



American Academy of Oral
& Maxillofacial Pathology

| Essay Program

Monday - May 17, 2010
8:00 am – 12:30 pm

Salon AB

Essay Abstracts – Monday, May 17, 2010

#1 – 8:00 am

AUTOSOMAL DOMINANT MESOMANDIBULAR FIBRO-OSSEOUS DYSPLASIA. I. Koutlas, A. Petryk, S. Kyrkanides. U Minnesota, Minneapolis, SUNY, Stony Brook. A hereditary congenital condition characterized by a fibro-osseous lesion sharing radiographic and histologic features with fibrous dysplasia and affecting the middle aspect of the mandible is presented. The condition was initially described by El Deeb, Waite and Gorlin (Congenital monostotic fibrous dysplasia - a possibly autosomal recessive disorder. J Oral Surg 1979;37:320) in two siblings, a male and a female. However, there is sufficient evidence that the disorder is autosomal dominant since it has been encountered in two of four children, both males, of the female propositus and one child, also a boy, of the male propositus. All patients presented at birth or right after birth with slow enlargement of the middle part of the mandible. Radiographs from affected individuals have shown mesomandibular enlargement with a “ground-glass” appearance. Histologically, samples from all patients revealed woven bone proliferation in a cellular fibroblastic stroma. Interestingly, both propositi, now adults in their 30s, have no evidence of jaw lesions either radiographically or clinically thus indicating that the condition is probably self-limiting. An autosomal dominant mode of inheritance with apparent male predilection is favored. The molecular basis of this condition is currently unknown. However, the location of the lesions in the middle aspect of the mandible suggests dysregulation of Bone Morphogenetic Protein (BMP) signaling since BMPs regulate mandibular morphogenesis in utero, particularly in the medial region. Thus, a mutation analysis of genes in BMP pathway, including BMP ligands, receptors, and downstream targets Msx1 and Msx2 may provide insight into the pathogenesis of this disease.

#2 – 8:12 am

PRIMARY T-CELL LYMPHOMAS OF THE ORAL CAVITY. S.Eljack, R.Reich, S.Kerpel, P.Freedman. New York Hospital Queens, New York. Most lymphomas that arise in the oral cavity are of B cell origin. Less than 10% of primary oral non-Hodgkin’s lymphomas (NHL) are T-cell in origin. They represent a unique and rare group of primary oral lymphomas. We present ten new cases of oral T-cell lymphoma. Six of the ten patients were female with an age range of 42 to 74 years and a mean age of 60. Six of the lesions were located in the tongue, two in the upper lip, two in the lower labial mucosa, two in the palate, two in the mandibular gingiva, one in the buccal mucosa and one in the floor of the mouth. All cases were diagnosed as Peripheral T-cell Lymphoma, NOS with the exception of one case that was diagnosed as Extranodal Natural Killer/T cell lymphoma, nasal type. EBV infection was determined by in situ hybridization for EBV-encoded RNA (EBER) and by immunohistochemistry for the EBV antigen latency membrane protein (LMP). EBV was detected in both the HIV positive patient and the NK/T cell lymphoma. Expression of EBER and not LMP in the HIV patient was noted. These results appear to be in accordance with previously reported studies. EBV exhibits marked tropism for B lymphocytes but infection of T lymphocytes appears to be a rare event. NHLs of B-cell origin in immunosuppressed patients often contain EBV. The role EBV plays in the pathogenesis of T-cell lymphoma is not well defined. EBV involvement in HIV-related T-cell lymphomas has not been widely reported and may represent a further manifestation of opportunistic EBV infection arising in the HIV-immunocompromised host. More studies are needed to further understand these oral T cell lymphomas and their interaction with EBV to better determine their prognosis and effective treatment approaches.

Essay Abstracts – Monday, May 17, 2010

#3 – 8:24 am

EPITHELIOID HEMANGIOENDOTHELIOMA OF THE ORAL CAVITY: REPORT OF 2 CASES. S. Fitzpatrick, R. Kuklani, D. Cohen, I. Bhattacharyya. U Florida, Gainesville. Epithelioid hemangioendothelioma is a rare neoplasm of uncertain malignant potential characterized by a proliferation of endothelial cells with epithelioid-cell like morphology. This tumor has primarily been reported to occur in the soft tissues of the extremities and occasional reports in the lung, liver, bones and skin are found. It is distinctly unusual in the head and neck region, especially the oral cavity with less than 30 cases reported in literature. Due to its histologic similarity to other entities occurring in the oral cavity this lesion may pose diagnostic difficulties. We report a series of two cases of epithelioid hemangioendothelioma occurring in the oral cavity to add to the collective literature. Case #1 is from a 21 year-old male with a mandibular gingival lesion, and Case #2 is from a 53 year-old male with an intra-osseous radiolucency of the mandible. The second case is of particular interest as very few of the previously reported cases are intra-osseous examples. We report the salient clinicopathologic and immunohistochemical features of these cases. In addition, we discuss the importance of correctly diagnosing this unusual neoplasm due to its variable prognosis and potential for uncertain biologic behavior.

