypia. The tumor “bursrows” into the supporting connective tissues creating branching crypt-like structures filled with keratin. Sometimes this lesion has been described histologically as resembling an inverted Schneiderian papilloma. The lesions usually exhibit an indolent clinical course and complete surgical removal is considered appropriate treatment. We present 6 additional cases of CC from the attached gingiva and vestibular/buccal mucosa. The average age at presentation was 66.5 yrs. All of our cases except 1 were treated conservatively: 1 required an en-bloc resection to achieve clear margins. In multiple cases of this study, treatment delays resulted from under-interpretation of small or superficial biopsies. Patients subsequently went on to obtain definitive diagnoses only after clinical correlation revealed an appearance inconsistent with a benign process. Therefore, since a pathognomonic microscopic appearance is often not seen in these cases, the caveat is given that appropriate clinical-pathologic correlations are required to achieve an accurate diagnosis of CC.

IMMUNOPHENOTYPING OF ORAL AMYLOIDOSIS AND CORRELATE WITH SYSTEMIC MANIFESTATIONS

N Bimmadi, C Intapa, T Meiller, M Scheper, King Abdulaziz University Jeddah, Saudi Arabia; University of Maryland, Baltimore, MD, USA

Amyloidosis is a rare localized or systemic disorder with extracellular deposition of fibrillar proteins into soft tissues and organs. It can be inherited or acquired, neoplastic, infectious, degenerative or associated with aging. More than 25 distinct biochemical forms of amyloid have been identified. These types have similar tertiary-pleated sheet structure, but different chemical compositions. It is recognized that the type of amyloid is important because the pathogenesis and treatment strategies are different. Amyloid was first described by Virchow in the 19th century; however, its etiology and pathogenesis have remained obscure. There are 1,275–3,200 new cases of primary systemic amyloidosis annually in the United States and AL amyloidosis and familial transthyretin-associated (ATTR) are the most common forms. Amyloid can be deposited in oral cavity, most often in the tongue. When the diagnosis of amyloidosis of the oral mucosa is made, further investigations are critical to evaluate the function of the organs most frequently involved, such as liver, kidney, and heart; and to exclude an underlying plasma cell dyscrasia. The aim of the present retrospective study was to diagnose a serious systemic condition as early as possible by typing the oral amyloid deposits. This study was conduct in 2 phases. First, 10 oral biopsy specimens from Oral Pathology Department of University of Maryland were collected, that were conclusive for a diagnosis of amyloidosis based on histology and Congo red stain. These were then assessed for the type of amyloid present using immunohistochemical staining with a routine antibody panel (AL, AA, ATTR, Ab2M). Next data was obtained to correlate the IHC findings with clinical parameters and follow-up of the patient’s medical status.

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER PRESENTING AS AN ORAL ULCERATION IN A RENAL TRANSPLANT RECIPIENT: DIAGNOSIS AND TREATMENT CHALLENGES

J O’Donnell, S Sheikh-Fayyaz, R Kelsch, J Fantasia, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY, USA

Background: Post-transplant lymphoproliferative disorders (PTLDs) represent a spectrum of lymphoid proliferations following transplantation. Most PTLDs are caused by Epstein Barr virus (EBV) infected lymphoid cells. PTLDs result from impaired cytotoxic T-cell response due to induced immunosuppression of the solid organ transplant recipient. Additionally, EBV related PTLDs can occur secondary to myeloablative regimens in the case of stem cell and bone marrow transplant. The WHO classifies PTLDs into 4 main groups; early lesions, polymorphic PTLDs, monomorphic PTLDs, and classical Hodgkin lymphoma-type PTLDs.

Observations: A 69-year-old woman presented with a rapidly evolving crateriform 2 cm ulcer of the right anterior maxillary gingiva extending onto the palate. She had a renal transplantation 10 years ago; her medications included prednisone, mycophenolate mofetil, azathioprine, and tacrolimus. Biopsy of the palatal lesion revealed a submucosal lymphocytic infiltrate with few Hodgkin-like cells. A diagnosis of EBV associated B−cell monomorphic PTLD was rendered based on the following immunophenotypic analysis: positive staining for CD79a, partial CD20, PAX5, CD30, dim BCL6, MUM1, with positive EBV, EBER (ISH) and Ki−67 60−70%; negative staining for CD3, CD15, CD34, CD138, CD4, CD117, CD99, EMA, TdT, MPO, Alk-1. Mucosal ulceration resolved upon discontinuing mycophenolate mofetil, and azathioprine and a reducing in the prednisone dose.

Conclusions: This case presentation describes an EBV associated monomorphic B-cell PTLD presenting as an oral ulcer and highlights the importance of recognizing PTLD for clinical purposes.

SYNCHRONOUS MULTIFOCAL ORAL MELANOACANTHOSIS: A CASE REPORT AND REVIEW OF THE LITERATURE

B Martin, C Allen, Ohio State University, Columbus, OH, USA

Oral melanocanthosis (OMA) is an uncommon melanocytic process found most often in black females in the third or fourth decade of life. OMA is regarded as a benign reactive process, based on a tendency to present in areas affected by trauma, regression after biopsy, and the histopathologic finding of increased vascularity and chronic inflammation. The exact cause, however, is unknown. A 44-year-old African-American woman was referred by her primary care physician for evaluation of multiple “spots” involving her maxillary and mandibular labial mucosa. The patient reported the sudden onset of these lesions approximately 2 months earlier, accompanied by an itching sensation. Several variably sized, homogenous, dark brown macules were observed in a background of otherwise unremarkable oral mucosa. A clinical diagnosis of OMA was rendered. Biopsy from the lower left labial mucosa revealed normally maturing oral keratinocytes exhibiting intercellular edema and dendritic melanocytes within the spinous layer. The dendritic melanocytes were confirmed with immunohistochemical studies using antibodies directed against S-100 and HMB-45, thereby confirming the clinical diagnosis. No melanocytic hyperplasia was present, but a light population of chronic inflammatory cells was seen in
the underlying connective tissue. Two months post-biopsy, the melanocytic nevus exhibited no significant clinical change in size or color.

**DIAGNOSTIC APPROACHES IN UNSUSPECTED ORAL LESIONS OF SYPHILIS**

**C Siquiera, F Silveira, J Lago, S. Sousa, University of São Paulo, São Paulo, Brazil**

**Background:** Awareness of the increased prevalence of syphilis is essential for early diagnosis, treatment and prevention of disease spreading. While serological studies are the primary tool used to confirm the diagnosis of secondary syphilis, biopsy of unsuspected oral lesions are not uncommon in oral pathology routine laboratory. In these cases histopathologic characteristics are likely to indicate the possibility of syphilis.

**Objective:** The aim of the present study was to test the efficacy of immunohistochemistry in the detection of T. pallidum in oral biopsies presenting histological aspects compatible with syphilis. Thirteen cases recently seen, were retrieved and submitted to immunohistochemical reaction with polyclonal antibody to Treponema pallidum (Biocare Medica). Clinically the cases had been provisionally diagnosed by the clinicians as histoplasmosis (1 case), viral infection (2 cases), lymphoma (2 cases), ulcer (1 case) pemphigus, pemphigoid (2 cases), erosive lichen planus (1 case), SCC, oral leukoplakia (2 cases) and sarcoma (2 cases).

