

#1 - 8:00 AM

LOCALIZED JUVENILE SPONGIOTIC GINGIVAL HYPERPLASIA ORIGINATES FROM JUNCTIONAL GINGIVAL EPITHELIUM- AN IMMUNOHISTOCHEMICAL STUDY

A. Naidu, Texas A&M University - Baylor College of Dentistry, K Lammert, Texas A&M University - Baylor College of Dentistry R Iwase, Texas A&M University - Baylor College of Dentistry R Spears, Texas A&M University - Baylor College of Dentistry I Allon, Tel-Aviv University, Tel Aviv, Israel J Wright, Texas A&M University - Baylor College of Dentistry

Localized Juvenile Spongiotic Gingival Hyperplasia (LJSGH) is a unique gingival lesion that predominantly affects patients in the second decade, with a mean age of 11.8 years. LJSGH is twice as common in females and 84% of cases affect the anterior maxillary gingiva. Histologically LJSGH is characterized by epithelial hyperplasia, spongiosis, inflammatory exocytosis, and a papillary surface architecture, resembling junctional epithelium. Previous researchers showed that junctional epithelium stained positively for CK 8/18, and gingival epithelium was negative. Gingival epithelium was strongly positive for CK1/10, and junctional epithelium was negative. Gingival epithelium typically shows strong reactivity for CK19, but only in basal cells, whereas CK19 reactivity is expressed throughout all strata of the junctional epithelium. Suprabasal cells of gingiva tend to be CK4 positive, whereas junctional epithelium is negative. In this study, it was hypothesized that cytokeratin expression in LJSGH would be similar to junctional epithelium and that gingival fibrous hyperplasia/fibromas, thought to originate in sites with normal surface epithelium, would stain similar to normal gingival epithelium. The immunohistochemical expression of CK 1/10, 4, 8/18 and 19 was semi-quantitatively evaluated in ten cases of LJSGH and ten control cases of fibrous hyperplasia/fibroma. Statistically significant differences were seen between LJSGH samples and the control group, with the staining pattern of LJSGH more closely resembling junctional epithelium ($p < 0.01$). The immunohistochemical staining pattern of cytokeratins in this study supports the hypothesis that LJSGH originates from junctional epithelium, which may be prone to irritation, resulting in inflammation and hyperplasia.

#2 - 8:18 AM

COMPARING NEW AND CURRENT METHODS OF MICROSCOPIC IMAGE PHOTOGRAPHY

Morrison, AS, Emory U, Atlanta, GA, K Magliocca, Emory U

Background: Microscopic image photography in pathology is essential for sharing histopathologic findings in consultation, interdepartmental communication, presentations, rounds, tumor boards, and teaching. Traditionally, images have been captured using photomicroscopes with digital cameras mounted onto a microscope with an adapter. In recent years, whole slide digital scanning has emerged as an alternative to photomicroscopes. Now that cellular phone technologies have advanced to have photographic capability equivalent or greater than many digital cameras, smart phones microscopic photography can be used as an alternative to mounted photomicroscopes and slide scanners for capturing photomicrographs. Design: Sixteen slides were photographed at 20x, 40x, 100x, and 200x magnification to obtain equivalent microscopic images using a mounted photomicroscope, a digital slide scanner, and a handheld smart phone. The time to capture and save the four images was recorded by two users. Results: The average times (min:sec) to obtain images for an inexperienced smart phone microscopic photographer was 3:40 while an experienced smart phone photographer only took 2:58. The average times to obtain images using a traditional microscope-mounted camera were 5:09 and 3:21. The average times to obtain images using digital slide scanning was 4:56 for an experienced user and 12:34 for an inexperienced user. Conclusion: Smart phone microscopic photography was the fastest method when employed by an experienced user in this pilot study. Digital whole slide scanning took the longest time to obtain images for an inexperienced user.

#3 - 8:30 AM

A QUANTITATIVE AND QUALITATIVE APPROACH TO EVALUATE THE EFFECTIVENESS OF RECUTS IN AN ORAL PATHOLOGY LABORATORY

Alqahtani M, U. Florida, Gainesville FL, Islam M, U. Florida, Gainesville FL Montague L, U. Florida, Gainesville FL Bhattacharyya I., U. Florida, Gainesville FL

INTRODUCTION: Recut sections of paraffin embedded tissue blocks submitted for diagnosis are routinely utilized in all pathology laboratories. These recuts improve the orientation of the tissue, when there is insufficient depth &/or are used for clarification of diagnosis. This study was undertaken to quantify the effectiveness of recuts and to evaluate the various reasons for the recut request. **MATERIALS AND METHODS:** The UFCD Oral Pathology Biopsy Service laboratory QA log was searched after IRB approval for recuts performed between 2012-2013. A total of 128 recut requests were identified and of these 113 were included in the study. Each original slide and recuts were examined by 4 investigators and stratified into 4 categories: A) technical errors; B) shallow/insufficient tissue; C) confirmation &/or additional information needed to support original diagnosis; and D) malorientation of tissue. The reviewers then assigned each recut with a score of 0 -no impact on diagnosis, 1- confirmed the diagnosis &/or added minimal additional information, 2-significantly altered or impacted diagnosis. **RESULTS:** The findings were tabulated and analyzed. In brief: 4% (5/113) of recuts were ordered to correct technical errors, 30% (34/113) insufficient tissue, 44% (49/113) for confirmation &/or clarification of diagnosis, and 22% (25/113) due to malorientation. When analyzing the value of recuts on the final diagnosis, we found that 31% of recuts significantly altered the diagnosis, 37% confirmed the diagnosis &/or provided additional information and 32% did not contribute to improving the diagnosis. **CONCLUSIONS:** Our study confirms that recuts are useful and valuable in majority of the cases and is essential in the standard of care in diagnostic oral and maxillofacial pathology.

