

AAOMP

ESSAY PROGRAM

April 24 – 25, 2006

San Antonio, Texas

Essay Program 1

Monday, April 24, 2006

#1 8:00 a.m.

SMOOTH MUSCLE HAMARTOMAS IN THE TONGUES OF YOUNG CHILDREN

PA Kreiger, LE Ernst, F Alawi, PA Russo. Children's Hospital of Philadelphia, Philadelphia, PA

Smooth muscle hamartomas of the tongue have been reported very rarely; generally in the context of individual case reports and typically in children under the age of six. We report the largest series of oral leiomyomatous hamartomas, and delineate the clinical and demographic features associated with such lesions. A retrospective review of all tongue lesions diagnosed since 1987 was performed utilizing the surgical pathology files at the Children's Hospital of Philadelphia. Where necessary, clinical history was obtained by standard chart review. Immunohistochemistry (CD31, D2-40, GLUT-1, SMA) and special stains (iron, Fontana, trichrome) were performed on selected cases. A total of 154 tongue lesions were identified of which just over 12% (19/154) of the cases were generically diagnosed as hamartomas. Variable amounts of benign, irregular smooth muscle bundles were identified in 15/19 of the lesions. In some lesions, the smooth muscle predominated whereas in others only scattered muscle bundles were identified with or without a variably prominent vasculature, admixed adipose tissue, salivary glands, and/or nerve bundles. In two cases, adnexal structures were identified and one lesion also contained cartilage. Most patients (17/19) were 5 years of age or less. Females outnumbered males by ~2:1. The majority of lesions were located in the dorsal tongue, and frequently in the anterior region (17/19). In all cases, the lesions were characterized as smooth, submucosal nodules. While most patients were otherwise healthy, four patients did present with clinical manifestations of oral-facial-digital syndrome. In cases with known follow-up, simple surgical excision was curative without evidence of any recurrence.

#2 8:12 a.m.

T-CELL RECEPTOR GENE REARRANGEMENT ANALYSIS OF TRAUMATIC ULCERATIVE GRANULOMA WITH STROMAL EOSINOPHILIA Hirshberg A, Amariglio N, Akrish S, Yahalom R, Rosenbaum H, Kaplan I. Tel-Aviv U, Sheba, Rambam and Rabin Medical Centers, Israel

To investigate the phenotypic profile and T-cell receptor gene rearrangement of the inflammatory infiltrate in oral traumatic ulcerative granuloma with stromal eosinophilia, 10 cases were analyzed using IHC for histiocyte, B&T cell markers, CD30 & Ki67. Automated high resolution PCR fragment analysis was used to detect T-cell receptor gene rearrangement. All cases showed ulcerated mucosa with dense inflammatory infiltrate, containing B&T lymphocytes, granulocytes, macrophages and abundant eosinophils. One case also showed atypical lymphoid cells with abundant mitotic figures. Large atypical cells were identified in 7 cases. Single CD30+ cells were scattered in 4 cases, and small aggregates of CD30+ cells were found in one case. Spectratyping analysis showed polyclonal rearrangement of the TCR-gamma genes in 4 cases and oligoclonality in 5. Monoclonality was detected in the case which showed histological features compatible with lymphoma. Healing was uneventful without recurrences in all cases. Conclusions: Most TUGSE are reactive, however, occasional cases may harbor a dominant clonal T-cell population. Although monoclonality does not necessarily indicate the existence of malignant lymphoid proliferation, follow-up is mandatory in these cases to exclude malignancy.

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#3 8:24 a.m.

CLINICAL AND DENTAL CT FINDINGS IN SYNOVIAL CHONDROMATOSIS. A Balasundaram, S Gordon and C.Hadgis. University of Detroit Mercy School of Dentistry, Detroit, Michigan.

Synovial chondromatosis is a rare disease featuring multiple cartilaginous bodies within the joint space due to metaplasia of synovial membrane. An 82-year-old Caucasian male presented with a swelling over the left TMJ that had developed over 5 years. He had episodic functional tenderness of the left TMJ since suffering painful repetitive jaw trauma while serving in the army in World War II. Radiographic evaluation of the lesion included a new 3-dimensional modality, Volumetric Cone Beam CT (Dental CT) study, which showed a well-defined radiopaque mass on the medial aspect and extending posterior to the left condylar head. The lesion measured 27 mm x 18mm. The mass encroached into the glenoid fossa, causing a uniform reduction in joint space. The lesion appeared heterogeneous in the posterior aspect showing patchy radiolucent areas within the radiopaque mass. The CT images clearly localized the extension of the lesion in the sagittal, coronal and axial planes. The patient was referred to an oral surgeon for treatment, but declined any form of intervention. He has been followed clinically for one year with little change. This case illustrates the uses and advantages of a novel 3-dimensional radiographic modality in evaluating a mass involving a joint with complex anatomy. The contribution of radiographic findings towards diagnosis is also discussed.

#4 8:36 a.m.

COMPARISSON OF CLINICAL AND HISTOPATHOLOGIC DIAGNOSIS IN LESIONS OF ORAL MUCOSA. R. Czerninski, C. Nadler, I. Kaplan, E. Regev, A. Maly. Hebrew U-Hadassah Medical Center, Jerusalem and Rabin Medical Center, Petah-Tiqva, Israel.

Objective: In order to investigate the accuracy of clinical diagnosis rendered by oral medicine specialists in lesions of the oral mucosa, as compared with histopathologic diagnosis, 136 cases of oral mucosal lesions treated between 2004-5 were retrieved from the files of the oral medicine department. Dental associated infections were excluded. The percentage of cases in which the histopathologic diagnosis coincided with one of the clinical differential diagnosis was calculated for the following diagnostic groups: dysplasia, hyperkeratosis, lichen planus, mucocele, non-specific ulcer/inflammation, papilloma, PV/MMP, reactive exophytic lesions, salivary gland tumors, SCC, and others. **Findings:** The histopathologic and clinical diagnosis were in agreement in a total of 106 cases (78%). The highest percent of correct diagnosis was found in 90-100% of cases with vesiculo-ulcerative diseases, dysplasia, mucocele, papilloma and lichen planus. The lowest percent of agreement was found in non-specific ulcerative/inflammatory lesions (38%), while all other groups reached 56-75% agreement. In these groups of lesions the clinical appearance was less homogenous and therefore more difficult to correctly diagnose clinically. **Conclusions:** Training in oral medicine allows for an accurate diagnosis in the majority of oral mucosal lesions, however there is a group of lesions in which the clinical presentation is non-specific and correct diagnosis is difficult to make on a clinical basis.