**Results:** All 13 cases were positive for the antibody anti-T. pallidum in the lower layers of the epithelium, and in an intercellular distribution. Thus, a histologic diagnosis of secondary syphilis was established. In all the cases serological examination confirmed the disease. Histologic characteristics that prompted a suspicion of syphilis were especially the presence of plasmacytic infiltration in a perivascular manner, and also diffuse or lichenoid, cellular distribution. Thus, a histologic diagnosis of secondary syphilis was established.

**Conclusion:** Histologic diagnosis of secondary syphilis was established in all the cases.

**STAFNE DEFECT OF THE ASCENDING RAMUS OF THE MANDIBLE: A RARE INCIDENTAL CONE BEAM COMPUTED TOMOGRAPHY FINDING**

**N Odingo, D Colosi, D Trochesset, State University of New York at Stony Brook, NY, USA**

The Stafne defect was first described in 1942. EC Stafne reported a series of asymptomatic radiolucent lesions located near the angle of the mandible. In subsequent reports of similar lesions, the condition was shown to represent a focal concavity of the cortical bone on the lingual surface of the mandible. The concavity is thought to result from or be associated with growth of the submandibular gland. Similar defects have been described in the region apical to the premolar teeth, associated with the sublingual gland, and very rarely, on the medial surface of the ascending ramus, associated with the parotid gland. We report an incidental finding of this latter occurrence in a 52-year-old female who presented for routine dental treatment. Cone beam computed tomography (CBCT) was completed as a component of treatment planning for placement of dental implants. CBCT findings included a well-corticated osseous defect of the lateral aspect of the right mandibular ramus. A panoramic radiograph acquired 12 months earlier revealed a similar defect at the same location, of about the same dimensions. A focused clinical history and examination revealed no symptoms or signs related to the right ascending ramus. A new panoramic radiograph was recommended for comparison. This new image showed no appreciable change in dimensions. The finding was interpreted as a Stafne defect of the right mandibular ramus. The etiology of the Stafne defect is unknown but it has been postulated to be a developmental anomaly, arising in patients aged as young as 11 years and as old as 30 years. The defects may continue to enlarge slowly. Treatment is not necessary for those arising in the posterior mandible, but close follow-up may be warranted for defects of the ramus of the mandible.

**RARE INTRAORAL SPITZ NEVUS-A CASE REPORT**

**C-C Li, VL Noonan, TJ Harrist, RJ Tannhyll III, SB Woo, Harvard School of Dental Medicine, Boston, MA; Boston University Goldman School of Dental Medicine, Boston, MA; StrataDx, Lexington, MA, USA**

Spitz nevi is very uncommon and accounts for only approximately 1% of all melanocytic nevi of the skin in children. Clinically, Spitz nevus presents as a solitary, asymptomatic, rapidly growing, symmetrical, dome-shaped, non-pigmented papule or nodule. It most frequently occurs on the skin of the head and neck region or extremities. Spitz nevi behave in a benign fashion and do not recur when completely excised; however, cytologic atypia or pleomorphism which is common in Spitz nevi may cause them to be misdiagnosed as melanoma. Here we report a case of an intra-oral Spitz nevus. An 11-year-old
male presented with a symmetrical, dome-shaped papule on the left buccal mucosa, measuring $0.5 \times 0.3 \times 0.2$ cm$^3$. Histopathological examination showed an unencapsulated but discrete proliferation of benign epithelioid and spindle-shaped nevus cells with minimal cytological atypia but without downward maturation, arranged in sheets and nests within the lamina propria. Melanin was present mostly within the superficial nests. A colllarette was present around the lesion. Nevo-melanocytic cells were focally present in nests within the basel cell layer. The nevus cells were both S100 and MART-1 positive. HMB-45 positive cells were superficially located. Less than 5% of the nuclei were positive for Ki-67 and these were limited to the superficial dermal component. Complete excision and follow-up evaluations are suggested for Spitz nevus. The prognosis is usually good, and the recurrence rate is low.

**SEMAPHORIN 4D AND PLEXIN-B1 PROMOTE PERINEURAL INVASION THROUGH RHOA AND ROK-MEDIATED PATHWAYS**

Perineural invasion (PNI) is a tropism of tumor cells for nerve bundles located in the surrounding stroma. It is a pathological feature observed in certain tumors, referred to as neurotropic malignancies, which severely limits the ability to establish local control of disease and results in pain, recurrent growth, and distant metastases. Despite the importance of PNI as a prognostic indicator, its biological mechanisms are poorly understood. The semaphorins and their receptors, the plexins, compose a family of proteins originally shown to be important in nerve cell adhesion, axon migration, and proper central nervous system development. Emerging evidence has demonstrated that these factors are expressed in tissues outside of the nervous system and represent a widespread signal transduction system that is involved in the regulation of motility and adhesion in different cell types. We believe that the plexins and semaphorins, which are strongly expressed in both axons and many carcinomas, play a role in PNI. In this study, we show that Plexin-B1 is overexpressed in tissues and cell lines from neurotropic malignancies and is attracted to nerves that express its ligand, Semaphorin 4D, in a Rho/Rho kinase (ROK)-dependent manner. We also demonstrate that nerves are attracted to tumors through this same system of proteins, suggesting that both Plexin-B1 and Semaphorin 4D are important in the promotion of PNI.

**ARCHITECTURAL CHANGES IN ORAL LEUKOPLAKIA ARE AS IMPORTANT AS EVIDENCE OF CYTOLeologic ATYPiA/DYSPLASiA:**

The current classification systems for assessing the presence and severity of oral epithelial dysplasia rely mostly on the cytological features of dysplasia with architectural features of dysplasia limited to irregular epithelial stratification, loss of polarity of basal cells, drop-shaped rete ridges, increased number of mitotic figures, abnormal superficial mitoses, premature keratinization of single cells (dyskeratosis) and keratin pearls within rete pegs. The purpose of this study is to determine whether other architectural features alone with minimal or only mild cytologic evidence of atypia/dysplasia is sufficient for a diagnosis of dysplasia, correlating the histopathology with the clinical appearance and behavior of such leukoplaikias. We present 10 patients where the original diagnosis had ruled out a dysplasia and correlate the histopathology with clinical findings. The architectural features that we considered were bulky epithelial proliferation, often endophytic and exophytic; papillomatosis, sharp demarcation of keratinization, skip lesions, and hyperkeratosis with atrophy without inflammation. In all 10 cases, some of these criteria were met and clinically many of these lesions represented proliferative or verrucous leukoplaikias. We propose that these architectural features are as important as the conventional ones in evaluation of leukoplaikias and that correlation with clinical findings is essential in arriving at an accurate diagnosis, and in facilitating treatment planning.