#4 - 8:42 AM

CHARACTERIZATION OF DIFFUSE LARGE B-CELL LYMPHOMAS OF THE ORAL CAVITY

N Marchese, University of Toronto, Toronto, Canada, I Leong, University of Toronto, Toronto, Canada G Bradley, University of Toronto, Toronto, Canada B Fernandes, University of Toronto, Toronto, Canada A Porwit, University of Toronto, Toronto, Canada

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma (NHL) of the oral cavity. There are two prognostically-defined subgroups of germinal center B-cell (GCB) and of non-germinal center B-cell (non-GCB) origin. A new category of NHL has been recently recognized that has features similar to both DLBCL and Burkitt lymphoma (BL) called B-cell lymphoma, unclassifiable with features intermediate between DLBCL and BL (BCLU), which was not well described in the oral cavity. **Objective:** To immunohistochemically characterize DLBCL of the oral cavity into GCB and non-GCB subtypes using the Hans and Natkunam (LMO2) algorithms and to identify BCLU using fluorescence in situ hybridization (FISH). **Methods:** 120 cases of oral NHL were reviewed and re-classified according to the WHO Classification of Haematopoietic tumours (2008). Immunohistochemistry was performed on cases of DLBCL with antibodies to CD20, CD10, BCL2, BCL6, MUM1, MIB-1, and LMO2. FISH was performed on cases of BCLU to detect c-MYC and IGH/BCL2 translocations. **Results:** Of the 120 cases of oral NHL, 44 were identified as DLBCL and 8 as BCLU. 42 of the 44 DLBCL cases were subtyped. Using the Hans algorithm, 21 cases of DLBCL were GCB (50.0%) and 21 were non-GCB (50.0%). Using the Natkunam algorithm, 32 were GCB (76.2%) and 10 cases were non-GCB (23.8%). **Conclusion:** The GCB subtype of DLBCL was the predominant subgroup of oral cavity NHL as determined by Natkunam algorithm, which seems to be better in determining GC origin. We identified 8 cases of the newly proposed category of NHL, BCLU, in the oral cavity.

#5 - 8:54 AM

CHARACTERIZATION OF EGFR EXPRESSION IN AMELOBLASTIC NEOPLASMS.

Y. LEI, U.OF PITTSBURGH, Susan Müller, Emory U. School of Medicine Elizabeth Bilodeau, U. OF PITTSBURGH

Epidermal growth factor receptor (EGFR) is overexpressed in over 90% of head and neck squamous cell carcinoma, and has emerged as a pivotal therapeutic target. An EGFR monoclonal antibody, cetuximab, has been recently approved by FDA for the treatment of advanced head and neck squamous cell carcinomas. Cetuximab activates immune effector natural killer (NK) cells, and shows significant therapeutic efficacy in a subset of patients. The activation and phosphorylation of pro-survival signal transducer and activator of transcription 3 (STAT3) constitutes a resistance mechanism against EGFR signaling blockade. Ameloblastoma and ameloblastic carcinoma are debilitating diseases that arise from the odontogenic epithelium. But the expression levels of EGFR and phospho-STAT3 in these tumors remain poorly characterized. We stained 10 ameloblastomas and 8 ameloblastic carcinomas with EGFR and phospho-STAT3 antibodies. Staining was interpreted by two pathologists independently, as we previously described. Comparison between two groups was made by Mann-Whitney U test. A p-value of less than 0.05 is considered significant. We showed that EGFR is expressed in both ameloblastoma and ameloblastic carcinoma, and that it is significantly overexpressed in ameloblastic carcinoma ($p=0.0013$). In agreement with previous literature, the constitutively activated phospho-STAT3 is a rare event in untreated patients. We showed phospho-STAT3 staining is generally weak and variably positive in a small fraction of tumor cells of both groups ($p=0.47$). Given the EGFR expression profile of ameloblastic neoplasms, EGFR targeted therapy may be a potentially promising intervening approach. Future study is necessary to elucidate the tumor cells response to cetuximab-mediated anti-tumor effects.

#6 - 9:06 AM

DESMOPLASTIC FIBROMA OF THE MANDIBLE: REPORT OF THREE CASES WITH A REVIEW OF LITERATURE

T Woods, U of Florida, Gainesville, D Cohen, U of Florida, Gainesville N Islam, U of Florida, Gainesville Y Rawal, U of Tennessee, Memphis I Bhattacharyya, U of Florida, Gainesville
DESMOPLASTIC FIBROMA OF THE MANDIBLE: REPORT OF THREE CASES WITH A REVIEW OF LITERATURE. TR Woods, DM Cohen, MN Islam, Y Rawal, I Bhattacharyya, U Florida, Gainesville, FL and U Tennessee, Memphis, TN. The desmoplastic fibroma (DF) is a rare, fibroblastic lesion of bone that histologically resembles the desmoid tumor of soft tissue. Although classified as benign, it frequently demonstrates aggressive behavior, often causing tooth mobility, extensive bone destruction, and has a moderate to high recurrence rate. We present three cases of DF occurring in the mandible: the first in a 13 year old female involving the body of the mandible in the region of #27-#28, the second in a 57 year old female with a lesion apical to tooth #30, and the third in a 20-year-old female involving the left posterior mandible. The clinical, histologic, immunohistochemical and radiographic features of this rare neoplasm are discussed. The challenges encountered in establishing an accurate diagnosis due to significant microscopic overlap with other spindle cell lesions are also detailed. We performed immunohistochemical stains including vimentin, smooth muscle actin, S-100 protein, β -catenin, HHF-35 and proliferation marker, Ki-67 for all 3 cases. The potential for misdiagnosis is high, especially in the early lesions, since immunohistochemistry has been reported in literature to be inconsistent when differentiating DFs from other spindle cell lesions. A comparative review of DF and similar lesions with current considerations in treatment and prognosis is presented.