#4 – 8:36 am

MELANOCYTIC NEVI OF THE ORAL CAVITY: A CLINICOPATHOLOGIC STUDY OF 84 CASES. L Ferreira, H Kessler, A Readinger. Baylor College of Dentistry, Dallas, Baylor University Medical Center, Dallas. Oral melanocytic nevi (OMN) are benign melanocytic proliferations of the oral mucosa. They are usually classified in five types: junctional, compound, intramucosal, blue nevus and combined. It is known that melanomas may arise from melanocytic nevi of the skin; however, the risk of transformation for oral nevi has not been determined. The purpose of this study is to report 84 cases of OMN retrieved from the files of the Oral Pathology service of Baylor College of Dentistry. We analyzed the data as to histologic type, location, presence of clinical pigmentation and configuration, as well as patient age, sex and race. Intramucosal nevus was the most common type (57.1%), followed by common blue nevus (23.8%), compound nevus (8.3%) and junctional nevus (3.6%). Combined nevus and cellular blue nevus were extremely rare (2.4% each). The hard palate was the most commonly affected site (38.1%), followed by the buccal mucosa (17.86%), vermillion border (17.86%) and gingiva (11.9%). We also report a case of intramucosal nevus with lipomatous-like changes and neurotization on the gingiva. In addition, we report two cases of junctional dysplastic nevus, one on vermillion border of the lip and the second on the hard palate. OMN and early developing melanoma can be clinically indistinguishable; therefore all unexplained pigmented lesions of the oral cavity should be biopsied. Melanocytic lesions presenting dysplastic or atypical changes should be completely excised.

Essay Abstracts – Monday, May 17, 2010

#5 – 8:48 am

CXCL13 IN SJÖGREN'S SYNDROME: A NOVEL BIOMARKER OF DISEASE. J Kramer, T Rothstein. Long Island Jewish Medical Center, New Hyde Park, The Feinstein Institute for Medical Research, Manhasset. Introduction: Sjögren's Syndrome (SS) is a rare autoimmune dyscrasia. Primary SS (pSS), or sicca syndrome, affects salivary and lacrimal glands predominantly, while secondary SS (sSS) occurs in conjunction with other autoimmune connective tissue disorders. In addition to reduced salivary and lacrimal function, serious systemic aspects of the disease are recognized. Care for SS patients is palliative, as no established therapeutics target the immune dysfunction directly. Initially, T cells were considered key mediators of disease; currently an important role for B cells is emerging, as B cell abnormalities are seen systemically and within salivary glands. However, the contribution of B cells to SS is poorly understood. In order for B cells to function most efficiently, they must be recruited to specific sites where they interact with other cells and secrete mediators to orchestrate immune responses. CXCL13 is a B cell chemokine that is elevated in many autoimmune diseases. Accordingly, we hypothesized that CXCL13 is upregulated during SS progression, and may serve as a valuable biomarker of disease. Methods: We quantified CXCL13 by real time PCR and ELISA at various disease time points using pSS and sSS models. Results: CXCL13 transcript and protein levels increase with disease severity in salivary tissue and serum, respectively. Moreover, CXCL13 co-localizes with lymphocytes in salivary tissue, and serum CXCL13 correlates with saliva levels during late stage disease. Conclusion: These data indicate that CXCL13 in salivary tissue and/or sera may be pathogenetically involved in SS disease and may serve as a marker of SS progression and severity. Therapeutic targets of CXCL13 may provide an innovative approach in the management of this debilitating disease.