**ORAL ULCERATION CAUSED BY CONCURRENT HERPES SIMPLEX, CYTOMEGALOVIRUS AND EPSTEIN-BARR VIRUS INFECTION IN AN IMMUNOCOMPROMISED PATIENT**

**Background:** In immunocompromised patients, oral ulcerations are common and have a wide spectrum of causes, including human herpes viruses. Co-infection by 3 different herpes group viruses simultaneously has rarely been reported.

**Objective:** To document an oral ulcer that was simultaneously infected by herpes simplex (HSV), cytomegalovirus (CMV) and Epstein-Barr virus (EBV) in a renal and pancreatic transplant recipient.

**Findings:** A 46-year-old female, hospitalized for CMV colitis, presented with a dorsal tongue ulcer of 3 months duration. Examination revealed a second ulcer of unknown duration on the hard palate. Their clinical appearance was nonspecific. Histopathologic and immunohistochemical evaluation of the tongue ulcer showed keratinocytes exhibiting herpetic viral cytopathic effect. CMV-related nuclear and cytologic alterations were seen in endothelial cells subjacent to the ulcer. In situ hybridization studies using probes directed against EBV showed intense nuclear reactivity among many large atypical mononuclear cells within the superficial lamina propria. Antibodies directed against VZV were negative, although antibodies directed against HSV and EBV were positive in the cells described above. Further hematologic testing showed no evidence of EBV-induced B-cell lymphoproliferative disorder.

**Conclusion:** HSV, CMV and EBV have each been recognized to cause oral ulcers in the context of defective cellular immunity. This appears to be the first well-documented report of their concomitant presence in an immunocompromised patient’s oral ulcer. Although the pathogenesis of co-infected ulcers remains unknown, this could suggest a synergistic effect.

**LOCALIZED SPONGIOTIC GINGIVAL HYPERPLASIA IN ADULTS**

In 2007, Darling et al first reported a benign reactive condition in 24 patients aged 5 to 28 years. This lesion clinically resembles pyogenic granuloma and microscopically, is characterized by hyperplastic stratified squamous epithelium with marked spongiosis and exocytosis of neutrophils. The underlying connective tissue demonstrates increased vascularity and chronic inflammation but no granulation tissue. They termed this lesion juvenile spongiotic gingivitis. Subsequently, Kessler et al reported 52 additional cases (mean age, 11.8 yrs) and proposed the name localized juvenile spongiotic ging-
gival hyperplasia (LJSGH). Recently, in our lab we have observed this lesion in adults. Therefore, the University of North Carolina and the Oral and Maxillofacial Pathology Laboratory, conducted a retrospective study from June 2005 to December 2011 on all cases of pyogenic granuloma, inflammatory papillary hyperplasia and inflammatory fibrous hyperplasia in adults over age 21 to determine the incidence of LJSGH in the adult population. Of the 804 cases that qualified for review, 10.1% (81) met the histopathologic criteria established by Darling and Kessler for LJSGH. There was no histopathologic difference between the cases reported in pediatric patients and our adult cases. Our findings suggest this lesion is present in both pediatric and adult populations. Based on clinical and histopathologic similarities between adult and pediatric cases, we propose modification of the name to localized spongotic gingival hyperplasia (LJSGH) and that the lesion be recognized as in both populations. Currently, no etiology for LJSGH has been confirmed. However, the presence of koilocytes in 44.4% of cases in our study warrants investigation of HPV as a possible etiologic agent.

MICROCYSTIC ADENOCARCINOMA OF THE TONGUE
M Romañach, B de Andrade, R Carlos, O de Almeida, Federal University of Rio de Janeiro, Brazil; University of Campinas, Piracicaba, Brazil; Centro Clínico de Cabeza y Cuello/Hospital Herrera Llerandi, Guatemala City, Guatemala

Microcystic adenocarcinoma has been recently described in the literature as a salivary gland tumor that shares microscopic features with the so-called microcystic adnexal carcinoma of the skin. Interestingly, some authors have claimed that this entity should be better diagnosed as a microcystic variant of the polymorphous low-grade adenocarcinoma. Regardless of some nomenclature controversy, we present a single case of microcystic adenocarcinoma affecting the tongue of a 92-year-old female patient. The lesion was first noted 3 months before the first consult and clinical examination revealed a 4 x 3 cm painful ulcer on the anterior dorsal tongue, with a tender consistency and limited motion. Microscopically, the tumor presented a distinct formation of double-lined small ductal structures, distributed in the superficial and deep connective tissue. The sub-epithelial ducts tended to be bigger and perpendicular to the surface epithelium, while the deeper ones presented as infiltrative small ducts in the highly sclerosing stroma, where perineural invasion was also evident. We did not find unequivocal features of polymorphous low-grade adenocarcinoma. By immunohistochemistry, the tumor ductal cells were positive for CK AE1/AE3, CK 34BE12, CK7, CK18, CK19 and epithelial membrane antigen, while only the outer ductal cells were positive for vimentin and N-cadherin, while reduced E-cadherin expression of vimentin and N-cadherin, while reduced E-cadherin.

ACTIVIN A INHIBITS APOPTOSIS AND INDUCES ACQUISITION OF EMT PHENOTYPES IN NORMAL KERATINOCYTES
A Bufalino, P Rodrigues, D Bastos, B Andrade, F Mariano, E Graner, R Coletta, University of Campinas, Piracicaba, São Paulo, Brazil

Oral squamous cell carcinomas (OSCCs) have a highly variable clinical course, and because it is often diagnosed only after it has reached an advanced stage, the overall survival rate is less than 50% in 5 years. As survival for patients with OSCCs varies considerably, better prognostic markers are of utmost importance. Activin A, a member of transforming growth factor superfamily, has been shown to be overexpressed in various cancers, where it controls cell proliferation, differentiation and apoptosis. The purpose of this study was to investigate the effects of activin A in the modulation of the key events associated with oral tumorigenesis, including proliferation, apoptosis and epithelial-to-mesenchymal transition (EMT). To assess the effects of activin A, the normal epithelial cell line HaCat was cultured in medium containing 0–100 ng/ml of recombinant activin A. Our results demonstrated that activin A promotes a significant and dose-dependent decreased of apoptosis and cell death, without influence on cell proliferation, as revealed by growth curves, cell cycle analysis and bromodeoxyuridine-labeling (BrdU) index. Additionally, activin A treatment stimulated significantly the expression of vimentin and N-cadherin, while reduced E-cadherin and catenin expression. These findings demonstrate that activin A modulates apoptosis and acquisition of EMT phenotypes, contributing to oral tumorigenesis.