#7 - 9:18 AM

IN VITRO DISSECTION OF MORPHOGEN GRADIENTS IN EARLY ODONTOGENESIS

C.-C. Li, Harvard School of Dental Medicine, Boston, S. Sant, University of Pittsburgh School of Pharmacy, Pittsburgh A. N. Ford Versypt, Massachusetts Institute of Technology, Cambridge A. Khademhosseini, Harvard Medical School, Brigham and Women's Hospital, Boston R. Maas, Harvard Medical School, Brigham and Women's Hospital, Boston

Introduction: Tooth agenesis seen in many syndromes is associated with dysregulation of morphogen signaling pathways. Morphogen gradients provide positional information to individual cells for differentiation during organogenesis. Inductive morphogens from the dental epithelium, such as bone morphogenetic protein 4 (BMP4) and fibroblast growth factor 8 (FGF8), form local gradients that activate odontogenesis via regulation of specific transcription factors (Msx1 and Pax9). However, concentration-dependent cell responses toward morphogen stimulation in early odontogenesis are not well defined. **Methods:** We established an in vitro platform that involves the generation of morphogen gradients using simple capillary flow in cell-laden gelatin methacrylate (GelMA) hydrogels. GelMA mimics natural tissues and provides an optimal 3D microenvironment. Mouse mandibular mesenchymal cells were encapsulated within the optimized in vitro gradient system with a morphogen gradient (BMP4 or FGF8). A mathematical model was constructed to describe the continuous morphogen gradient. **Results:** The mandibular mesenchymal cells responded to morphogen stimulation and differentiated toward odontogenic fate (e.g. odontoblasts). BMP4 up-regulated Msx1 but down-regulated Pax9 in a dose-dependent manner. FGF8 up-regulated both Msx1 and Pax9 in a dose-dependent manner. A BMP4 gradient then was incorporated with the uniformly-distributed FGF8, showing a synergistic effect on Msx1 expression, and a rescue effect on Pax9 expression. **Conclusion:** This in vitro gradient system can be used to dissect transcriptional responses of key genes in the odontogenic pathway and clarifies how morphogen gradients coordinate with each other, providing us with insights into the underlying mechanisms of tooth agenesis.

#8 - 9:30 AM

PRIMARY SMALL CELL CARCINOMA OF THE PAROTID GLAND: A CASE SERIES

C Fisher, U. Michigan, Ann Arbor, J McHugh, U. Michigan, Ann Arbor P Harms, U. Michigan, Ann Arbor P Edwards, Indiana U., Indianapolis T Danciu, U. Michigan, Ann Arbor

Aim: Small cell carcinoma (SmCC) of salivary gland origin is a rare malignant tumor composed of small, undifferentiated cells that exhibit neuroendocrine differentiation, and has a predilection for the parotid. SmCC accounts for less than 1% of all salivary gland tumors. Salivary gland SmCC must be differentiated from metastatic SmCC and Merkel Cell Carcinoma (MCC). Non-pulmonary neuroendocrine carcinomas stain positive for CK 20 and one or more neuroendocrine markers. Merkel cell polyomavirus (MCPV) is a relatively new diagnostic tool used to study Merkel cell carcinoma. The aim of this study is to document three new cases of primary SmCC of the parotid gland. **Methods:** One case of parotid SmCC was retrieved from the School of Dentistry OMP Biopsy Service and four from the UMHS Department of Pathology. Two cases were metastatic in nature and excluded. Clinical workups and histories revealed no signs of cutaneous Merkel cell carcinoma for the remaining patients. IHC analysis of the cases was performed with neuroendocrine and epithelial markers, as well as for MCPV, which was PCR verified. **Results:** The three cases were diagnosed in two male and one female patient with an average age of 76. One patient presented with local metastasis to an intraparotid lymph node; none had distant metastasis. All were treated with total parotidectomy. IHC analysis demonstrated immunoreactivity for CK20, in a paranuclear dot-like pattern (3/3), CAM 5.2 (3/3) and neuroendocrine markers (Chromagranin 2/3, NSE 3/3, CD 56 2/3). All tumor cells were negative for CK 7 and TTF-1. MCPV was positive in two of the three cases. **Conclusion:** Our cases are consistent with the clinical and histological findings in the literature. Our study also supports the findings that MCPV is not specific to MCC.