#6 – 9:00 am

VIRAL G PROTEIN-COUPLED RECEPTOR UPREGULATES ANGIOPOIETIN-LIKE 4 PROMOTING ANGIOGENESIS AND VASCULAR PERMEABILITY IN KAPOSI'S SARCOMA. B Jham, T. Ma, J. Hu, E. Friedman, J. Basile, A. Sodhi, S. Montaner. U. Maryland, Baltimore, Johns Hopkins U, Baltimore. Kaposi's sarcoma (KS) is an enigmatic vascular tumor thought to be a consequence of dysregulated expression of the human herpesvirus-8 (HHV-8 or KSHV)-encoded G protein-coupled receptor (vGPCR). Indeed, transgenic animals expressing vGPCR in just a few cells manifest vascular tumors histologically identical to human KS through a remarkable paracrine mechanism. Both human and vGPCR experimental KS lesions are characterized by prominent angiogenesis and vascular permeability attributed to the paracrine release of angiogenic mediators, most notably vascular endothelial growth factor (VEGF). To date, the relative contribution of these paracrine mediators to the angiogenic and exudative phenotype of KS lesions remains unclear. Here we show that vGPCR upregulation of the VEGF/KDR conduit is not sufficient to explain the potent angiogenesis and vascular permeability observed in KS. Rather, we demonstrate that vGPCR upregulation of Angiopoietin-like 4 (ANGPTL4) plays a prominent role in promoting the angiogenic and exudative phenotype of this tumor. Inhibition of ANGPTL4 effectively blocks vGPCR promotion of angiogenesis and vascular permeability in vitro and tumorigenesis in vivo. These observations suggest that ANGPTL4 is a previously unrecognized target for the treatment of patients with KS. As angiogenesis and increased vessel permeability are common themes in all solid tumors, these results may have a broad impact on our understanding and treatment of cancer.

Essay Abstracts – Monday, May 17, 2010

#7 – 9:12 am

DEVELOPMENT OF A WELL DOCUMENTED DATABASE FOR PATIENTS WITH ORAL BISPHOSPHONATE RELATED OSTEONECROSIS OF THE JAWS. K Magliocca, R Cohen, J Green, E Lewis, J Ojha, M Islam, R Kuklani, I Bhattacharryya, D Cohen. U Florida, Gainesville, Washington U, St. Louis, U Detroit, Detroit, U Indiana, Indianapolis. Bisphosphonates are commonly used pharmaceutical agents in the management of diseases involving high bone turnover. Intravenous bisphosphonates are associated with a high incidence of bone necrosis in the jaws also called bisphosphonate related osteonecrosis or BRON. Only about 2 to 3 % of the patients with BRON take the oral preparations. As a major referral center we have accumulated detailed information on 34 patients with this complication and with funding from Merck and Co. have initiated a study to create a detailed database of these patients. We use the AAOMS guidelines for defining the disease (exposed necrotic bone in the oral cavity for 6 to 8 weeks, unresponsive to therapy in a patient on any of the high potency bisphosphonates). We document the radiographic changes associated with BRON and any changes that may precede bone exposure (pre-osteonecrosis). Triggers such as extractions, presence of lobulated tori, prominent mylohyoid ridge etc. are examined. Importantly, the time of initiation of oral bisphosphonate therapy, duration of therapy, the presence of periodontal disease and the onset of osteonecrosis have been documented.

#8 – 9:24 am

MODULATION OF JAW BONE STEM CELL PRECURSORS BY ITS UNIQUE MECHANOBIOLOGY MIGHT EXPLAIN ITS VULNERABILITY TO BISPHOSPHONATE RELATED OSTEONECROSIS OF JAW. P Arany, J Umanzor, S Pernia, D Mooney. Harvard School of Engineering & Applied Sciences, Boston. Of the four commonly speculated mechanisms for BRONJ namely, repetitive micro-trauma, primary osteoclastic dysfunction, anti-angiogenic effects and a primary bacterial infection from oral commensal microflora, the osteoclastic dysfunction and anti-angiogenic effects do not explain the jaw site specificity while the minimal inflammation noted with associated microorganisms inundates the infectious theory. The most plausible explanation is the rigorous, repetitive and cyclic stretch regimen of the jaw bones making them more susceptible to failure of bone homeostasis in the presence of bisphosphonates in the osteoprogenitor compartment as compared to other skeletal bone sites. We subjected two osteoprogenitor cell lines, RAW 264.7 and D1 to various stretch regimens simulating the rigorous jaw versus appendicular skeletal motions in the presence of bisphosphonates and assessed cell proliferation and differentiation. We found a significant decrease in cell proliferation of D1 (osteoblast progenitors) but surprisingly a robust proliferative response in the RAWs (osteoclast progenitors) in response to the drug. Similarly, we observed a decrease in Osteoblast differentiation while an increase in Osteoclast differentiation was noted. While this increase in number and differentiated osteoclasts is paradoxical to the presence of necrotic bone observed with BRONJ, we are presently exploring the molecular pathways and functionality of these neo-differentiated osteoclastic population using in vitro assays. From our observations, we report for the first time that the rigorous stretch regimens in the presence of bisphosphonates can lead to a perturbation of the jaw bone homeostatic mechanisms which, in turn, would result in BRONJ.