MULTI-SPECTRAL FLUORESCENCE AND REFLECTION: IMAGE ANALYSIS AND QUANTIFICATION OF HUMAN PAPILLOMAVIRUS ORAL LESIONS
A Zuluaga, M Nichols, C Flaitz, Remicalm LLC, Houston, TX; Bering Omega Dental Clinic, Houston, TX; University of Texas School of Dentistry, Houston, TX, USA

The rise in oral human papillomavirus (HPV) incidence underscores the importance of early detection and monitoring of HPV-induced lesions. This feasibility study assessed the value of multi-spectral optics using an imaging program for detecting HPV lesions. Clinical images were obtained with IRB approval, using white light reflectance, violet-excited autofluorescence (AF) (405 nm), and narrowband (NB) green reflectance (575 nm) from 31 consecutive, biopsy-proven HPV cases in HIV-positive patients. Using an open source imaging program, Fiji (http://fiji.sc/), representative affected and normal mucosa from each patient were outlined and captured in every image. After quantification of absolute intensity (average) and intensity heterogeneity (standard deviation), parameters for each color (red, green, blue) in regions of interest were documented. Paired t-test analysis was performed to determine whether statistically significant differences existed between lesion and normal areas (p < .05). Paired t-test analysis was also performed to determine if differences in lesional appearance were noted under 3 illumination conditions. Results showed that 75% (8/12) of parameters calculated in white light images, 92% (11/12) in violet images, and 83% (5/6) in green images were significantly different. Also, 67% (10/15) of intensity-based parameters and 87% (13/15) of heterogeneity-based parameters were significantly different. Violet images displayed significantly larger lesion areas than white or green images. Findings suggest that quantification of clinical images can be used to enhance detection of HPV oral disease with lesion heterogeneity playing an important role. Furthermore, AF and NB provide additional differentiation over white light images, alone. (Sponsored by Trimira.)

EXPRESSION OF MCM-2, KI-67 AND GEMINIIN IN ORAL NEVI AND MELANOMA
B de Andrade, M Romañach, R Carlos, W Delgado-Azahiero, A Mosqueda-Taylor, O de Almeida, University Campinas, Piracicaba, Brazil; Federal University of Rio de Janeiro, Brazil; Centro Clínico de
Cabeza y Cuello/Hospital Herrera Llerandi, Guatemala City, Guatemala; Universidad Peruana Cayetano Heredia, Lima, Peru; Universidad Autónoma Metropolitana, Xochimilco, México

Evaluation of cell cycle using antibodies against nuclear proteins involved in regulating DNA replication, has gained special interest in the effort to predict biological behavior of benign and malignant tumors. The aim of this study was to analyze the expression of Mcm-2, Ki-67 and geminin in oral nevi and melanomas. Expression of these cell proliferation markers was evaluated by immunohistochemistry in 51 oral melanocytic lesions, including 38 intramucosal nevi and 13 primary oral melanomas. Mcm-2, Ki-67 and geminin were rarely expressed in intramucosal nevi, in contrast to oral melanomas, which showed high levels of these cell proliferation markers, particularly Mcm-2, indicating it is a more sensitive marker in primary oral melanomas than Ki-67 and geminin. These results indicate that these markers may be involved in the pathogenesis of oral melanomas, and could be eventually useful as an additional diagnostic tool for differential diagnosis of oral benign and malignant melanocytic lesions.

ANALYSIS OF ANTIBODIES IN SJÖGREN’S SYNDROME: SOURCE AND SECRETION J Kramer, T Rothstein, The Feinstein Institute for Medical Research, North Shore-LIJ Health System, Manhasset, NY, USA

Sjögren’s Syndrome (SS) is a debilitating autoimmune disease. In addition to xerostomia, patients may develop serious systemic disease manifestations. While B cells have been shown to play an important role in SS disease pathogenesis, it is not known whether autoantibodies originate from glandular tissue predominately.

Hypothesis: Activated B cells from SS mice secrete more immunoglobulin (Ig) than B cells isolated from healthy controls. Further, we propose that this may lead to increased Ig levels in the sera of SS animals.

Methods: To determine the most significant source(s) of Ig production in SS, we isolated B cells from a mouse model of SS with advanced disease (n=5) along with age and sex matched controls (n=5). To examine Ig secretion, we used sort purified B cells from spleen, cervical lymph nodes, submandibular gland tissue, and bone marrow. Cells were stimulated with lipopolysaccharide (LPS) for 3 days, and ELISPOT assays were performed. Total serum IgM and IgG was measured by ELISA.

Results: Preliminary data suggest activated B cells isolated from the spleen and cervical lymph nodes from SS mice secrete twice as much IgM and IgG in response to LPS than control B cells. In addition, total serum IgM is higher in control animals, while SS mice have higher serum IgG.

Conclusions: Activated B cells isolated from the spleen and cervical lymph nodes of SS mice secrete higher levels of IgM and IgG than control B cells. Moreover, SS mice have higher serum IgG titers than control animals. Such studies suggest that both basal and stimulated B cell activity is increased in SS mice, and this hyperactivity is not restricted to salivary tissue. Thus, B cell dysfunction in SS extends to primary and secondary lymphoid organs, and likely contributes to SS pathogenesis.

A LOW GRADE MYOFIBROBLASTIC SARCOMA OF THE ALVEOLAR RIDGE B Aldape, B Cruz, Legorreta, R Lopez, UNAM, Mexico City, Mexico

The low grade myofibroblastic sarcoma is an heterogeneous neoplasm, with a biological spectrum from a benign to malignant neoplasm. Misdiagnosis as benign lesion can be made. Identifying neoplastic myofibroblasts is important for diagnosis as a myofibroblastic neoplasm. The currently accepted markers for identifying myofibroblasts are muscle-specific actin (MSA), smooth muscle actin (SMA), desmin, and calponin.

Case presentation: A 74-year-old woman presented with a normal colored 1 cm. growth in the right alveolar ridge of the first lower molar area. The lesion was asymptomatic, had been present for 1 year, and showed sauceration of the underlying bone on radiograph. Gross examination revealed a smooth firm, brown nodule measuring 1.5 × 1.5 × 1.0 cm. Microscopic examination with H&E stain showed a spindle myofibroblastic proliferation, with pushing margins and compression of the surrounding tissue, with mitotic activity. Immunohistochemical studies were performed which revealed: Actin (focal +), Ki 67 10%, HCaldesmon (−), S-100(−), this result supported the diagnosis of low grade myofibroblastic sarcoma.

Conclusion: The LGMS is a rare tumor in this location. To establish the diagnosis it is important to obtain immunohistochemical markers, as well as ultrastructural (EM) studies to support the myofibroblastic differentiation. These are being performed. The differential diagnosis includes leiomyosarcoma and fibrosarcoma. The cytogenetic and molecular genetic studies indicate that sarcomas can be divided into 2 genetic groups. The focal inflammatory infiltration can help to aid the differential diagnosis. The LGMS contain more poorly developed myofibroblasts and tends to be more uniform in appearance with a higher cellularity.