#9 - 9:42 AM

NEUTROPHILS INCREASE ORAL SQUAMOUS CELL CARCINOMA INVASION THROUGH AN INVADOPODIA-DEPENDENT PATHWAY

M Magalhaes, U. of Toronto, J Glogauer, U. of Toronto C Sun, U. of Toronto G Bradley, U. of Toronto M Glogauer, U. of Toronto

Neutrophils have recently been shown to promote invasion and correlate with a poor prognosis in different cancers including head and neck squamous cell carcinomas. In this study we analyze the effects of neutrophils in the invasion of oral squamous cell carcinoma (OSCC) using a combination of conditioned media, direct and indirect co-culture of human peripheral blood neutrophils and UMSCC47 cells (OSCC cell line). Invasion and matrix degradation were determined using a modified in vitro invasion assay and an invadopodia assay respectively (Magalhaes et al 2011). Direct UMSCC47 and neutrophil co-culture increased UMSCC47 invasion in the presence of an EGF gradient. Indirect co-culture increased UMSCC47 invasion even in the absence of EGF, suggesting that neutrophils created a signaling gradient for UMSCC47 cells. Invasion was completely blocked by the broad-spectrum MMP inhibitor GM6001 (ilomastat) while specific inhibition of MMP9 reversed the increase mediated by neutrophils. Conditioned media from co-cultures of UMSCC47 and neutrophils also increased the invasion of naïve UMSCC47 cells. Invadopodia assays show that neutrophils promote a significant increase in the number of invadopodia and matrix degradation by UMSCC47 cells. Our results show that neutrophils increase the invasiveness of OSCC both directly and indirectly through the activation of invadopodia. These results suggest that the presence of neutrophils in the oral environment may modulate the clinical behavior of OSCC.

#10 - 9:54 AM

SYNCHRONOUS MULTIFOCAL PERIPHERAL AND INTRA-OSSEOUS CALCIFYING EPITHELIAL ODONTOGENIC TUMORS

M. Cuevas-Nunez, Harvard School of Dental Medicine. Boston, MA, S. Kabani, Center for Oral Pathology, StrataDx, Lexington, MA A. Jones, Private practice, Fall River, MA V. Noonan, Boston U. Henry M. Goldman School of Dental Medicine, Boston, MA. Center for Oral Pathology, StrataDx, Lexington, MA

The calcifying epithelial odontogenic tumor (CEOT) is a benign uncommon neoplasm occurring both as intra-osseous and extra-osseous variants. The intra-osseous type is more common and represents (96%) of all reported cases. Multifocal CEOTs have been previously reported occurring as multiple intra-osseous tumors in three patients, as well as bilateral peripheral gingival tumors in another patient. We report an unusual case of a 37 year-old female with synchronous intra-osseous and peripheral CEOTs affecting different sites. The intra-osseous tumor was located in the anterior mandible and presented as a well-demarcated radiolucency between the roots of teeth #25 and #26. The peripheral tumor was confined to the soft tissue overlying the left posterior mandibular alveolar ridge in the area of teeth #18 and #19 with associated cupping of the superior cortical bone on radiographic examination. Histopathologically, both tumors were identical and were characterized by a proliferation of polyhedral epithelial cells arranged in small and large islands and strands in a stroma of dense fibrous connective tissue. The cells had prominent eosinophilic cytoplasm and distinct intercellular bridging. Pools of Congo red-positive, amorphous, extracellular, amphiphilic material were appreciated throughout the lesions. Discrete foci of calcification were also noted. The etiology of multifocal CEOTs in a subject is poorly understood, however; this phenomenon when coupled with CEOT-like areas reported in association with dental follicles, lends support to the link of these tumors with tooth formation.

#11 - 10:06 AM

ANALYSIS OF MATRIX METALLOPROTEINASE LEVELS AND ACTIVITY IN ORAL VESICULOEROSIVE DISEASE

Mair Y, Aguirre A., Department of Oral Diagnostic Sciences, SUNY at Buffalo, Buffalo, NY, Jhamb T, Department of Oral and Maxillofacial Medicine & Diagnostic Sciences, Case Western Reserve University School of Dental Medicine, Cleveland, OH Fantasia JE , Department of Dental Medicine, Division of Oral and Maxillofacial Pathology, North Shore-LIJ Health System, Manhasset, NY Kramer JM, Department of Oral Biology, SUNY at Buffalo, Buffalo

Oral vesiculoerosive disease (VE), such as lichen planus and pemphigoid, are immune mediated pathoses. VE disease is treated with non-specific immunosuppressants. These medications often have untoward effects and do not address disease etiology. It is important to identify mechanisms critical to disease pathogenesis in order to design targeted therapeutics. Matrix metalloproteinases 2 and 9 (MMP2 and MMP9) are elevated in oral lesional biopsies of VE patients. However, there have been no studies examining systemic levels of MMP2 and MMP9 in this patient population, and the ability of these enzymes to degrade substrate (activity) in disease is also unknown. Our objective is to perform a pilot study to determine whether levels and activity of MMP2 and MMP9 are elevated in the sera and saliva of patients with VE disease in order to identify novel therapeutic targets. Methods: We recruited patients with a known or suspected diagnosis of VE disease (n=9), and age and sex matched healthy controls (n=19). We collected sera and saliva, and performed ELISAs to measure MMP levels. We used gelatinase zymography and ELISA based activity assays to determine MMP2 and MMP9 activity. Results: Preliminary results demonstrate MMP2 and MMP9 are present and active in sera of healthy control and VE patients. MMP2 levels are elevated in both sera (p = 0.005) and saliva (p = 0.012) of VE patients. There was no difference in MMP9 levels or activity in VE patients as compared to controls. Conclusion: MMP2 and MMP9 are detected in both sera and saliva of healthy controls, and MMP2 is elevated in VE patients. Therefore, therapeutics that diminish MMP activity may have efficacy in the treatment of VE disease.