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#5 8:48 a.m.

INTRAOSSSEOUS PLEOMORPHIC ADENOMA OF THE MANDIBLE: REPORT OF A CASE AND REVIEW OF LITERATURE. J. Ojha, I. Bhattacharvva, N. Islam, S. Manhart, D. Cohen. U. of Florida, Gainesville. Salivary gland tumors constitute approximately 3% of all head and neck tumors. The most common salivary gland neoplasm involving both major and minor salivary glands is pleomorphic adenoma. Pleomorphic adenoma is a painless, slowly progressing and insidious tumor which can reach grotesque proportions if not treated surgically. They are predominantly seen in the salivary glands and account for majority of tumors (70-80%) effecting these organs, but these lesions have been sporadically described in unusual locations including other regions of the head and neck, the extremities, the trunk, and the genitals. We present a rare case of intraosseous pleomorphic adenoma of the mandible mimicking a lateral periodontal cyst along with a detailed review of literature. Pleomorphic adenomas arising within the jaws as primary central lesions are extremely rare with only a few cases reported. An extensive review of literature revealed a total of only nine cases of intraosseous pleomorphic adenoma. Radiographically and clinically these tumors may resemble lesions of odontogenic origin and typically present as radiolucencies with swelling along with pain and discomfort. Due to their relatively high rate of recurrence, continued and careful long term clinical and radiographic follow up is required. Strict evaluation criteria are required to prevent a false interpretation regarding their central bony origin. Clinicians should be aware of this possibility, emphasizing the need for submission of so called cystic lesions for histopathological analysis.

#6 9:00 a.m.

DIAGNOSIS OF THE PATHOLOGY OF THE KANAM MANDIBLE. J. Phelan, MJ Weiner, JL Ricci, T. Plummer, S. Gauld, R. Potts, TG Bromage. NYU College of Dentistry, New York City. Queens College, City University of New York, New York City. Santa Monica College, Santa Monica, California. Smithsonian Institution, Washington DC. The "Kanam Mandible" is the anterior portion of a fossilized mandible that was discovered by Louis Leakey's team in Kanam, Kenya in 1932. It has been assigned to archaic *Homo* of the African Middle or Late Pleistocene. The lingual aspect exhibits an exophytic mass that has been examined by anthropologists and pathologists with differential diagnoses that have included osteosarcoma, bone keloid, Burkitt lymphoma and osteomyelitis secondary to fracture. This study presents a re-examination of mandible and its exophytic mass. **Methods:** A Hitachi 3500-N SEM, fitted with a Robinson detector and a PGT x-ray microanalysis system, permitted backscattered electron imaging and mineral composition analysis respectively. Elemental maps of elements: Ca, P, S, and Si from sectioned sample surfaces were generated. These maps were used to determine where bone mineral (calcium phosphate) was located in relation to the sedimentary matrix surrounding the fossilized bone (calcium carbonates, silicates, etc.) **Results:** The Kanam mandible contains cancellous bone composed of calcium phosphate of varying mineral density; there is no discrete cortex. Space in the bone consists of a calcium carbonate and silicate material. The microstructure shows lamellae and osteocyte lacunae and many areas of bone remodeling with abundant osteocyte spaces and reversal lines. Trabecular fragmentation appears to be related to geologic processes. **Conclusion:** The Kanam mandible has retained its calcium phosphate bone composition and although geological processes have fractured components of the specimen, both macro and microanatomy are consistent with bone pathology secondary to fracture.

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#7 9:12 a.m.

ORAL MANIFESTATIONS OF LUPUS ERYTHEMATOSUS: CLINICAL AND HISTOLOGICAL STUDY OF 46 CASES AND IMMUNOHISTOCHEMICAL ANALYSIS OF EPITHELIAL MATURATION S.V. Lourenço; M.N. Sotto; M.A.C. Vilela; F.R.G. Carvalho; E.A. Rivitti ; M.M.S. Nico. Department Of Dermatology, Medical School, University Of São Paulo, Brazil

Background: lupus erythematosus (le) is an autoimmune disease of unknown cause. Prevalence of oral involvement in patients with le is uncertain, but may vary from 9-45% in patients with systemic disease and from 3-20% in patients with chronic cutaneous involvement. **Methods:** forty-six of oral lesions of le and their clinical aspects were investigated. Their histopathologic features were analyzed and the status of epithelial maturation was assessed through the expression patterns of cytokeratins. **Results:** from the forty-six cases detected with oral lesions, 34 were females and 12 males. Clinical aspects of these lesions varied and lips and buccal mucosa were most affected. Histologically, lesions revealed lichenoid mucositis with perivascular infiltrate and thickening of basement. Cytokeratins profile showed hyperproliferative epithelium, with expression of ck5/6, and ck14 on all epithelial layers, ck16 on all suprabasal layers and ck10 on prickle cell layers only. **Conclusions:** oral lesions of le show a variety of aspects with main microscopic features of lichenoid mucositis with deep inflammatory infiltrate. Patterns of cytokeratins expression are of hyperproliferative epithelium and this phenomenon must be analysed in relation to the inflammatory cytokines for a better understanding of the mechanisms of the disease.

#8 9:24 a.m.