MALIGNANT EPITHELIOID HEMANGIOENDOTHELIOMA DETECTED ON PANORAMIC RADIOGRAPH V Woo, A Ruisinoski, A Miyat,E Herschaft, B Lawenda, University of Nevada, Las Vegas, NV, USA

Epithelioid hemangiendothelioma (EH) is a rare vascular neoplasm composed of epithelioid endothelial cells embedded in a distinct myxohyaline stroma. The majority of cases arise within or adjacent to blood vessels of the liver, lungs and extremities. Head and neck involvement is seldom seen. EHs typically present as painful masses that may be associated with edema and thrombophlebitis owing to their vascular origin. Ossification is an uncommon finding that is mostly observed in deeply situated tumors. On histopathologic examination, approximately one-third of cases show nuclear atypia, mitotic activity, marked spindling of cells or necrosis that warrant a malignant designation. We describe an unusual case of malignant EH in a 53-year-old female that was first detected on dental radiographs. A routine screening panoramic film revealed a mixed lesion with speckled internal characteristics in the right carotid artery region. On clinical examination, a firm mass was noted anterior to the sternocleidomastoid muscle, evident only on palpation. Following appropriate diagnostic tests, she underwent resection and a modified radical neck dissection. Microscopic examination showed the classic features of EH with formation of metaplastic bone. Increased mitotic activity and significant necrosis were seen. Metastasis was identified in 1 node. Immunohistochemical analysis showed positive staining for CD31 and CD34. Due to the close proximity of the tumor to the carotid artery, the patient was treated with adjuvant radiation therapy and chemotherapy and...
remains disease-free 6 months post-surgery. Though unusual, vascular neoplasia is a diagnostic consideration for mixed radiolucent-radiopaque lesions presenting in the head and neck soft tissues.

ECTOSENCHYMAL CHONDROMYXOID TUMOR OF THE ORAL CAVITY: REPORT OF THREE CASES MA Copete, MR Darling, TD Daley, University of Saskatchewan, Saskatoon, SK; University of Western Ontario, London

Ectomesenchymal chondromyxoid tumor (EMCT) is a rare neoplasm first described by Smith et al. in 1995. Most tumors present as asymptomatic, slow growing submucosal nodules, particularly in the anterior tongue and infrequently in the posterior tongue. EMCT is histopathologically characterized by a well circumscribed, but unencapsulated, lobular proliferation of round, polygonal, ovoid or fusiform cells, which are present in a myxoid to chondromyxoid stroma that may show areas of hyalinization. The immunohistochemical profile reveals positivity of the lesional cells with variable reactivity patterns for antibodies directed against glial fibrillary acidic protein (GFAP), cytokeratins, S-100 protein and CD-57 in most tumors. Additionally, other reported markers for vimentin, CD56, EMA, SMA, desmin, p63, CD99 and Calponin have also shown variable reactivity. Treatment consists of conservative surgical excision. Limited recurrence potential is observed after complete conservative surgery.

GIANT CEMENTOBLASTOMA TREATED WITH RESECTION R Assi, H Kessler, G Ghali, M Yeoh, Texas A&M Health Science Center-Baylor College of Dentistry, Dallas, TX; LSU School of Medicine, Shreveport, LA, USA

Benign cementoblastoma is a rare odontogenic tumor that often occurs in the mandibular molar area, affecting mostly young adults. Although considered benign, cementoblastoma may be a locally aggressive neoplasm in some cases, with significant bony expansion, pain and swelling. We present a case of benign cementoblastoma in a young male associated with an impacted lower left third molar that was managed with an enbloc resection. A 25-year-old African American male presented with continued pain and swelling following an extraction by a general dentist. Physical examination revealed a left mandibular swelling of about 4x4 cm in size with a lucent border, occupying the left mandibular body, angle, and ramus area and fused with the lower left third molar roots. The clinical differential diagnosis was giantiform cementoma, osteosarcoma and CEOT. An incisional biopsy was suggestive of benign cementoblastoma. An enbloc excision of the lesion was planned. A segmental mandibulectomy from the left first molar region to the left subisgoid area was completed for excision of the lesion. Reconstruction was performed with placement of a reconstruction plate with a crib containing bone morphogenetic protein-2 in a collagen sponge. Post operatively, the patient is progressing well without complications. This case represents a rare example of a locally aggressive benign cementoblastoma in a young patient that required surgical management.

FUTURE STUDIES WILL FOCUS ON THE RELATION BETWEEN C6 CERAMIDE, REDUCED SURVIVING LEVELS AND POTENTIAL INCREASE IN SUSCEPTIBILITY OF HSC-3 CELLS TO VARIOUS ANTI-CANCER AGENTS.

GIANT CEMENTOBLASTOMA TREATED WITH RESECTION R Assi, H Kessler, G Ghali, M Yeoh, Texas A&M Health Science Center-Baylor College of Dentistry, Dallas, TX; LSU School of Medicine, Shreveport, LA, USA

Benign cementoblastoma is a rare odontogenic tumor that often occurs in the mandibular molar area, affecting mostly young adults. Although considered benign, cementoblastoma may be a locally aggressive neoplasm in some cases, with significant bony expansion, pain and swelling. We present a case of benign cementoblastoma in a young male associated with an impacted lower left third molar that was managed with an enbloc resection. A 25-year-old African American male presented with continued pain and swelling following an extraction by a general dentist. Physical examination revealed a left mandibular swelling of about 4x4 cm in size with a lucent border, occupying the left mandibular body, angle, and ramus area and fused with the lower left third molar roots. The clinical differential diagnosis was giantiform cementoma, osteosarcoma and CEOT. An incisional biopsy was suggestive of benign cementoblastoma. An enbloc excision of the lesion was planned. A segmental mandibulectomy from the left first molar region to the left subisgoid area was completed for excision of the lesion. Reconstruction was performed with placement of a reconstruction plate with a crib containing bone morphogenetic protein-2 in a collagen sponge. Post operatively, the patient is progressing well without complications. This case represents a rare example of a locally aggressive benign cementoblastoma in a young patient that required surgical management.

OBJECTIVES: to investigate the effect of C6 ceramide, a sphingolipid metabolite, on cell proliferation and levels of anti-apoptotic cell protein survivin in human HSC-3 OSCC (oral squamous cell carcinoma) cell lines and its potential therapeutic target for OSCC.

Methods: Plain and C6 liposomes were added to the HSC-3 cell cultures; in the conc. range 0.1-50 μM of C6. After incubation for 24 h at 37°C, 5% CO2, cell survival was evaluated by Alamar Blue and Live/Dead viability assays. Survivin levels were measured by ELISA.

Results: Liposomal C6 ceramide treated cells showed decreased cell viability and Alamar Blue assay showed a linear reduction with increased concentration of C6 ceramide. The viability with plain liposomes was 93±5% of the control. For 5 and 10 μM liposomal C6 ceramide, the viability was reduced to 72±3% and 44±0% of untreated cells respectively. Survivin ELISA results showed a decrease of survivin levels with increasing concentrations of C6 ceramide (4462±28 pg/mg protein in untreated cells; 4558±577 pg/mg protein cells treated with plain liposomes, and 3099±72 pg/mg protein at 5 μM C6 ceramide and 1574±279 pg/mg protein at 10μM C6 ceramide).

Conclusions: Liposomal C6 ceramide exerted a desirable effect by reducing cell proliferation, probably because of a decrease in the levels of survivin. Thus, HSC-3 cells are vulnerable to liposomal C6 ceramide in a dose-dependent manner. Further future studies will focus on the relation between C6 ceramide, reduced surviving levels and potential increase in susceptibility of HSC-3 cells to various anti-cancer agents.
requires no treatment and should be differentiated from the more common white plaque of infancy, thrush. We propose the diagnostic term “breast feeding keratosis” for this entity.