Essay Abstracts – Monday, May 17, 2010

#9 – 9:36 am

ANALYSIS OF BONE ACTIVITY OF JAWS USING SCINTIGRAPHY ON PATIENTS BEFORE, DURING AND AFTER TREATMENT WITH IV BISPHOSPHONATES: A RETROSPECTIVE STUDY. N Handoo, J Hellstein, S Vincent, M Finkelstein, Y Menda, M Zimmerman. U Iowa, Iowa City. During the early stages of BON, areas of reduced uptake of technetium-99 methylene diophosphonate on scans are consistent with the decreased level of vascularity of the bone. However, with disease progression, scintigraphy is able to show areas of radionuclide uptake representative of osteoblastic hyperactivity. However, increased uptake of technetium-99 in the scintigraphy of the jaws of patients who receive bisphosphonates should always be considered as an indicator of probable BON. The purpose of this retrospective study is to correlate nuclear medicine study findings in relationship to rate of inflammation and bone activity prior to dispensing any IV bisphosphonates and identify any potential confounding or evolving changes thereafter. This retrospective study involved a review of a patient's previous medical record and bone scintigraphies which were images made for initial metastatic workup and subsequently compared to images after the commencement of any bisphosphonate regimen to establish a baseline for further readings. Review of all available follow-up images was also carried out. The amount of uptake of the radiotracer was graded as 0 (no uptake), 1 (mild), 2 (moderate), 3 (intense). Results: The study showed that base grade and cumulative dose with statistically significant results. A three-way correlation to see the effect of base grade and cumulative dose on the jaw shows that it is twice more likely to see changes in mandible than maxilla. The presence of pre-existing "hot-spots" in the jaws prior to bisphosphonate therapy makes future identification of BON difficult. It was also seen that series of scintigraphs of same subject showed changes and possibility of predicting BON.

#10 – 9:48 am

THE HISTOPATHOLOGY OF CHRONIC ISCHEMIC BONE DISEASE (CIBD)-PARAMETERS AND DISEASE CLASSIFICATION. J Bouquot, R McMahon. U Texas, Houston, Valparaiso, Indiana. Over the past 3 decades our understanding of the histopathology of ischemic bone disease has dramatically improved but a classification system has not been well established. We present current concepts of CIBD histopathology and propose a useful disease classification. This summary is based on: review of a convenience sample of >11,000 jawbone marrow samples from a large archival oral pathology database; an extensive literature review; and collaboration with well known medical experts in osteonecrosis. Ischemic bone death is represented by focal (not scattered) loss of osteocytes and is not found in most jaw CIBD. Marrow changes include: wispy (not dense) ischemic myelofibrosis streaming between adipocytes; variation in adipocyte size; dilated marrow capillaries, typically with few remaining erythrocytes and with passive endothelial cells; few, if any, chronic inflammatory cells; occasional mast cells; oil cysts; granular cytosol in nonviable adipocytes; fatty microvesicles; intramedullary cavitation; frequent intravascular thrombi; focal hemorrhage (microinfarction); plasmotaxis (serous ooze); and calcific/proteinaceous detritus. While microscopic features are similar, a distinction between inflammation and CIBD can usually be made and some lesions will show both diseases. A suggested CIBD classification system includes: avascular necrosis, bone marrow edema, regional ischemic osteoporosis, ischemic myelofibrosis, ischemic osteosclerosis, ischemic marrow atrophy (honeycombed bone), intramedullary fibrous scar, and ischemic cavitation. The microscopic parameters are distinct enough to allow a confident diagnosis of CIBD and distinguish it from inflammatory marrow changes. A classification system is proposed.

Essay Abstracts – Monday, May 17, 2010

#11 – 10:00 am

NON-INVASIVE DETECTION OF ANEUPLOID CELLS CAN PREDICT THE MALIGNANT POTENTIAL OF ORAL LICHEN PLANUS. A Hirshberg, N Yarom, T Shani, I Kaplan, M Vered, G Rechavi, N Amariglio, L Trakhtenbrot. Tel Aviv U School of Dental Medicine, Tel Aviv, Rabin Medical Centre, Petah-Tiqva, The Chaim Sheba Medical Center, Tel-Hashomer. The malignant potential of OLP has been the subject of controversy in the literature. The present study aimed to evaluate the presence of chromosomal numerical aberrations in cells collected by brush sampling from OLP patients for early detection of potentially malignant cells even before cytologic changes are apparent by traditional histopathology. Brush samples from affected and non-affected mucosa of 57 patients with OLP and 41 control subjects were simultaneously analyzed for morphology and fluorescent in-situ hybridization (FISH) using chromosomes 2 and 8 centromeric probes. Over 2% aneuploid cells (ACs) were detected in 14 OLP patients (24.5%); in 10 (17.5%) over 5% of the cells were aneuploid. ACs were also detected in the normal looking mucosa in 7 patients. Three patients developed squamous cell carcinoma in 5 years follow-up; the brush sample of these patients contained a significant number of ACs. In the control group over 2% ACs were detected only in 3 subjects (7%). OLP carry an increased risk for chromosomal instability. Identifying aneuploid cells in a brush sample and the combined morphological and FISH analysis can increase the specificity in predicting the malignant potential of OLP.