KI-67 EXPRESSION IN *CANDIDA*-ASSOCIATED ORAL LESIONS. M. Moldauer, R A. Safadi, C. Kleinegger, J. Hellstein, F.Qian, S. Timmons, Z.B. Kurago. U of Iowa, Iowa City and Oregon Health & Science U, Portland. **Background:** Reportedly, chronic hyperplastic candidosis is associated with 16% frequency of epithelial dysplasia. High proliferation rates and cell cycle disturbances in dysplasia and squamous cell carcinoma (SCC) are reflected in high expression levels of Ki67 and p53 proteins, respectively. **Objective:** Determine how keratinocyte proliferation rates (Ki67 expression) in *Candida*-associated lesions compare to those in dysplasia and in SCC. **Methods:** Fifteen archival specimens per group: 1) SCC, 2) epithelial dysplasia, 3) *Candida*-associated epithelial dysplasia, 4) candidosis, 5) non-specific mucositis, 5) normal epithelium. Duplicate sections per case were stained by standard IHC for Ki67 using monoclonal antibodies (clones MB67 and KiS5) or negative control and the ultravision HRP-DAB detection system (Lab Vision Corp.). Digital images at 220x were analyzed with Image j software. At least 500 cells per section were counted, and the % of Ki67+ cells was determined. **Statistical analysis:** The % of Ki67+ cells in all groups were compared using ANOVA. Pairwise multiple comparisons were performed with post-hoc Tukey-Kramer test. A two-sample t-test was also used to compare candidosis with mucositis, and candidosis with *Candida*-associated dysplasia. **Results:** Mean Ki67 expression in SCC was greater than in all other groups ($p < 0.0001$). Dysplasia and *Candida*-associated dysplasia had higher Ki67 expression than mucositis and normal epithelium ($p < 0.05$). Interestingly, Ki67 expression in candidosis was not different from that in both dysplasia groups ($p = 0.0904$) and higher than in mucositis ($p = 0.0114$). These results are comparable to p53 analysis obtained previously. **Conclusion:** epithelial proliferation in candidosis appears similar to that in dysplasia.

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#9 9:36 a.m.

THE PRESENCE OF *HELICOBACTER PYLORI* IN LABIAL SALIVARY GLANDS OF SJÖGREN'S SYNDROME PATIENTS. E. Piperi, E. Chrysomali, Ch. Kouvidou, J. Papanikolaou, R. Chaisuparat, N. Nikitakis, A. Sklavounou-Andrikopoulou. U. Athens and Elpis Hospital, Greece, and U. Maryland, Baltimore. Sjögren's Syndrome (SS) is an autoimmune disease characterized by lymphocytic infiltration of the exocrine glands and an increased risk of developing extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) type, mainly of the major salivary glands. MALT accumulates secondarily in response to antigenic stimulation, presumably by a still unidentified exogenous agent. *Helicobacter pylori* (Hp)-associated gastritis predisposes to acquired MALT formation and eventually gastric MALT lymphoma development but, although Hp is a common resident of oral microbial plaque and saliva, its presence in labial salivary glands (LSG) of patients with SS has not been investigated. The purpose of this study was to investigate the presence of Hp in LSG of patients with SS. A labeled streptavidin-biotine method using a primary antibody against Hp was applied to 40 formalin-fixed, paraffin-embedded LSG biopsies of patients with SS and 20 control cases of chronic non-specific LSG sialadenitis. Giemsa stain was also performed for comparative evaluation. Rod forms of Hp were detected in excretory ducts surrounded by intense lymphoid infiltration in 7 cases (17.5%) of SS, 3 of which were also positive with Giemsa stain. All Hp-positive cases showed acquired MALT development, three of them also exhibiting monoclonality; these correlations did not reach statistical significance. None of the control sialadenitis cases were positive for the bacterium in either stain. We suggest that Hp may serve as an antigenic stimulus for acquired MALT development in SS at least in some cases, perhaps through LPS activation of Toll-like receptors on ductal epithelial cells and subsequent TLR4-LPS activation of B-lymphocytes.

#10 9:48 a.m.

HEAD AND NECK MALIGNANCIES IN EGYPTIAN PATIENTS WITH COMBINED HCV AND SCHISTOSOMIASIS INFECTION. S. Aboualzm, A. Nour El Din, E. Yonan, G. Eltawil, and M. Fata. Alexandria U., Egypt. Hepatitis C virus (HCV) infection has reached epidemic proportions. In Egypt, it was found that the prevalence of HCV in Nile delta is high especially in the fifth decade of life. The aim of the present work is to study the oral mucosal lesions in patients with viral hepatitis C infection alone or combined with Schistosomiasis (SCH) infection. Clinical and oral examination was applied on two hundred cases with positive HCV infection or combined with SCH infection. They were randomly collected from Alexandria's governmental hospitals and medical centers. Sixteen instances of oral squamous cell carcinoma (OSCC) were recorded in positively infected patients with HCV and SCH. Ten patients had extranodal oral malignant lymphomas (NHL) with positive HCV infection. Immunohistochemical assay using monoclonal mouse anti-hepatitis C virus and tissue PCR were performed to detect the viral particles in the cells of these lesions. The result revealed HCV expression in two cases of OSCC and three cases of NHL. Using tissue PCR, the previous cases showed positive tissue PCR together with another case of OSCC and five cases of NHL. From these findings, it was established that OSCC and NHL could be considered as extrahepatic lesions associated with HCV infection. Is HCV and co infection with SCH playing a significant oncogenic role in head and neck cancer? This is a question that needs further studies on a larger group of the Egyptian population.

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#11 10:00 a.m.

RHINO-CEREBRAL ZYGOMYCOSIS - AN INCREASINGLY FREQUENT CHALLENGE: UPDATE AND SURPRISING OUTCOMES IN TWO CASES. N. Islam, I. Bhattacharyya, J. Ojha, D. Cohen. U. of Florida, Gainesville.

Zygomycosis or mucormycosis is a life threatening infection increasing in frequency which was first reported in 1885. It includes all zygomycotic infections regardless of the etiologic organism. Regional designations such as rhino-cerebral, disseminated, cutaneous etc are used and are important predictors of pathogenesis and outcomes. This disease is caused by opportunistic fungal organisms of the class Zygomycetes. Despite the varied forms the disease takes, the pathognomonic feature is the presence of invasive mycelium in the tissues. These hyphal forms exhibit haphazard branching, are rarely septate and are larger than other filamentous fungi. These infections occur mostly in patients with immunosuppressive conditions, including diabetes (43% exhibit the rhino cerebral form), organ transplants and hematologic malignancies. Despite advances in diagnosis and treatment, the disease frequently follows a dismal and fatal course (44% mortality), unless aggressive treatment is initiated early. No appreciable change in the mortality rate has occurred in the last 40 years. We present two cases, a 63 year old female and a 58 year old male, both poorly controlled diabetics, with maxillary lesions suggestive of osteomyelitis. The patients were leading a near normal life with minimal discomfort or signs and symptoms of underlying mycosis. Despite long delays and inadequate initial therapy these patients survived with little outward morbidity. The prognosis for this condition may therefore be considered less dire than previously thought.