#12 - 10:18 AM

CENTRAL ANGIOLEIOMYOMA OF THE JAW BONES: A SERIES OF FOUR CASES AND REVIEW OF THE LITERATURE

A. Kalgi, New York hospital Queens, New York, A. Kalgi, New York Hospital Queens A. Kumar, New York Hospital Queens B. Krost, J. Stein, R. Reich, New York Hospital Queens P. Freedman, New York Hospital Queens

Angioleiomyoma is a benign smooth muscle tumor arising in the walls of arteries and veins, found most commonly in the uterus, gastrointestinal tract and skin. In the oral cavity, they are found most frequently as soft tissue lesions on the lips, palate, tongue or gingiva. Intraosseous oral angioleiomyomas are exceedingly rare with only seven cases reported. Only one case of extragnathic intraosseous angioleiomyoma was found in the English literature. Intraosseous oral angioleiomyomas are most commonly found in the posterior mandible and present as a unilocular or multilocular radiolucency, with either ill-defined or well-defined sclerotic borders. Here we present a series of four cases of intraosseous oral angioleiomyomas to add to the seven cases already published. Cases 1 and 2 were asymptomatic, multilocular radiolucent lesions of the mandibular right premolar region. Cases 3 and 4 were asymptomatic, unilocular radiolucent lesions of the anterior mandible and anterior maxilla respectively. Interestingly, all four patients were women in their fifth and early sixth decades. Only one case (case 3) was reported to have caused expansion. Biopsies of the lesions revealed well delineated tumors composed of a collection of numerous vascular channels with muscular walls. In areas, the smooth muscle of the vascular walls streamed into the supporting stroma of the tumor. Three of the four cases were treated by conservative surgical excision. Surgery for the fourth case has been scheduled for in the near future. Recurrences are rare as long as the lesion is completely excised.

#13 - 10:30 AM

DIRECT IMMUNOFLOUORESCENCE TESTING RESULTS IN CASES OF ORAL DYSPLASIA AND SQUAMOUS CELL CARCINOMA

L. Montague, U. Florida, Gainesville, I. Bhattacharyya, U. Florida, Gainesville M. Alqahtani , U. Florida, Gainesville MN. Islam, U. Florida, Gainesville D. Cohen, U. Florida, Gainesville S. Fitzpatrick, U. Florida, Gainesville

Oral premalignant and malignant lesions may occasionally demonstrate histologic features that mimic oral lichen planus (LP). For clinically lichenoid lesions, direct immunofluorescence testing (DIF) is recommended to confirm a diagnosis of LP (fibrinogen positivity along basement membrane zone). Though fibrinogen positivity supports a diagnosis of LP, similar findings may be noted in dysplasia and squamous cell carcinoma (SCC). This phenomenon has not been well described in the literature. The purpose of this study was to examine fibrinogen positivity in oral dysplasia (OD) and SCC and identify clinical patterns of expression. The UF Oral Pathology Biopsy Service archive was searched from 2003 to 2013 for all cases with DIF coded as verruco-papillary hyperkeratosis (VPHK), OD, atypical epithelial proliferation, SCC and verrucous carcinoma (VC). Fibrinogen staining, demographic and clinical information were collected. A total of 163 cases were identified, of which 68 cases were fibrinogen positive. The majority were VPHK (22 cases, 32.4%), followed by low grade OD (21, 30.9%). A total of 11 fibrinogen positive cases of SCC, including VC, were identified. Females made up 66.2% of cases, while 33.8% were males. The majority of fibrinogen positive lesions occurred on the buccal mucosa (22, 32.4%) and gingiva (21, 30.9%). Pathologists should be aware that fibrinogen positivity may be seen in premalignant and malignant oral lesions. Significant overlap of histologic features and DIF findings in lichenoid lesions may complicate discrimination, particularly between true LP and low grade OD or VPHK. Therefore, when cytologic and morphologic atypia are encountered, pathologists should be cautious about rendering a diagnosis of lichen planus, regardless of fibrinogen positivity.

#14 - 10:42 AM

HPV 16 IN ORAL EPITHELIAL DYSPLASIA

S Almazrooa, Harvard School of Dental Medicine, Massachusetts , M Lerman, Harvard School of Dental Medicine, Massachusetts & StrataDx, Massachusetts N Lindeman, Brigham and Women Hospital, Massachusetts D Zepf, Brigham and Women Hospital, Massachusetts S Woo, Harvard School of Dental Medicine, Massachusetts & StrataDx, Massachusetts, Brigham and Women Hospital, Massachusetts

Background: The role of high-risk human papilloma virus (HPV) in oropharyngeal and cervical neoplasia has been well established and HPV 16 is the most common sub-type. However, there have been limited studies evaluating HPV in oral epithelial dysplasia (OED). The objective of this study is to identify specific types of virus in HPV-associated OED. Methods: Cases of HPV-associated OED were identified from the archives of StrataDx, a private surgical pathology laboratory in Lexington, MA. Only cases with specific histopathology for HPV-associated OED and that were positive for p16 and by in situ hybridization for high risk types of HPV were further analyzed. DNA was isolated from tissue sections using QIAgen QIAamp DNA Tissue Kits and samples were digested overnight. DNA underwent amplification and digestion with restriction enzymes and was run on a polyacrylamide gel. Digestion patterns were then visually compared to a database of known HPV type digestion patterns for identification. These studies were performed at Brigham and Women's Hospital in Boston, MA. Results: There were 27 specimens included in the analysis, of which the histopathology on 19 had been previously reported. Of the 27 cases, the quantity of DNA extracted was insufficient for analysis in 10 cases. Of the 17 cases remaining, there were 13 men (M:F ratio 3.3:1) with a mean age of 58.6 years. The most common site of involvement was the ventral tongue/floor of mouth (65% of cases). HPV 16 was identified in 15/17 (88%) cases. One case each was associated with HPV 33 (6%) and HPV 58 (6%). Conclusion: HPV 16, the most common HPV type associated with oropharyngeal and cervical cancers was identified in 88% of 17 cases of HPV-associated OED; other high risk types included HPV 33 and 58.