#12 – 10:12 am

ZD6474 IS AN EFFECTIVE CHEMOPREVENTIVE AGENT IN THE MOUSE 4-NQO MODEL OF ORAL CARCINOGENESIS. M Lingen, G Zhou, R Hasina, L Martin, K Kasza. University of Chicago, Chicago. Despite numerous advances in treatment, the 5-year survival rate for head and neck squamous cell cancer (HNSCC) has remained largely unchanged for the last 50 years. This poor outcome is due to a number of variables including the development of multiple primary tumors. Therefore, it is essential to supplement early detection with effective chemopreventive strategies. Using the carcinogenic agent 4-Nitroquinoline 1-Oxide (4-NQO) to produce HNSCC in a mouse model, we tested the hypothesis that ZD6474 is an effective chemopreventive agent in a pre-clinical animal model of HNSCC. CBA mice were treated with 4-NQO (100 ug/ml) in their drinking water for a period of 8 weeks. The mice were then randomized to either no treatment or oral lavage of ZD6474 (25 mg/Kg/day) for 24 weeks (total time of experiment 32 weeks). At the completion of the study, the proportion of mice with Dysplasia or HNSCC was significantly different between the two treatment groups (96% in the control and 28% in the ZD6474 group; Fisher's exact test $p < 0.001$). Similarly, the proportion of animals with HNSCC was significantly different between the two treatment groups (71% in the control and 12% in the ZD6474 group; Fisher's exact test $p < 0.001$). In addition, animals treated with ZD6474 displayed a lower proliferative index, a decrease in microvessel density, and the inhibition of phosphorylation of EGFR and VEGFR2 when compared to the control mice. These data support the hypothesis that ZD6474 may be promising chemopreventive agent for individuals at risk for developing HNSCC.

Essay Abstracts – Monday, May 17, 2010

#13 – 10:24 am

ISOLATION OF COMPONENTS OF SQUAMOUS CELL CARCINOMA (SCC) PARENCHYMA AND STROMA FOR FUNCTIONAL STUDIES. Z Kurago, E Wagner, L Ramanathapuram, EL Lamb, JH Lee. NYU, New York, U South Dakota/Sanford Health. Malignant cell success depends in part on the support of its microenvironment. The microenvironment of oral squamous cell carcinoma is complex and the interactions between the various components are poorly understood. Our long-term goal is to provide a system for ex-vivo testing of treatments that target both the parenchyma and the stroma of SCC, and potentially enable individualized approach to patient treatment. The purpose of the current study is to develop an ex-vivo approach to the analysis of the stromal composition of SCC and the interactions between the parenchyma and stroma. To do this, fragments of a HPV-negative squamous cell carcinoma of the tongue were processed, sectioned and stained by H&E and immunohistochemistry. Several fragments were explanted in complex media to support various cell types. A variety of culturing conditions, assays and antibody-based analyses were used. We found SCC cells and multiple mesenchymal cell populations, including fibroblasts, macrophages, dendritic cells, lymphocytes, neutrophils, and cells with characteristics of smooth muscle and of endothelium. Some mesenchymal populations were highly migratory. Several cell types were persistent in culture for 2+ months, which facilitates multiple tests. Our studies currently focus on stromal fibroblasts and monocyte lineage cells. Functional studies include responsiveness to microbial stimuli, migration assays, assessment of colony formation, and organotypic cultures to compare the functions of tumor-associated and normal mesenchymal counterparts and their impact on SCC cell survival and migration.

#14 – 10:36 am

LOSS OF DYSKERIN FUNCTION DISRUPTS THE ACCUMULATION OF SUBSETS OF SMALL NUCLEOLAR RNA AND MICRORNA. F. Alawi, P Lin. U Pennsylvania, Philadelphia. Dyskerin is a multifunctional protein that is commonly upregulated in neoplasia, including oral squamous cell carcinoma (OSCC). Dyskerin binds to and stabilizes non-coding RNAs, including a subset of small nucleolar RNAs (snoRNA), which are characterized by a common H/ACA secondary structure. Since dyskerin is a ubiquitous protein, we hypothesized that its loss of function would reduce the accumulation of all H/ACA snoRNA, irrespective of cell type. To test this hypothesis, we transfected UM-SCC1 OSCC cells and U2OS osteosarcoma cells with dyskerin siRNA; siRNAs directed against GAPDH and a non-specific target served as negative controls. Forty-eight hours later, total RNA was extracted, reverse transcribed, and subjected to real time PCR analysis. Loss of dyskerin function significantly reduced the levels of three randomly selected H/ACA snoRNA, including U17A, U19, and U66, by more than 2-fold in both cell lines relative to the controls. In contrast, the levels of C/D box snoRNA, small nuclear RNU5A and miR-let-7g remained essentially unchanged; dyskerin is not known to bind to these RNA. However, dyskerin was recently shown to directly bind to microRNA (miRNA) sequences that are embedded within and processed from H/ACA snoRNA. MiRNAs are a class of small non-coding RNA that regulates post-transcriptional gene expression. We have now shown for the first time that loss of dyskerin also significantly decreased the levels of the miRNA miR-664, miR-1248 and miR-1291, and their corresponding precursors, respectively. The roles of these dyskerin-regulated non-coding RNA in tumorigenesis are not currently known. Nonetheless, these findings suggest new and novel avenues of investigation into the molecular mechanisms by which dyskerin may contribute to neoplasia.