PAPILLARY VARIANT OF SQUAMOUS CELL CARCINOMA ARISING ON THE GINGIVA: A SERIES OF 61 CASES WITHIN A LARGE DATABASE OF GINGIVAL SQUAMOUS CELL CARCINOMA S Fitzpatrick, A Newman, I Bhattacharyya, D Cohen, University of Florida, Gainesville, FL, USA

Papillary squamous cell carcinoma (PSCCA) is a rarely occurring variant of squamous cell carcinoma (SCCA) with distinctive exophytic and papillary features and a more favorable prognosis than conventional SCCA. The larynx is the most commonly affected site in the head and neck. The oral cavity, oropharynx, sinonasal tract, and nasopharynx are also affected. Within the oral cavity cases have been reported on the alveolar ridge, oral mucosa, floor of the mouth, ventral tongue, and rarely other areas. We identified 61 cases of gingival PSCCA within the parameters of a larger study of 519 cases of gingival SCCA. We evaluated the clinical and histologic features of these lesions. The average age of the PSCCA patient was 74 years, with a very slight male predominance. The mandible was affected nearly twice as often as the maxilla, and the most common location by far was the mandibular posterior region. Most lesions of those with a timeline reported were present over 2 months in duration. The most common clinical presentation was that of an erythematous or mixed white and red exophytic mass. 62% of submitting clinicians considered a malignant or premalignant lesion in their differential diagnosis, but other clinical impressions included papillomas, reactive gingival lesions, and fungal infections. Histologically, 88% of the lesions were either well or moderately-well differentiated. In conclusion, PSCCA is a rare subtype of SCCA which has been reported infrequently involving the gingiva or alveolar ridges but should be considered by clinicians in the differential diagnosis of papillary gingival masses.

INCREASED MARROW ADIPOSE TISSUE ENHANCES SERUM ADIPONECTIN IN STATES OF CALORIE RESTRICTION E Scheller, W Cawthorn, B Learman, H Mor, B Simon, A Bree, Y Yao, O MacDougald, University of Michigan, Ann Arbor, MI, USA

White adipose tissue (WAT) plays a central regulatory role in energy homeostasis, not only as a site for storage of excess energy, but also as an endocrine organ that impacts whole body metabolism. Marrow adipose tissue (MAT) can comprise up to 70% of total bone marrow in humans. Although early studies concluded that MAT does not have a function, more recent work suggests that increased MAT in response to starvation, osteoporosis, and diabetes may have important endocrine roles. Adiponectin is a 30kDa adipocytokine that was identified as a unique transcript of adipocytes. Paradoxically, despite being one of the most highly expressed transcripts in WAT, circulating adiponectin decreases with obesity and increases in states of decreased body mass such as anorexia. Unlike decreases in WAT, MAT increases during calorie restriction (CR). Thus, we hypothesize that increases in serum adiponectin with CR are driven in part by enhanced marrow adipogenesis. To increase marrow adipogenesis, female control or OCN-Wnt10b transgenic mice were placed on a diet of 30% CR from age 9 to 15 weeks. Whereas conventional markers of WAT, such as leptin and FABP4, were virtually absent in MAT, adiponectin was highly expressed. CR by 30% significantly increased marrow fat in tibias of both control and OCN-Wnt10b animals. Marrow fat accumulation in OCN-Wnt10b mice was lower than in controls. Circulating adiponectin increased in both restricted animal models, but was blunted to a similar extent as the marrow fat in OCN-Wnt10b mice. Our data suggest that MAT contributes substantially to circulating adiponectin. Furthermore, accumulation of MAT during CR may explain the paradoxical increase in adiponectin in lean individuals. (Supported by R24DK092759.)

MIDKINE EXPRESSION IN AMELOBLASTOMAS C Intapa, M Scheper, E Verissimo, M Zhang, A Batista, B Jham, University of Maryland, Baltimore, MD, USA; Federal University of Goias, Goiania; Midwestern University, Downers Grove, IL, USA

Background: Ameloblastoma is a locally aggressive benign neoplasm with a tendency to invade the surrounding tissues and a relatively high recurrence frequency. It is the most common clinically significant odontogenic tumor, with studies from different regions of the world showing it accounts for 9–88% of all odontogenic neoplasms.

Objective: The aim of this study was to investigate the expression of midkine, a heparin-binding growth factor, in ameloblastomas and correlate the results with clinicopathological parameters.

Methods: Cases of ameloblastoma seen at the University of Maryland between 1999 and 2010 were identified. Clinical information was collected regarding age, gender, race and location. Cases were classified as solid, multicystic, unicystic and peripheral. The expression of midkine was assessed using immunohistochemistry, and reactivity was graded in a semi-quantitatively manner. A statistically significant difference was considered to be present at p < 0.05.

Results: A total of 27 cases of ameloblastoma were identified. Midkine was expressed in 84% of the lesions (weak expression was seen in 29%, moderate in 18% and strong expression in 37% of the cases). No statistically significant correlation was observed between expression of midkine and clinicopathological parameters.

Conclusion: Midkine is expressed in the majority of ameloblastomas, suggesting a role of the protein in the development of the tumor. Midkine may possibly serve as a molecular-based therapeutic target for the treatment of ameloblastomas.

A CLINICOPATHOLOGICAL STUDY OF HEAD AND NECK SARCOMAS E Verissimo, A Gomes, L Nascimento, T Almeida, E de Paula, E Mendonca, B Jham, Federal University of Goias, Goiania; Araujo, Jorge Hospital, Goiania, Goias; Midwestern University Downers Grove, IL, USA

Background: Sarcomas are malignant tumors of mesenchymal origin, which account for 1% of all cancers. Lesions of the head and neck account for 5–15% of all adult and 35% of pediatric sarcomas. The combination of rare occurrence and poor prognosis make head and neck sarcomas a challenge for health professionals and highlights the need for a thorough understanding of the clinical and pathological features of these tumors.

Objective: The aim of this study was to describe the profile of head and neck sarcomas seen in a single institution.

Methods: The files of 36 patients with head and neck sarcomas seen between 1987 and 2010 were retrieved from the
archives of the Araujo Jorge Hospital. All lesions had a histological diagnosis of sarcoma primary to the head and neck region. Charts were analyzed and the following information was collected regarding patients and lesions: age, gender, symptoms, signs, location, size, clinical aspect, radiographic description, histological diagnosis, treatment and follow-up information.

**Results:** Patients were 22 females and 14 males, with mean age of 32.1 years. Most lesions presented as a painful tumoral mass in the mandible. Average size at diagnosis was 6 cm. Radiographic imaging of intraoral lesions revealed the majority were osteolytic and destructive. Histologically, the most common subtype was osteosarcoma, followed by chondrosarcoma. The majority of lesions were treated with surgery and postoperative radiotherapy. The average patient follow-up time was 46 months. Of patients with follow-up information of at least 6 months (n=26), 8 were deceased and 18 still alive.