#12 10:12 a.m.

PYOGENIC GRANULOMAS AND PEMPHIGUS VULGARIS: AN UNUSUAL ASSOCIATION.

R. Abdelsayed, J. Dudelzak, and J. Leshner. Medical College of Georgia, Augusta.

A 45 year-old male African-American male with a 3 year-history of oral pemphigus vulgaris presented with a new onset of multiple painful, smooth, broad-based, red, and ulcerated nodules on his right buccal mucosa and dorsum and right lateral border of tongue. These intraoral sites, among others, were previously involved with pemphigus vulgaris, and the biopsies of these recent nodules showed pyogenic granulomas (PGs) developing in association with persistent pemphigus in the adjacent mucosa. The patient's oral pemphigus, which had initially led to a 60 pound weight loss, has been refractory to a number of aggressive combination of immunosuppressive therapies including; prednisone, azathioprine, cyclophosphamide, cyclosporine, mycophenolate mofetil and intravenous immunoglobulin and methylprednisolone, with concomitant use of several topical corticosteroid, tacrolimus, and antihistamine-anesthetic rinses. It can be hypothesized in this case that a group of factors including; the acantholytic process, inflammation with associated growth factors elicited by the disease, and the use of immunosuppressive agent, such as cyclosporine, and local trauma may have led to the development of multiple PGs.

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#13 10:24 a.m.

GENE EXPRESSION PROFILE ANALYSIS USING MICROGENOMICS IN FORMALIN FIXED, PARAFFIN EMBEDDED, DECALCIFIED AMELOBLASTOMA TISSUE. P. DeVilliers, C. Suggs, D. Simmons, T. Wright. U. of North Carolina at Chapel Hill.

Microgenomics implies the precise molecular analysis of very small pure cell population that has been microdissected from biopsies. Gene expression profile analysis using microarrays provides information to elucidate the signaling pathways that drive tumorigenesis and behavior of tumors. RNA was isolated and amplified from five samples of formalin fixed paraffin embedded, (FFPE) decalcified ameloblastoma tissue using laser capture microdissection technique.

To assess the quality and quantity of the RNA, samples were analyzed using the NanoDrop™ spectrophotometer as well as the 2100 ribosomal RNA Bioanalyzer. The aminoallyl antisense RNA (aa-aRNA) was hybridized to 40,000-oligonucleotide expression microarray using Human Universal Reference RNA. GeneSpring™ software was used to analyze the microarray data and the PathArt™ database was utilized to perform gene signaling pathway enquiries. The results showed a total of 38 upregulated genes, 2 fold, in 5 out of the 5 samples and 988 overexpressed genes, 2 fold, in 2 out of 5 samples. Among the 38 genes, WNT and LGR4, part of the breast cancer pathway, were overexpressed, as well as Tenascin from the melanoma pathway.

#14 10:36 a.m.

INFANTILE FIBROMATOSIS OF THE TONGUE: A CLINICOPATHOLOGIC AND IMMUNOHISTOCHEMICAL ANALYSIS OF 11 CASES. M. Kernig, J. Fetsch, M. Miettinen, R. Foss, S. Williams. Armed Forces Institute of Pathology (AFIP), Washington, D.C. Eleven cases of a distinctive form of infantile fibromatosis affecting the tongue (IFT) were reviewed. The lesions were morphologically and clinically separable from the desmoid-type fibromatoses that affect the head and neck. **Objective:** To evaluate the clinicopathologic and immunohistochemical features of IFT. **Methods:** Eleven cases of IFT were identified in the AFIP files. Clinical, histomorphologic, and immunophenotypic characteristics were evaluated and follow-up data was obtained. **Results:** There were 3 male and 7 female patients (one unknown). Ages at treatment ranged from newborn to 29 months (median 3 months.) All cases were treated by local surgical excision, with one lesion known to be incompletely excised. Three patients with long-term follow-up were alive, free of disease 16-37 years after treatment. Five patients with short-term post-operative follow-up were alive free of disease 4 months to 4 years after treatment. Follow-up was unavailable for three patients. No significant functional or speech deficits were present in the three patients with long-term follow-up. The tumors were immunoreactive for SMA, actin, desmin, CD9, and fibronectin. Stains for S100, MyoD1, MYF4, and myogenin were non-reactive. Beta-catenin showed cytoplasmic reactivity but no nuclear staining. **Conclusions:** The distinctive histomorphology and interesting immunophenotype suggest that this fibromatosis-like process of the tongue is separate from that of desmoid-type fibromatosis. Preliminary follow-up data suggests that these lesions may have a lower recurrence rate and less aggressive behavior than desmoid-type fibromatosis of the head and neck.

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Monday, April 24, 2006

#15 10:48 a.m.

THE EFFECTS OF COX INHIBITORS ON STAT3 SIGNALING AND SURVIVIN EXPRESSION IN ORAL CANCER. MA Scheper, JJ Sauk, NG Nikitakis. U. Maryland, Baltimore. Cyclooxygenase (COX) inhibitors exert anti-proliferative and pro-apoptotic effects on various cancers. We assessed the effects of both non-selective (sulindac or indomethacin) and selective (nimesulide or celecoxib) COX inhibitors, as well AG490 (JAK kinase inhibitor) and PD153035 (EGFR tyrosine kinase inhibitor), on the cell proliferation and apoptosis of oral squamous cell carcinoma lines (SCC9 and 25) and correlated them with induction of changes in the oncogenic signal transducer and activator of transcription 3 (Stat3) pathway and the inhibitor of apoptosis, survivin. SiRNA methods were used to selectively target survivin or Stat3. Further, transfection studies using forced expression vectors for survivin or constitutively active Stat3 mutant were performed. The effects on cell growth and apoptosis were determined by cell counting and Annexin V assay, respectively; while protein and mRNA expression of survivin and Stat3 were measured by Western blot and real time-PCR. Treatment with sulindac, inhibited cell growth, induced apoptosis, and mediated a downregulation of Stat3, with a corresponding decrease in survivin protein and mRNA expression; in contrast, other COX inhibitors did not mimic these effects. Stat3 targeting by means of AG490, PD153035 or Stat3 SiRNA treatment downmodulated survivin expression. SiRNA treatment against survivin and Stat3 inhibited oral cancer cell growth and apoptosis. Finally, survivin forced expression and transfection with constitutively active Stat3 mutant diminished the effects of sulindac. Our data indicate that survivin is a downstream effector of the oncogenic Stat3 signaling. Sulindac's ability to specifically downregulate survivin expression in a Stat3-dependent manner provides an explanation for its antineoplastic effects in oral cancer cells.