Essay Abstracts – Monday, May 17, 2010

#15 – 10:48 am

AUTOANTIBODIES TO P63 IN A CASE OF ORAL SPINDLE CELL SQUAMOUS CELL CARCINOMA. L Solomon, N Laver, D Zoukhiri. Tufts U, Boston. Spindle cell squamous cell carcinoma (SCSCC) is a rare, bimorphic, malignant neoplasm of the upper aerodigestive tract and skin. This tumor is composed of a squamous cell carcinoma and a malignant spindled component, thus diagnosis on H&E sections alone presents a challenge. This case also had serendipitous findings of tissue bound and serum autoantibodies on direct and indirect immunofluorescence (IF) respectively. Objectives: To report the immunohistochemical (IHC) findings in a case of oral SCSCC and to further investigate the nature of the patients circulating autoantibodies using an enzyme linked immunosorbent assay (ELISA). Findings: IHC showed the carcinomatous portion of the tumor expressed pankeratin, EMA and E-cadherin; the sarcomatoid component expressed vimentin, SMA and N-cadherin; both carcinomatous and sarcomatoid portions of the tumor expressed p63 and CK34BE12. Direct and indirect IF showed autoantibodies in a stratified epithelial specific-antinuclear antibody (SES-ANA) pattern; ELISA showed these patient antibodies are of the IgG class, and are immunoreactive with recombinantly produced deltaNp63. Conclusions: Studies have shown that overexpression of the p63 gene is reported in 85% of oral SCC cases and that overexpressed p63 functions as an oncogene. This case shows p63 is useful as an IHC marker of both the squamous and sarcomatoid phenotypes in SCSCC. In addition, we present evidence of a humoral immune response to the overexpressed p63 protein. Autoantibodies to p63 were previously demonstrated in chronic ulcerative stomatitis (CUS) and lichen planus (LP). This case raises the question whether p63 autoantibodies may represent potentially malignant cases of CUS or LP. Ongoing studies are exploring the role of p63 autoantibodies as SCC biomarkers.

#16 – 11:00 am

PITFALLS IN DIAGNOSTIC TESTS FOR HIGH-RISK HUMAN PAPILLOMAVIRUS. P DeVilliers, A Andea, E Kerr, L Novak. U Alabama, Birmingham. High-risk human papillomavirus (HR-HPV) is associated with some cases of oral and pharyngeal invasive squamous cell carcinoma (OPSCC). The preferred methods for detecting high-risk HPV are in-situ hybridization (ISH) and polymerase chain reaction (PCR). There are conflicting reports on the reliability of immunohistochemical (IHC) detection of HPV types 6, 11, 16, 18, 31, 33, 42, 51, 52, 56 and 58 as well as the significance of p16 as a surrogate marker of HR-HPV status. This study evaluated the potential utility of combining IHC for HPV and p16 as less expensive alternative testing methods to ISH or PCR for detecting high-risk HPV. Immunohistochemical expression of p16 (MTM Laboratories, Westborough, MA) and HPV (Dako, Denmark) was analyzed in tissue blocks from patients recently diagnosed with oral and pharyngeal epithelial dysplasia or invasive squamous cell carcinoma with confirmed HPV status by ISH and PCR. Cases were evaluated for distribution, extent, and degree of intensity of p16 and HPV IHC stain. Cases of OPSCC which were originally diagnosed as high-risk HPV-positive by PCR were also positive by ISH and were strongly positive for p16. Cases of squamous papilloma and dysplasia which were diagnosed as low-risk HPV-positive by PCR showed only focal staining for p16. The degree of p16 expression correlated with the severity of dysplasia. Cases of OPSCC with negative high-risk HPV expression by PCR/ISH were negative for p16. All cases were HPV-negative by immunohistochemistry. These data imply: a) immunohistochemical expression of p16 is a reliable surrogate marker for high-risk HPV expression in OPSCC; b) high-risk HPV detection by ISH is a reliable alternative when PCR testing is not available; c) HPV detection by IHC is not dependable.