**Conclusion:** Although rare, sarcomas represent an important group of malignant neoplasms and should be considered in the differential diagnosis of head and neck masses.

**GRANULOMATOUS FOREIGN BODY REACTION TO POLY-L-LACTIC ACID FILLER. REPORT OF SIX CASES**

SS Farahani, V Noonan, S Kabani, S-B Woo, Harvard School of Dental Medicine, Boston, MA; Strata Pathology Services, Lexington, MA; Boston University, School of Dental Medicine, Boston, MA, USA

Dermal fillers are often used to smooth out wrinkles and treat facial atrophy. They are classified into biostimulatory, filling, and combined fillers. An example of biostimulatory fillers is poly-L-lactic acid (PLA), a synthetic peptide polymer of the ±-hydroxy-acid family that is commonly used in absorbable sutures. PLA is a resorbable dermal stimulatory agent which stimulates fibroblasts to produce collagen. Although injectable PLA is considered a biocompatible dermal filler, nodules and foreign body granulomas have also been described and this is a report of 6 cases of such an adverse reaction. Patients were female aged 40 to 69 years (median, 55 yrs), all with a history of PLA (Sculptra, Dermik, Berwyn, PA) injection to the nasolabial fold or lip for cosmetic reasons. Except 1 case who presented a nasolabial nodule, all developed firm nodules intraorally (two in the mandibular vestibular mucosa and the other 3 in the maxillary buccal vestibule). Histopathologically, each showed a well-circumscribed, partially encapsulated nodule consisting of nonneocrotizing granulomas with many foreign body-type multinucleated giant cells associated with abundant ovoid, needle-shaped and geometric, refractile foreign materials. Some of this material was identified within the giant cells. Scattered lymphocytes were noted.

**Conclusion:** PLA fillers may migrate from the site of injection to produce intraoral nodules that are foreign body granulomas with a distinct appearance.

**MASSIVE, AGGRESSIVE ADENOMATOID ODONTOGENIC TUMOR (AOT): REPORT OF AN UNUSUAL MANDIBULAR LESION**

H Qari, G Blandell, N Demian, M Covinsky, JE Bouquot, University of Texas School of Dentistry, Houston, TX, USA

**Background:** Since 1905, 700+ examples of adenomatoid odontogenic tumor (AOT) have been reported. It has a strong predilection for females (up to 2.3:1), for the maxilla (1.8:1 vs. mandible) and for young persons (<30 years of age). It is virtually always <3 cm in size and rarely resorbs roots but occasionally displaces them. Since the last major review in 1990, only 4 cases (all mandibular) have been larger than 3 cm.

**Objective:** To present possibly the largest, most aggressive AOT reported.

**Case:** A 37-year-old male presented with a 7x6x4 cm expansive radiolucency of the mandible, extending from the right first mandibular molar to the left first molar, associated with an impacted left canine. The lucency contained scattered small grayish radiopacities, had massively expanded the chin, thinned the cortex considerably and leading to several perforations. The mental nerves were intimately associated with the tumor. Almost all overlying teeth were displaced and all overlying roots were resorbed, with some roots missing as much as half of their structure. At surgery, more than 85% of the lesion was represented by a single fluid-filled cystic space. The lesion was removed by enucleation and the defect was filled with autologous bone; there has been no recurrence to date but only 6 months of follow-up have occurred.

**Conclusion:** This appears to be the largest, most aggressive AOT yet reported.

**AXENFELD-RIEGER SYNDROME: DIFFERENTIAL DIAGNOSIS IN CASES OF OLIGODONTIA**

A Bufalino, M Andrade, A Silva, R Coletta, M Lopes, University of Campinas, Piracicaba, São Paulo, Brazil

Axenfeld-Rieger syndrome (ARS) is a rare autosomal dominant condition characterized by a variety of malformations in the anterior chamber of the eyes, which can lead to blindness. The clinical spectrum also includes systemic malformations and craniofacial and dental features. ARS is caused by mutations in 2 transcription factors, PITX2 and FOXC1, although the underlying genetic defect is unknown in 60% of the cases. We reported herein a 9-year-old girl with oligodontia that led to the diagnosis of a family with ARS. Her medical history showed bilateral congenital glaucoma, and physical examination revealed redundant peri-umbilical skin, corectopia in the right eye, polycoria in the left eye, slightly protruding lower jaw and oligodontia characterized by the absence of 14 teeth. The clinical examination of the family members revealed that her mother presented typical features of ARS, including loss of vision at age 10 years and absence of 14 teeth. Proband’s father and older sister did not show similar alterations. Genomic DNA was extracted from oral mucosa cells and sequencing analysis of PITX2 and FOXC1 exons and their flanking splice junctions was performed. Mutations were not found in both affected members. In conclusion, ARS should be considered in the differential diagnosis of patients with oligodontia, and dentists should be able to recognize this uncommon syndrome. Early diagnosis is essential for an appropriate treatment of the affected patients and genetic counseling.

**CALCIFYING EPITHELIAL ODONTOGENIC TUMOR: REPORT OF A SERIES OF TEN CASES**

J Whitt, B Barker, J Rokos, C Dunlap, University of Missouri, Kansas City, MO, USA

The Calcifying Epithelial Odontogenic Tumor (CEOT) is an uncommon odontogenic tumor arising from odontogenic ectoderm which usually presents in adults. It exhibits a wide variation in radiographic appearance, but most frequently presents as a mixed radiolucent-radiopaque lesion. Approximately 15% of the lesions...
may be expected to recur after conservative local excision. We report a series of 10 cases with an age range from 12 to 77 years (mean, 43 yrs). Six of the lesions arose centrally within bone; 4 arose peripherally within the gingival soft tissue. The tumors were equally distributed between the mandible and maxilla and exhibited a slight female gender predilection. Three of the 4 peripheral lesions arose in females. All central lesions presented as well-circumscribed mixed-density lesions; 1 lesion was markedly radiodense. One peripheral lesion also exhibited a crestal mixed-density radiographic appearance. All of the lesions were located anterior to the molar area. The intra-osseous lesions ranged from 3 to 5 cm. No size information was available for the peripheral lesions; the clinical diagnoses included peripheral giant cell granuloma, peripheral ossifying fibroma and localized gingival fibrous hyperplasia. The relative proportions of the tumor components varied widely from epithelium-predominant, stroma-poor to epithelium-poor, stroma-rich lesions. One intra-osseous lesion exhibited predominately clear epithelial cells. Two of the peripheral lesions exhibited mild cytologic atypia. Histologically, 2 of the lesions were combined odontogenic tumors, exhibiting the histomorphology of both CEOT and another odontogenic tumor (Adenomatoid Odontogenic Tumor in 1 central lesion and Calcifying Cystic Odontogenic Tumor in 1 peripheral lesion).