#16 11:00 a.m.

SQUAMOUS CELL CARCINOMA-MONOCYTE-LIPOPOLYSACCHARIDE INTERACTIONS INDUCE FACTORS THAT ACTIVATE STAT3. A. Lam-ubol and Z. Kurago. U. of Iowa, Iowa City.

Background: Interleukin (IL)-6 is associated with head and neck squamous cell carcinoma (HNSCC) progression. IL-6 can activate STAT3, and activated STAT3 is important in carcinogenesis. Monocyte (MO)-lineage cells are common in HNSCC and are associated with HNSCC metastases to lymph nodes. MO-lineage cells produce large amounts of IL-6 in response to microbial products. As mucosal surface integrity is typically disrupted in HNSCC, microbial products are likely components of the HNSCC environment. **Objective:** To determine the impact of MOs and microbial products on the production of IL-6 and on STAT3 activation in HNSCC cells. **Methods:** HNSCC lines and healthy donor MOs were cultured independently and together, with or without E. coli lipopolysaccharide (LPS). The culture supernatants and cells were evaluated for IL-6 production by ELISA, and intracellular staining with flow cytometry. Cell phenotype was determined by flow cytometry. Phosphorylation of Y705-STAT3 in HNSCC cells in response to recombinant IL-6 and to culture supernatants with IL-6-neutralizing or control antibodies was determined by Western blotting. **Results:** IL-6 production varied among HNSCC lines. However, all HNSCC-MO-LPS co-cultures consistently produced high levels of IL-6. Both MO and HNSCC produced IL-6, but MOs were the major source. HNSCC cells had little to none constitutively active STAT3, however, both IL-6 and supernatants from HNSCC-MO-LPS co-cultures potently activated STAT3 in HNSCC cells. This activation was decreased by IL-6 neutralization. **Conclusions:** IL-6 and other factors induced by HNSCC-MO-LPS interactions consistently activate STAT3 in HNSCC cells.

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Monday, April 24, 2006

#17 11:12 a.m.

HIV SALIVARY GLAND DISEASE: A ROLE FOR VIRAL INFECTION. A. Dovigi, J. Webster Cyriaque. U. of North Carolina at Chapel Hill.

HIV-associated salivary gland disease (HIVSGD) is an AIDS defining condition associated with significant morbidity and lymphoma development in HIV-positive individuals. Understanding HIVSGD becomes increasingly important as the burden of HIV disease expands globally. The epidemiology of HIVSGD suggests the involvement of a viral opportunist in its pathogenesis. Based on this and on histologic correlates we hypothesized that HIVSGD is a manifestation of DNA tumor virus infection/reactivation during immunosuppression. Analysis of HIVSGD lesions determined that while herpesviral gene products were not consistently detected in HIVSGD, Polyomavirus nucleic acids and antigens were detected. The subcellular localization of the viral-oncoprotein in HIVSGD was similar to that in a mouse model of polyomavirus-associated salivary gland disease. In HIVSGD the polyomavirus oncoprotein, Tag, was consistently colocalized with p53 implicating the deregulation of this tumor suppressor in the HIVSGD pathogenesis. Collectively, these studies underscore the potential for polyomaviruses to be key etiologic agents in HIVSGD development.

#18 11:24 a.m.

RECURRING MUCOSAL MALIGNANT MELANOMA IN-SITU: CASE REPORT AND REVIEW. S. Kemp, G. Gallagher, and S. Kabani, Boston University, Boston, Massachusetts.

Oral melanoma is a rare lesion representing less than 1% of all melanomas. It affects 1.2 persons per 10 million annually. Mucosal melanoma, at the time of diagnosis, is typically more advanced than the much more common cutaneous form. Whether this discrepancy is due to differences in clinical detectability or is a true difference in biologic behavior is not clear. However, the prognosis for mucosal melanoma, even in less advanced stage I cases, is still poor with less than 50% surviving according to most studies. We present a case of persistent melanoma in-situ that presented clinically as a patchy brown macular lesion with irregular borders affecting the maxillary ridge, palate, and buccal mucosa area of a 74-year-old male. There were two recurrences after excision over a 3 year period. The original incisional biopsy showed lentiginous melanocytic hyperplasia with moderate to severe atypia consistent with the early radial growth phase of malignant melanoma in-situ. The lesions have continued to recur at the previous excision site and at the margins of the previous excisions. Interestingly, no invasive component has been detected in any of the recurrences. Based on the poor prognosis of mucosal melanoma, close long-term follow-up of such cases seems necessary. The microscopic features of the case will be presented along with a brief review of the literature.

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Monday, April 24, 2006

#19 11:36 a.m.

MUCINOUS ADENOCARCINOMA OF THE PALATE: REPORT OF A CASE AND REVIEW OF THE LITERATURE. B. Shumway, J. Kalmar, R. Steiner, and C. Allen. The Ohio State University, Columbus.

Primary mucinous adenocarcinoma of salivary gland origin is a rare malignant neoplasm that appears analogous in many ways to mucinous adenocarcinoma of the skin and breast. We present a case that may have arisen from the minor salivary glands of the palate. A 72-year-old male had a non-tender, firm, bluish nodule at the junction of his left hard and soft palate for several months. Incisional biopsy showed collagenous bands separating variably sized pools of mucin, many containing suspended islands of atypical ductal epithelial cells. The atypical cells were strongly positive for CK7 and negative for CK20, CDX2, villin, PSA, PSAP and TTF-1. No occult primary tumor was identified, despite extensive imaging studies and clinical evaluation. Treatment consisted of wide excision with post-operative radiation, and there is no recurrence after eight months. Although classification of these tumors has been controversial, 15 cases have been previously reported in the head and neck region. Salivary mucinous adenocarcinoma typically affects patients over 50 years of age and presents as a slow-growing swelling with occasional dull pain. Complete surgical excision is the treatment of choice.