Essay Abstracts – Monday, May 17, 2010

#17 – 11:12 am

THE ROLE OF DIRECT VISUAL FLUORESCENT EXAMINATION (VELSCOPE) IN TUMOR MARGIN DELINEATION AND ROUTINE SCREENING FOR ORAL CANCER. K McNamara, A Agrawal, T Teknos, E Ozer, E Evans, C Allen, J Kalmar. Ohio State U, Columbus. VELscope is a commercially available oral cancer screening system based on principles of tissue fluorescence. It has been proposed that direct visual fluorescent examination (DVFE) of the oral cavity may be a useful adjunct to conventional oral examination (COE), however, evidence for this role is lacking. In addition, DVFE reportedly improves tumor margin delineation in the operating room. We present initial results from a two-arm study to evaluate DVFE in both surgical margin delineation and in routine screening of the oral cavity. 20 patients presenting for surgical excision of prior biopsy-confirmed oral epithelial dysplasia or squamous cell carcinoma were included in the high-risk study arm. Lesional tissue margins were assessed by both COE and DVFE and punch biopsy was used to provide histopathologic correlation. 33.3% of tumors exhibited positive DVFE extension beyond the clinically visible tumor margin and 58.3% of these extensions demonstrated microscopic evidence of premalignancy (sensitivity = 64%; specificity = 62%). The general population study arm consisted of 40 patients presenting for routine dental care. Study subjects received a comprehensive COE followed by DVFE and all positive DVFE areas were referred for scalpel biopsy. DVFE positivity was not significantly related to biopsy evidence of cancer or precancer (P=0.0016). These results confirm that DVFE may be useful in tumor margin delineation during surgical management of patients with oral (pre)cancer. False positive test results, however, may limit the utility of VELscope as a routine screening device.

#18 – 11:24 am

KERATOAMELOBLASTOMA AND SOLID VARIANT OF KERATOCYSTIC ODONTOGENIC TUMOR. F Kratochvil, J Stewart, C Kleinegger. Oregon Health & Science U, Portland. The diagnosis of ameloblastoma or keratocystic odontogenic tumor (odontogenic keratocyst) is usually a routine matter for the practicing oral and maxillofacial pathologist due to well-established microscopic criteria. There are a number of cases reported as keratoameloblastoma (KAB) or solid keratocystic odontogenic tumor (SKOT) where this distinction is not so clear-cut. Less than 15 cases of KAB have been reported. Three cases of a SKOT have been documented in the literature. This is a report of a case that demonstrates the dilemma that a pathologist may face in distinguishing between these two rare microscopic presentations of two of the most common odontogenic neoplasms. During a routine dental examination, a 25-year-old woman was discovered to have an asymptomatic, 1.0 cm ovoid radiolucency in the right mandibular body between the roots of vital teeth #28 & #29. The lesion was biopsied and a microscopic diagnosis of “odontogenic keratocyst, solid variant” was rendered. Microscopic criteria as well as the clinical significance for the diagnosis of KAB and SKOT will be discussed.

Essay Abstracts – Monday, May 17, 2010

#19 – 11:36 am

BILATERAL CALCIFYING EPITHELIAL ODONTOGENIC TUMORS OF THE MANDIBLE: A CASE REPORT AND REVIEW OF THE LITERATURE. A McLean, C Kleinegger, F Kratochvil. Oregon Health & Science U, Portland. First described by Pindborg in 1955, the calcifying epithelial odontogenic tumor (CEOT) is a benign, locally invasive neoplasm of odontogenic epithelium without odontogenic ectomesenchyme. This lesion is uncommon, with only about 200 cases reported in the literature. Radiographically, CEOTs present as uni- or multilocular mixed lucent/opaque lesions of varying size. CEOTs typically appear as solitary lesions. In rare instances, multiple lesions may occur within the same patient. We report the case of a 39-year-old Hispanic female, presenting with bilateral mandibular mixed radiolucent/radiopaque lesions associated with three impacted molars. Bilateral incisional biopsies revealed findings that supported the diagnosis of CEOT, including islands, nests and cords of epithelial cells within a fibrous to myxoid stroma; the presence of amyloid-like material; and Liesegang ring calcifications. This unique case demonstrates the ability of CEOTs to occur synchronously within the same jaw. Radiographic findings and histopathology of the current case and a review of the literature will be presented.