ENHANCER OF ZESTE HOMOLOG 2 AS A MARKER FOR CARCINOMATOUS CHANGES IN AMELOBLASTIC CARCINOMA R Younis, L Mao, B Levy, M Scheper, Department of Oncology and Diagnostic Sciences, Dental School, University of Maryland Baltimore, MD, USA

Ameloblastic carcinoma is a rare malignant odontogenic tumor that arises de novo or from a pre-existing ameloblastoma. Because of the rarity of ameloblastic carcinoma its immunohistochemical profile is still to be investigated. The diagnosis of ameloblastic carcinoma also can sometimes be a challenge to differentiate from atypical ameloblastoma. We presented before the epigenetic modulator Enhancer of Zeste Homolog 2 (EZH2), which is a methyl transferase enzyme that methylates lysine 27 of histone 3, resulting in gene silencing as a biomarker for early detection of malignancy in oral leukoplakia. In this work we introduce EZH2 as a biomarker for detection of carcinomatous changes in a case of ameloblastic carcinoma. EZH2 shows moderate nuclear staining in ameloblastic carcinoma versus negative staining in ameloblastoma and tooth follicles. The data produced from this study suggests new diagnostic criteria that can help in the diagnosis of ameloblastic carcinoma. In addition it provides better understanding of the underlying molecular profile of ameloblastic carcinoma and opens new avenues for molecular and therapeutic targets.

C-JUN AND PC-JUN EXPRESSION IN ORAL LEUKOPLAKIAS FROM SMOKERS AND NON-SMOKERS J Lima, G. Rabelo, L. Corrêa, S. Sousa, University of São Paulo, São Paulo, Brazil

OSCC is usually preceded by a premalignant stage. The study of these premalignant stages can provide a better understanding of the carcinogenesis. However, most underlying mechanisms remain obscure. Oral epithelial dysplasia is the histopathologic sign of the potential transformation to carcinoma. Tobacco is known to act as a risk factor for the development of OSCC; however, despite this negative potential, there are limited studies comparing smokers and nonsmokers lesions and its relation to the development of carcinoma. It is already known that the main component of the transcription factor AP-1, c-Jun protein and its phosphorylated form (p-c-Jun), participate in the cell cycle and that their inhibition compromises cell proliferation. The aim of this study was to access the role of the smoking habit in the expression of these proteins. For this, 40 cases clinically diagnosed as oral leukoplakias and that presented a moderate or intense degree of epithelial dysplasia and could not be diagnosed as any other diseases were selected. Twenty cases were from smokers (>20 cigarettes/day) and 20 from non-smokers. Histological sections of each lesion were subjected to the streptavidin biotin immunohistochemical method for detection of c-Jun and p-c-Jun. A semi quantitative analysis was performed. There was a significant difference between c-Jun and p-c-Jun in both, smokers (p<0.0001) and non-smokers (p=0.0055). However, the results showed no statistical differences between the expressions of c-jun (p=0.4626) and p-c-jun (p=0.2905) comparing smokers and non-smokers. In conclusion, despite the similarity in the groups, the expressive positivity of the proteins in many cases indicates a possible role in the process of oral carcinogenesis.

DETECTION OF SALIVARY HUMAN PAPILLOMAVIRUS DNA IN HIV-INFECTED PATIENTS WITH ORAL LESIONS: A CLINICOPATHOLOGIC STUDY M Nichols, C Flatz, A Zulaigua, Bering Omega Dental Clinic, Houston, TX; University of Texas School of Dentistry, Houston, TX; Remicahn LLC, Houston, TX, USA

Human papillomavirus (HPV) is commonly detected in the saliva of HIV-infected individuals, but the types are less well defined. The purpose of this retrospective study was to document salivary HPV DNA results with clinical and histopathologic findings in HIV-infected patients with oral lesions. Following IRB approval, all patients from Bering Omega Dental Clinic, who had a salivary HPV DNA test (OraRiskSM HPV, OralDNA Labs) were included. Demographics, HIV exposure, social history, CD4 count, HIV PCR viral load, combined antiretrovirals (CARV), oral lesion diagnosis and HPV DNA results were collected. Results included 31 subjects (mean age, 49 yrs; 29M/2F; 20 white, 6 black, 5 Latino). HIV exposure included 24 MSM, 7 HS with mean CD4 count=433 and 94% on CARV. History of oral sex was 90%; tobacco use was 45%. HPV results were positive in 52% with HPV 16 in 6.5% (tonsillar cancer, condyloma with dysplasia). HPV lesions were diagnosed in 17/31 (76% HPV+), squamous cell carcinoma/moderate to severe dysplasia in 6/31 (33% HPV+), hairy leukoplakia in 1/31 (100% HPV+) while other lesions in 7/31 (lichen planus, fibroma, hyperkeratosis ± dysplasia, erythema migrans) were all HPV-negative. High-risk HPV (16, 68) was documented in 3 subjects; low risk (6, 72, 83, 84, C6P108) in 5; unknown risk (32, C6P8061, unknown) in 8. MSM exposure, oral sex, and low CD4 count were correlated with the presence of any HPV types (p < 0.05). Four patients had dual infections. HPV 72, 83, 84, C6P108, C6P8061 and unknown types were primarily detected in patients with low CD4 counts (<200 mm³). In conclusion, the clinical presence of oral warts was associated with the detection of HPV in saliva. Also, HPV 16 was only detected in HIV patients with oropharyngeal cancer and condyloma with dysplasia.

PERSISTENT EXPOSED NON-VITAL BONE NOT ASSOCIATED WITH BISPHOSPHONATE USE E Peters, A Khan, N Sifideen, University of Alberta, McMaster University, Hamilton, Ontario, Canada
The incidence of bisphosphonate related osteonecrosis of the jaws (BRONJ) in patients taking oral bisphosphonates has been estimated between 0.0004% and 0.06%. Case definition in the incidence studies typically has required the presence of exposed bone for greater than 8 weeks in patients who have been treated with bisphosphonates and with no history of radiotherapy. The objective of this preliminary study was to assess the presentation profile of BRONJ type cases in the absence of bisphosphonate use. All sequestration cases, which were submitted for histopathologic exam, during a 3-year period, before bisphosphonates were approved for clinical use, were reviewed. 48 cases with histories indicating the clinical presentation and suspected cause were included in the study. 34 of these cases (71%) could be attributed to a range of etiologic factors (post-surgical complication, infection, trauma, radiation, eruption) and did not match the BRONJ type profile. A further 14 case (29%) were characterized by idiopathic bone exposure before surgical intervention. 7 cases involved the posterior lingual mandible, 4 cases involved developmental exostoses and 3 cases involved recessed gingiva. In 7 of the 14 cases, lesion duration had been recorded and indicated a mean time of 4.6 weeks (SD= 4.0) before surgical management. In 3 of the 7 cases (lingual mandible = 2; recessed gingiva = 1), the lesions had persisted for over 8 weeks. Thus, a minimal 6% of BRONJ type presentations could be identified from the total sequestration cases. These preliminary results indicate that studies attempting to assess BRONJ incidence need to account for the unknown incidence or background noise associated with BRONJ type sequestrations that occur in the absence of bisphosphonate use.