Primary mucinous adenocarcinoma of the salivary glands appears to act aggressively with frequent lymphatic extension. Of the twelve cases with available follow-up, six patients died of disease from 12-72 months following initial diagnosis and two had local recurrence or metastasis. Clinical stage of disease seems to be the most important prognostic indicator for this rare neoplasm.

Essay Program 2

Tuesday, April 25, 2006

#20 8:00 a.m.

THE HISTORY AND MYSTERY OF CARNOY SOLUTION: AN ASSESSMENT OF THE NEED FOR CHLOROFORM. J. Hellstein, T. Hopkins, and T. Morgan. U. of Iowa, Iowa City Carnoy first reported use of his fixative for the study of nematodes in 1887. His goal was to fix the tissue and preserve nuclear detail. Chloroform laden Carnoy solution has been reported for treatment of odontogenic keratocysts. However, fixation is not really the effect that Oral Surgeons desire, they are after the cauterization effect that the solution produces. The preference for chloroform began in 1931 in an oft cited article on the use of Carnoy solution for “cysts”. The fact that Carnoy solution in the lipid rich environment of the brain produced less destruction and inflammation than Zenker solution and 40% formaldehyde is often reported. The fact that 3 of the 11 dogs treated with Carnoy solution died and the lesions were not cysts, is not well reported. Voorsmit studied the penetration of Carnoy solution and reported a penetration of 1.54 mm after 5 minutes of exposure. This was actually 2-10 times deeper than the soft tissue samples. Only 2 or 3 bone specimens were actually analyzed in that study and the question of how bone penetration could be so much higher than the soft tissues was not well addressed. The use of chloroform in humans is problematic with FDA Compliance Policy Guide, Chapter 4 sub-chapter 460 specifically preventing the compounding of chloroform in any therapeutic agent. The objective of this study was to assess the need and effect of chloroform. We utilized 20 bone, connective tissue and mucosal specimens then compared the effects of classic Carnoy solution with ferric chloride, to a solution using 9 ml of 95% ethanol, 3 ml of glacial acetic acid and 1 g of ferric chloride. The study found very similar penetration values for all tissue types with little or no benefit seen for the use of chloroform. The non-chloroform version has been used in 15 patients with a recurrence rate similar to classic Carnoy solution and we conclude that chloroform is an unnecessary constituent of Carnoy solution.

#21 8:12 a.m.

EXPRESSION OF OPG, RANKL AND TRAIL IN ODONTOGENIC KERATOCYSTS (OKC). AN IMMUNOHISTOCHEMICAL STUDY. A. Zakopoulos, K. I. Tosios, D. Vlachodimitropoulos, S. Tseleni-Balafouta, G. Fanourakis, and IG Koutlas. Faculty of Dentistry and Medical School, University of Athens, GREECE and University of Minnesota, Minneapolis.

The aggressive biologic behavior of the OKC, the presence of gene alterations and its association with the Gorlin syndrome support the current concept that it is a benign cystic neoplasm. The molecular mechanisms underlying the infiltrative behavior of OKC have not been elucidated. The aim of the present study was to evaluate the immunohistochemical expression of molecules involved in osteoclastogenesis, namely Receptor Activator NF- κ B Ligand (RANKL), osteoprotegerin (OPG), and TNF-Related Apoptosis-Inducing Ligand (TRAIL) in OKCs and compare this expression to that in dentigerous (DC) and residual cysts (RC). The study material consisted of 58 OKC, 10 DC, and 10 RC. Epithelial expression of RANKL was seen in 52 OKCs (89.6%), in 10/10 DC and 9/10 RC, while the expression in the connective tissue wall was 96.5% for OKC and 100% for DC and RC. OPG was expressed in the epithelium of 50 OKCs (86.2%), 7 of 10 DC, and 6 of 10 RC, and in the connective tissue wall of 49 OKC (84.5%), 6 of 10 DC, and 5 of 10 RC. None of the lesions expressed TRAIL. In conclusion, the molecular system OPG/RANKL/TRAIL is variably expressed in OKC, DC and RC and may be involved in the osteoclastogenetic mechanisms in OKC.

Essay Program 2
Tuesday, April 25, 2006

#22 8:24 a.m.

KERATOAMELOBLASTOMA OF MAXILLA. J. Whitt, C. Dunlap, J. Sheets, M. Thompson, U. of Missouri Kansas City.

A 45 year-old male presented with an expansile, radiolucent lesion of the left anterior maxillary alveolar ridge, containing a number of internal densities. The lesion had been present for at least 6 months and had produced expansion the facial cortex and divergence between the left lateral incisor and canine tooth roots. The radiographic margin, while distinct, was not sharp and crisp and extended from the distal surface of tooth #9 to the mesial surface of tooth #12, extending from the alveolar crest to the tooth apices. Surgical exposure of the lesion to obtain an incisional biopsy specimen revealed erosion the facial cortical plate. The lesion was solid, with a uniform, tan surface that cut with a gritty consistency. Histopathologic examination of the incisional biopsy specimen revealed a generally solid, unencapsulated lesion in which islands and anastomosing cords of epithelium formed lamellated stacks of parakeratin with foci of dystrophic calcification. The lamellated, pacinian-like stacks of parakeratin protruded into the collagenous tumor stroma without invoking a response, obscuring the distinction between the keratin and collagen in routine H&E stained sections. Rare areas exhibited histologic features of odontogenic keratocyst, with transition to areas exhibiting reverse polarity and subnuclear vacuolization, typical of ameloblastoma. A diagnosis of keratoameloblastoma was made. The patient received a wide local excision of the lesion, including removal of teeth #9-12.

#23 8:36 a.m.

PERIPHERAL GRANULAR CELL ODONTOGENIC FIBROMA. J. Rinaggio, R. Koshy, A. Gallante, and N. Mirani. U. of Medicine and Dentistry of New Jersey, Newark.