#20 – 11:48 am

A CASE REPORT OF AN EXTRANODAL HISTIOCYTIC SARCOMA PRESENTING IN THE ORAL CAVITY. B Accurso, K McNamara, W Marsh, C Allen, J Kalmar. Ohio State U, Columbus. Histiocytic sarcoma (HS) is a rare neoplasm that often presents as an extranodal mass of the GI tract, skin, or soft tissue. Multifocal presentations including nodal involvement have been rarely reported. We report a 65-year old male who presented with a 1-month history of a gingival mass surrounding an implant in the left posterior mandible. The lesion had exhibited rapid growth and was firm to palpation. The patient's medical history was notable for kidney and lung masses. Two months prior, a needle core biopsy of the renal lesion was signed out descriptively as "histiocytic and lymphocytic infiltrates," with a recommendation to obtain a larger sample. A biopsy of the gingival lesion demonstrated sheets of medium to large mononuclear cells with vacuolated to foamy eosinophilic cytoplasm. The nuclei demonstrated pleomorphism with vesicular chromatin, prominent eosinophilic nucleoli, and numerous as well as abnormal mitotic figures. Immunohistochemical studies demonstrated strong lesional cell positivity for CD68, CD163, CD4, and CD45RO. Variable positivity was demonstrated with lysozyme and MPO; Ki67 was expressed in 70-80% of lesional cells. Probes for CD1a, CD79a, CD138, S100, CD21, CD117, and cytokeratins were negative, as was a Leder stain. To the best of our knowledge, this is the 2nd case in the English language literature of a HS in the oral cavity confirmed by immunohistochemistry, and the first as part of multifocal disease. It is an aggressive neoplasm with a poor response to therapy. The majority of patients present at a late stage (III/IV), and most will succumb to progressive disease.

Essay Abstracts – Monday, May 17, 2010

#21 – 12:00 pm

AMORPHOUS BASOPHILIC DEPOSITS IN THE NODULAR LESION OF LIP: REPORT OF TWO CASES WITH HISTORY OF RESTYLANE INJECTION. S Farahani, S-B Woo. Harvard School of Dental Medicine, Boston. Many fillers have been used for reducing facial skin lines, and for providing lip augmentation, one of which is hyaluronic acid (HA), a non-animal-based material. There are two main commercial forms of HA: Restylane (Q Med, Sweden), produced by microbiologic engineering techniques, and Hyaloform (Biomatrix, USA), an extract derived from rooster combs. Although HA is non-toxic and non-immunogenic, hypersensitivity and granulomatous foreign body reactions have been reported as adverse reactions against this material. We report two patients (females, aged 55 and 57) who presented with firm nodular lesions of the lip (one in upper lip, the other in lower lip) clinically diagnosed as adenoma, fibrous hyperplasia, or inflammatory minor salivary gland lesion. Histopathologically, both cases showed pools of amorphous hematoxyphilic material surrounded by densely collagenized connective tissue with no inflammation or foreign body reaction. The Alcian blue stain confirmed the presence of acid mucopolysaccharides such as hyaluronic acid. Both patients had undergone lip augmentation with Restylane (Q Med, Sweden) before. Conclusion: Restylane (Q Med, Sweden) is an inert filler that may persist at an injection site, resulting in a tumor-like nodule.

#22 – 12:12 pm

A RETROSPECTIVE REVIEW OF MINOR SALIVARY GLAND SIALOLITHIASIS. N Narayana, J Casey. UNMC College of Dentistry, Lincoln. A review of the literature shows that sialoliths (SL) of minor salivary glands (MISG) are infrequent compared with those of major salivary glands (MASG). AIMS: This study evaluated the frequency of SL in the MISG in the files of the University of Nebraska Medical Center (UNMC) Oral Pathology Biopsy Service documenting agreement or lack thereof between the clinical and histologic diagnoses. Material and methods: All cases with a final diagnosis of SL from 1987 through 2009 were reviewed. Results: 103 cases (0.3%) with a final diagnosis of SL were identified from 38,472 cases during this period. Among SL, the MISG SL formed 64 %, occurring most commonly in Caucasian males (59%) with a mean age of 64 yrs. The upper lip (56 %) was the most common location compared with the cheek (30 %) and lower lip (14%). 20% of the clinical diagnoses matched the histologic diagnosis. In 76% of SL of MISG, the clinical diagnosis included mucocele, benign mesenchymal lesions, phlebolith and salivary gland tumors. Conclusion: We saw fewer SL MASG as compared with MISG. There was a statistically significant difference between the clinical and histologic diagnostic agreement in MASG as compared with MISG. The SL MASG is correctly diagnosed clinically more often (92%) than MISG (20%). SL in the MISG was more frequent at ages above 60 yrs compared with SL in MASG. Lower lip lesions occurred at a younger age as compared with those of the upper lip and cheek. This review demonstrates that SL MISG occurs more often than clinically suspected and should be considered in the differential diagnosis of nodules in the upper lip, cheek and lower lip.