#15 - 10:54 AM

PRIMARY MUCOUS PRODUCING PAPILLARY ADENOCARCINOMA OF SALIVARY GLAND ORIGIN

A Bhattacharya, Texas A&M U Baylor College of Dentistry, Dallas, J Fantasia, Long Island Jewish Medical Center, NY R Carlos, Centro Clinico de Cabeza y Cuello, Guatemala City, Guatemala F Pires, State University of Rio de Janeiro, Brazil R Miller, ProPath, Dallas, TX J Wright, Texas A&M U Baylor College of Dentistry, Dallas

Primary intestinal-like adenocarcinoma is a recently reported entity in the major salivary glands. The microscopic architecture of these tumors is identical to colonic adenocarcinoma, however their immunoprofile (CK7 and Muc-1 positive) is distinct from their colonic counterparts (CK20, CDX2 and Muc-2 positive). We sought to determine if this entity exists in minor salivary glands, and we present a report of six cases from intraoral sites. The tumors were well circumscribed with papillary columnar to cuboidal epithelium and mucous producing cells similar to colonic adenocarcinoma. The tumors demonstrated diffuse IHC positivity for CK7 and were negative for colonic markers CDX2, MUC2, CK20, villin, SATB2 and nuclear beta-catenin. We ruled out metastatic adenocarcinoma from thyroid and lung (TTF-1), kidney (Pax8), breast (GATA3, GCDFP-15, S100 and ER). These tumors were negative for mammaglobin a marker of mammary analog secretory carcinoma. We believe primary mucous producing papillary adenocarcinoma is the most appropriate designation for this entity. These tumors are distinct from colonic type sinonasal adenocarcinoma which has been reported in base of tongue, as well as metastatic colonic adenocarcinoma. It is essential to recognize this entity as a primary salivary neoplasm as it has important consequences for patient management.

#16 - 11:06 AM

REAPPRAISAL OF BENIGN LYMPHOEPITHELIAL SIALADENITIS FOR EVIDENCE OF EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA.

R Werner, Naval Postgraduate Dental School, Bethesda MD, G Wang, Joint Pathology Center, Silver Spring MD S Zhang, Joint Pathology Center, Silver Spring MD P Shick, Joint Pathology Center, Silver Spring MD R Foss, Naval Postgraduate Dental School, Bethesda MD

Background: Lymphoepithelial sialadenitis or benign lymphoepithelial lesion (BLEL) represents the initial presentation of acquired salivary mucosa-associated lymphoid tissue and is generally considered the precursor lesion of extranodal marginal zone B-cell lymphoma (EMZBCL).

Objective: The aim of this study was to evaluate the features of historic cases of BLEL for evidence of monoclonality and cytogenetic alterations. Methods: Twenty cases of BLEL involving major salivary glands (18 parotid/2 submandibular) were retrieved from the Joint Pathology Center Tissue Repository and evaluated for morphologic, immunophenotypic, molecular and cytogenetic abnormalities associated with EMZBCL. Results: Cases comprised 19 female patients and 1 male patient, ages 16-78 years (median age 47). All cases displayed lymphoepithelial lesion formation with epitheliotropic monocytoid lymphocytes. Fourteen cases demonstrated monoclonal heavy chain gene rearrangements (PCR) and 8 cases demonstrated increased copy number of chromosome 3 (FISH). No cases revealed translocations involving the MALT1 gene. Epitheliotropic B cells exhibited a CD20, CD79a and PAX 5 positive B cell immunophenotype; aberrant CD43 expression was present in 17 cases (85%) and 2 cases demonstrated aberrant CD5 expression. Conclusion: A significant portion of historic cases classified as BLEL demonstrate features indistinguishable from EMZBCL based on current diagnostic criteria, including morphology, heavy chain rearrangement and cytogenetic alterations.

#17 - 11:18 AM

TRIP13 ENHANCES DNA REPAIR TO PROMOTE TREATMENT RESISTANCE IN CANCER.

R. Banerjee, U of Michigan, Ann Arbor. , N Russo, , U of Michigan, Ann Arbor. M Liu, , U of Michigan, Ann Arbor. V Basrur, , U of Michigan, Ann Arbor. E Bellile, , U of Michigan, Ann Arbor. N Palanisamy, , U of Michigan, Ann Arbor. C Scanlon, , U of Michigan, Ann Arbor. E Van Tubergen,, U of Michigan, Ann Arbor.