Soft tissue masses arising on the gingiva are a relatively common finding, and are typically a response to local irritation. In contrast, benign odontogenic tumors are quite rare in this location. A 58-year-old female presented with an asymptomatic pedunculated mass arising from the facial gingival margin of the left mandibular lateral incisor. The involved tooth was unrestored, non-mobile, and had no gross adherent calculus. There was no significant medical history. A periapical radiograph demonstrated intact underlying bone with no evidence of a central lesion. The lesion was excised, and microscopic examination revealed a non-ulcerated nodular growth characterized by numerous polygonal cells with a slightly basophilic, granular cytoplasm and uniformly stained nuclei within a fibrocollagenous stroma. Islands of odontogenic epithelium exhibited peripheral hyalinization. There were no calcifications, areas of necrosis, or mitotic figures. The granular cells showed positive immunohistochemical staining to vimentin and KP-1, and were negative for cytokeratin AE 1/3 and S-100 protein. A diagnosis of peripheral granular cell odontogenic fibroma was rendered, and confirmed by AFIP consultation. To our knowledge, this represents the fourth detailed case description of this entity.

Essay Program 2

Tuesday, April 25, 2006

#24 8:48 a.m.

BISPHOSPHONATE ASSOCIATED OSTEONECROSIS: A REVIEW OF REPORTED CASES.

D. Fischer. Marquette U. School of Dentistry, Milwaukee, Wisconsin.

A recent clinical entity has become evident in current literature. Four hundred twenty six cases of osteonecrosis of the jaws have been reported since 2003. Various terms have been suggested to describe this entity, including avascular necrosis of the jaws, osteonecrosis of the jaws, bis-phossy jaw (Hellstein 2004), and bisphosphonate-associated osteonecrosis. Bisphosphonates are synthetic analogs of pyrophosphate administered intravenously or orally. The majority of reported cases, 93%, involved intravenous bisphosphonates. Patients treated for multiple myeloma represent 219 (52%) of reported cases. The majority of remaining cases were being treated for metastatic breast cancer (36%) and metastatic prostate cancer (5%). Of the reported cases of osteonecrosis of the jaws, 222 (53%) occurred in the mandible, 78 (18%) in the maxilla, and 27 (6%) in both jaws. The main dental procedure leading to osteonecrosis was dental extraction (48%), followed by periodontitis (8%), spontaneous cases (17%), ill-fitting dentures (1%), periodontal surgery (1%), implant placement (1%), and endodontic therapy (1%). Additional reported comorbidities include chemotherapy (49%), Dexamethasone (20%), history of radiotherapy (2%), and unspecified corticosteroids (3%). Current treatment has been focused on prevention of osteonecrosis for patients taking bisphosphonates as well as maintaining a pain-free state in those who develop osteonecrosis of the jaws.

#25 9:00 a.m.

AMYLOID DEPOSITION IN A SPLIT THICKNESS SKIN GRAFT. V. Woo, C. Pulse, A. Yoon, W. Pochal, V. D'Agati, and D. Zegarelli. Columbia U., New York, New York.

Amyloid deposition can be observed in a variety of clinical situations, such as in the setting of multiple myeloma and long-term renal dialysis. Secondary amyloidosis characteristically develops as a complication of a chronic inflammatory process, and has been recognized in patients with suffering from persistent osteomyelitis and tuberculosis. We report a case of a 64-year-old female who presented with a large mass at the distal extent of an autogenous split thickness skin graft placed 30 years ago for ridge augmentation. Review of the patient's past medical history was unremarkable for systemic illnesses and no osseous abnormalities were detected on intraoral radiographs. Histologic examination of the submitted tissue revealed diffuse masses of amorphous, eosinophilic material exhibiting cracking artifact and interspersed foci of chronic inflammatory cells. Sections stained with congo-red demonstrated birefringence under polarized light microscopy and metachromasia was noted with crystal violet stains. A diagnosis of amyloid deposits and associated mucosal inflammation was rendered. Although the exact etiology of the amyloid seen in this case is not clear, we propose that long-standing chronic inflammation related to the patient's graft procedure may have played a role. To our knowledge, amyloid occurring in a skin or oral mucosal graft has not been previously described; however, a case of amyloid involving a corneal graft has been documented.

Essay Program 2
Tuesday, April 25, 2006

#26 9:12 a.m.

ORAL AND MAXILLOFACIAL SCLEROSING EPITHELIOID FIBROSARCOMA: REPORT OF FIVE CASES. G. Folk, S. Williams, R. Foss, and J. Fanburg-Smith, Armed Forces Institute of Pathology, Washington, D.C.

Sclerosing epithelioid fibrosarcoma (SEF) is a variant of low-grade fibrosarcoma with distinctive histologic features. It occurs primarily in the deep soft tissues of the extremities of adults. Lesions involving the oral and maxillofacial region (OMFR) or intraosseous examples have not been well characterized. We present five new cases of OMFR SEF. There were three male and two female patients, age 19-47 years, (median 35 years). Tumors involved the zygomatic-temporal, buccal (recurrence extended into bone), anterior mandible (intraosseous), parotid and submandibular gland regions. Histologically, the tumors were well delineated, multinodular with fibrous septa. The primarily epithelioid to spindled tumor cells formed moderately cellular sheets and cords with irregularly contoured medium/large round/oval occasionally overlapping nuclei, indistinct to small nucleoli, wispy eosinophilic to clear (retracting) cytoplasm, and distinct cytoplasmic borders. Tumor cells were positive for vimentin and CD99 (3/3) and weak for CD34 (1/5). S100 protein, keratins, EMA, desmin, and SMA stains were negative. The differential diagnosis for these tumors includes a wide array of neoplasms arising in the OMFR: sclerosing carcinoma, Ewing/PNET, osteosarcoma, osteoblastoma, and salivary gland tumors with myoepithelial differentiation (benign and malignant).

#27 9:24 a.m.

MYOEPITHELIAL CARCINOMA OF ANTERIOR MAXILLA. J. Whitt, B. Barker, R. Taylor, U. of Missouri Kansas City.

A 65 year-old male presented with a 2 x 3 cm circumscribed, midline radiolucency of the anterior maxilla. The lesion was centered over the apices of the vital central incisor roots, accompanied by expansion of the anterior hard palate and was believed to represent a nasopalatine duct cyst. Upon enucleation, the lesion had eroded the overlying cortex and proved to be solid, rather than a cystic lesion. It consisted of uniform cells with well-defined borders and eosinophilic cytoplasm in a chondroid matrix, proliferating with broad pushing margins. There was infiltration into the adjacent trabecular bone. Immunohistochemical markers were positive for cytokeratin, S100 protein, glial fibrillary acidic protein, vimentin, epithelial membrane antigen, actin and desmin, supporting myoepithelial differentiation. Subsequently, a wide local excision was performed and the defect was reconstructed with a bone graft and a fixed dental prosthesis. The tumor recurred after 10 years, presenting as a 1 cm mass expanding into the maxillary labial vestibule, beneath the nasal ala. A second wide local resection was performed and the defect was reconstructed with an obturator. Eleven years after the initial presentation of the tumor, the patient is alive without evidence of disease. This tumor represents the unusual occurrence of an intraosseous salivary gland neoplasm, apparently arising for salivary tissue within the incisive canal.