RC Inglehart, T Metwally, RS Mani, A Yocum, MK Nyati, RM Castilho, S Varambally, AM Chinnaiyan, and NJ D'Silva. U of Michigan, Ann Arbor. Head and neck cancer (HNC) is a common, aggressive, chemoresistant cancer with a high recurrence rate and mortality, but the mechanism of treatment resistance remains unclear. Aim: The goal of this study was to establish the mechanism by which TRIP13 promotes treatment resistance. Methods: TRIP13 was nominated as an oncogene using bioinformatics. Expression and function were investigated in HNC cells. Mass spectrometry and network analysis were performed to identify TRIP13's binding partners and the signaling mechanism, respectively. Results: Overexpression of TRIP13 in non-malignant cells leads to malignant transformation. High expression of TRIP13 in HNC leads to aggressive, chemoresistant tumors and enhanced repair of DNA damage. Stable downregulation of TRIP13 was incompatible with cell viability. In vivo, doxycycline-induced shTRIP13 arrested tumor growth compared to control tumors. Mass spectrometry identified DNA-PKcs complex proteins that mediate non homologous end joining (NHEJ), as TRIP13 binding partners. Using repair reporter systems, we uncovered that TRIP13 promotes NHEJ and chemoresistance. Overexpression of TRIP13 sensitizes HNC to DNA-PKcs inhibitors in vivo. Conclusion: Taken together, TRIP13-overexpressing HNCs have non-oncogene addiction to DNA-PKcs. Thus, DNA-PKcs is a target to overcome treatment resistance in TRIP13-overexpressing tumors with competent homologous recombination. Funding: DE019513, DE018512, and DE022567.

#18 - 11:30 AM

SHINING LIGHT FROM LAB TO OPERATING ROOM - THE COOLS STUDY

C Poh, U. of British Columbia and Vancouver, S Durham, U. of British Columbia, Vancouver P Brasher, U. of British Columbia, Vancouver K Berean, U. of British Columbia, Vancouver C MacAulay, BC Cancer Agency Research Centre, Vancouver M Rosin, Simon Fraser University

High local recurrence rate followed by aggressive disease is a major concern for patients diagnosed with oral cancer. The objective of the Canadian Optically-guided approach for Oral Lesions Surgical (COOLS) trial is to investigate the efficacy of an emerging optical technology using Fluorescence Visualization to guide surgical margins and reduce local recurrence rates. Methods:

Funded by the Terry Fox Research Institute (TFRI), the COOLS study is a multi-centre phase III randomized controlled trial with a total of 400 patients. From September 2010, 7 cancer centres from coast to coast have joined the COOLS trial and are actively recruiting eligible patients across Canada. Each eligible patient will complete baseline questionnaires on socio-demographic factors, risk factors, cancer history, and quality of life prior to the surgery. Results: Up to January, 2014, 357 patients have received assigned surgical interventions (89% of the projected) with 12 patients reached the primary endpoint, local recurrence; 28 patients failed the first pass margin; 14 patients developed regional lymph node metastasis; and 9 patients died of disease. The median follow-up time is 12 months. The follow-up rate (every 3 months for the first 2 year and 6 months up to 5 years) is ~90%. Additionally, screening logs have been used to monitor site accrual activities.

Quality assurance for the adoption of the new technology is reinforced through frequent checking images taken at the initial and intraoperative assessments. Conclusion: The trial is not only an excellent example of translational research but also an integral in building the first-ever pan Canadian surgical network for oral cancer control. If validated, it can potentially change clinical practice.

#19 - 11:42 AM

MECHANISM OF PERINEURAL INVASION IN HEAD AND NECK CANCER

C Scanlon, U of Michigan, Ann Arbor, C Scanlon, R Banerjee, RC Inglehart, M Liu, N Russo, A Hariharan, E Van Tubergen, S Corson, I Asangani, C Mistretta, AM Chinnaiyan, NJ D'Silva U of Michigan, Ann Arbor Perineural invasion (PNI) is correlated with poor survival in head and neck cancer (HNC), and leads to sensory disturbances and pain. The mechanisms of PNI are poorly understood due to inadequate in vivo models to study nerve-tumor interactions. Elucidation of mechanisms will identify treatment targets. Objectives: a) Present a novel in vivo model of PNI; b) Use this model to investigate neural-tumor interactions in HNC progression; c) Investigate potential anti-PNI therapy. Methods: To investigate the role of GAL and its receptor (GALR2) in tumor-nerve interactions, we used murine xenograft tumors and a new in vivo model. We used ChIP, immunoblot and ELISA to determine the mechanism of GALR2-induced PNI. Findings: Meta-analyses determined that the neuropeptide galanin (GAL) is upregulated in HNC, and GAL expression correlates with poor survival. Nerves promote HNC growth and metastasis and initiate PNI via release of GAL, which induces GALR2 in HNC cells. Stimulated GALR2 induces NFATC2-mediated transcription and secretion of GAL and PGE2. In a feedback loop, HNC-released GAL promotes neuritogenesis. PGE2 promotes HNC invasion. Clinical data show proteins involved in this cascade correlate with poor survival. Importantly, the GALR2 inhibitor M871 blocks PNI. Conclusions: This study provides evidence of dynamic nerve-tumor interactions driving PNI. Targeting GALR2/GAL disrupts nerve-tumor crosstalk, suggesting these proteins as PNI treatment targets. Funding: DE019513, DE018512, DE022567 and UM-ADVANCE (NJD), DE021293 (CSS), NIDCD DC009982 (CMM).

#20 - 11:54 AM

CDH11, A NOVEL BIOMARKER OF EMT IN HNC: DISCOVERY USING AN IN SILICO APPROACH, AND VALIDATION

R Inglehart, U of Michigan, Ann Arbor, C Scanlon, U of Michigan, Ann Arbor N Russo, U of Michigan, Ann Arbor A Hariharan, U of Michigan, Ann Arbor R Banerjee, U of Michigan, Ann Arbor N D'Silva, U of Michigan, Ann Arbor

Epithelial-mesenchymal transition (EMT), a change of non-motile epithelial cells into motile cells, occurs during embryonic development and wound healing. In cancer, EMT facilitates invasion and metastasis. The clinical significance of EMT in progression and prognosis of head and neck cancer (HNC) is increasingly recognized. HNC is a disease with poor prognosis, unchanged in the last ~5 decades. Discovery of new oncoproteins will provide potential new treatment targets. Aim: This study's goal is to present a bioinformatics-based strategy to suggest new EMT biomarkers and evaluate cadherin-11 (CDH11) with this strategy. Methods: Meta-analyses of gene array datasets evaluated the expression of established EMT biomarkers in HNC (ACTA2, SNAI2, TGFB1 and VIM), as well as a novel putative EMT biomarker, CDH11. Expression of these markers in cancer versus normal tissues, and correlation with clinical outcome were determined. CDH11 expression was evaluated via immunohistochemistry on human HNC cell lines and a tissue microarray. Results: In meta-analyses, CDH11 was overexpressed in cancer compared to normal tissue and in samples from patients with metastases who died within 5 years of diagnosis. In validation studies, CDH11 was overexpressed in HNC cell lines. Moreover, CDH11 was overexpressed in intensity and proportion in human HNC versus normal tissue. Conclusions: Bioinformatics analyses of existing datasets can be used to nominate novel biomarkers in HNC, which can be validated by immunohistochemistry on human HNC tissue. Funding: DE019513, DE018512, DE022567 (NJD) and DE021293 (CSS).

#21 - 12:06 PM

ARE ATYPICAL JUVENILE GINGIVAL EPITHELIAL HYPERPLASIAS (JUVENILE GINGIVAL KERATOACANTHOMAS) REALLY SQUAMOUS CELL CARCINOMAS AND VICE VERSA? CONTRADICTIONARY CLINICAL AND MOLECULAR FINDINGS.

I Koutlas, U of Minnesota, M Lingen, U of Chicago S Binder, UCLA R Gopalakrishnan, U of Minnesota P Argyris, U of Minnesota X Li, UCLA J Wright, Baylor College of Dentistry

Background: There are rare atypical juvenile gingival squamous proliferations (AJGSP) reported as pseudoepitheliomatous hyperplasia (PEH) and intraoral keratoacanthoma (IKA) that appear indistinguishable from reported cases of juvenile squamous cell carcinoma of the gingiva (JSCCG).

This distinction, as it will be presented, is subjective, however, it leads to considerably different treatment approaches. Herein, we present our clinicopathologic experience on AJGSP, critically review the literature on AJGSP and JSCCG and discuss molecular findings. Materials and methods: Three cases, 2 diagnosed as AJGSP and 1 as IKA, are described. Gene expression pattern was investigated by multiplex qRT-PCR that apparently distinguishes cutaneous PEH from SCC.

Results: All 3 cases affected young males of 5-17-years with no history of trauma to the area. Clinically, 2 manifested as subgingival expansile masses, while the third was an exophytic granular/verruroid lesion. Conservative surgical excision was performed with no recurrences being reported in a follow-up period between 8-27 months. Interestingly, qRT-PCR revealed that the expression of C15orf48 (NMES1) was significantly higher than that of KRT9, thus suggesting a SCC profile. Conclusions: 1) AJGSP/IKA lesions are not pseudoepitheliomatous hyperplasias. 2) Although the molecular method utilized herein supports the diagnosis of SCC, based on clinicopathologic features and their behavior, such lesions resemble cutaneous KA more than conventional SCC. 3) Based on recent evidence that KA is molecularly different from SCC we opine that it is of great value to further study and define the molecular signature of such lesions highlighting their distinction from oral SCCa.

#22 - 12:18 PM

A COMPARATIVE STUDY OF ORAL HAMARTOMA AND CHORISTOMA

I.Kaplan, Rabin Medical Center, Tel-Aviv Sourasky Medical Center and Goldschleger School of Dental Medicine, Tel-Aviv U, I.Allon, Tel-Aviv U B.Shlomi, Tel-Aviv Sourasky Medical Center and Tel-Aviv U V.Raiser, Tel-Aviv Sourasky Medical Center S.Kleinman, Tel-Aviv Sourasky Medical Center D.M.Allon, Rabin Medical Center and Tel-Aviv U

Aim: To describe a new large series of hamartomas and choristomas of the oral mucosa and jaws, compare clinical and microscopic characteristics, analyze the literature and discuss the challenges in diagnosis. Materials and methods: Retrospective analysis, cases diagnosed 2000-2012, and literature search. Results: 61 new cases and 154 from the literature were included. The age ranged from infancy to old age, (mean 43 years), with a female predominance. The lesions most frequently occurred in the tongue, lips and palate, and exhibited limited growth potential. Hamartoma and choristoma were composed of either a single tissue type or were mixed. The majority of choristomas were single tissue type (60%), of which respiratory, cartilaginous and gastric were most prevalent. Epidermal/hairy choristoma were the most prevalent mixed choristomas. The vast majority of hamartomas (81%) exhibited multiple tissue types, most frequently neurovascular hamartoma. Other common components in multiple tissue hamartoma were smooth muscle and adipose tissue. The majority of the single tissue type hamartomas were composed of smooth muscle. Conclusion: Due to the rarity of these lesions and the wide variety and combination of structures, the correct classification of an individual lesion as hamartoma or choristoma may be complex. Differentiating choristoma from hamartoma depends to a great extent on the recognition of the normal tissues expected at every individual location.