Essay Program 2

Tuesday, April 25, 2006

#28 9:36 a.m.

EXTRAMAMMARY PAGET'S DISEASE OF THE FLOOR OF MOUTH ASSOCIATED WITH MINOR SALIVARY GLAND CARCINOMA AND CONCURRENT INVASIVE SQUAMOUS CELL CARCINOMA. MJ Bullock and CG Robertson, Dalhousie University, Halifax, Nova Scotia, Canada.

Extramammary Paget's disease (EPD) of the oral mucosa is extremely rare, limited to a few case reports. We present the case of a 52-year-old Native Canadian woman with EPD of the floor of the mouth (FOM) associated with high grade in situ and microinvasive salivary gland carcinoma, and concurrent invasive squamous cell carcinoma. The patient, a smoker with a history of heavy alcohol consumption, presented with a 6 week history of a painful FOM ulcer. On examination, there was a 3 cm area of erythroplakia of the right FOM with a central 0.5 cm ulceration, a biopsy of which showed invasive squamous cell carcinoma. Following definitive resection, the area of erythroplakia demonstrated highly atypical malignant cells arranged in a Pagetoid fashion throughout the surface epithelium. No typical squamous dysplasia was identified. A 0.4 cm focus of microinvasive SCC arose within the affected area. The EPD cells, in situ and invasive salivary gland tumor, and a level 1 lymph node metastasis were all CK7 positive. No glandular differentiation was demonstrated with mucin stains. The invasive SCC was CK7 negative. GCDFP-15 and Her2/neu immunostains were negative in all malignant cells. EPD is an extremely rare cause for oral erythroplakia; the association with typical invasive SCC in this case appears to be unique. The literature regarding EPD of the oral mucosa, the possible pathogenesis of concurrent salivary gland and squamous cell carcinoma, and the relationship to oral adenosquamous carcinoma, are discussed.

#29 9:48 a.m.

ATYPICAL CARCINOID TUMOR (MODERATELY DIFFERENTIATED NEUROENDOCRINE CARCINOMA) OF THE SALIVARY GLANDS. REPORT OF 3 CASES N. Said-Al-Naief, K. Sciandra, J. Fantasia, R. Lopez & D. R. Gnepp. The U. of Alabama at Birmingham, Rhode Island Hospital, Providence, & LIJ Hospital, New Hyde Park NY. Primary Neuroendocrine carcinomas (NEC) of the salivary glands are rare, comprising only ~1 % of all salivary malignancies with a well-documented prevalence for the parotid gland. Most reported NECs are small cell carcinomas with a few cases of carcinoid tumor. This is the first report of 3 atypical carcinoid tumors. All involved the parotid gland; 2 were women and 1 a man, ages 57, 59 & 82 yrs. All were initially treated with parotidectomy, with selective lymph node excision in one, & radiation in another. Follow-up was available for 2 cases (18 & 79 mo). One patient had 2 local recurrences, developing lymph node & liver metastases requiring further surgery & chemotherapy. Currently, she is alive with disease, on supportive care. The second patient is alive with no signs of recurrence. Patient work-up excluded the possibility of metastatic neuroendocrine tumor to the salivary glands in all patients. The histomorphological features were similar with infiltrating round, oval to spindle shaped, mild to moderately pleomorphic cells, with moderate to focally abundant eosinophilic cytoplasm, small to prominent nucleoli & chromatin stippling. Cells were arranged in nests, cords & trabeculae with scattered rosette-like structures in 1 tumor. Prominent mitotic activity was noted in 1 tumor, necrosis (focal & abundant) in 2 tumors and perineural invasion in 1 tumor. Immunohistochemistry staining was diagnostic showing uniform positive labeling with broad spectrum cytokeratin (with paranuclear punctuate pattern in 2 cases), chromogranin & synaptophysin antibodies. CK20 was negative in 2 tumors & stained rare cells (<1%) in the 3rd. Calponin & smooth muscle actin were negative.

Essay Program 2

Tuesday, April 25, 2006

#30 10:00 a.m.

TERATOCARCINOSARCOMA OF THE NASAL CAVITY. S. Wei, A. J. Lazenby, W. Bell, R. Lopez & N. Said-Al-Naief. U. of Alabama at Birmingham. Teratocarcinoma (TCS) is a unique, highly malignant neoplasm with high grade polymorphous features that combines carcinosarcoma and teratoma. We present a case of nasal teratocarcinoma in a 42 y.o. Guatemalan man who complained of left nasal fullness, obstruction, pain, bilateral frontal headaches and epistaxis for several weeks. Laryngoscopic exam. showed total obstruction of his left nostril with a large fleshy mass that pushed the nasal septum to the right. Imaging studies revealed a large mass filling the left nasal cavity & extending to the cribriform plate & sinuses with involvement of the lamina papyracea & orbit but w/o gross intraorbital extension. He underwent anterior craniofacial resection and medial maxillectomy. The tumor followed an aggressive course in the following 4 months which required further Surg.+Chemo+RT. No residual tumor or recurrence was seen in his last F/U visit. A review of the English literature revealed a total of 54 similar cases. The tumor primarily involved adult ♂ (M: F ≈ 7:1, age ranged from 18 -79 ys) (except 1 neonate). 44/54 (81%) patients were treated with S.+RT+ Chemo. In 14 of those (initially received S.+ other treatment later), 2 were lost to F/U & in the remaining 12; 8 (66.7%) had local recur.+/- mets and 4 had NED (FU period=6m-7y). In 10 patients (initially received RT.+ other treatment later); 8 had recurr., mets or unresponsiveness and 2 had NED(FU period=9m-5y). 17 patients (10 received S.+RT, 3 RT only, 2 S.only, 1 S.+Chemo.only and 1 S.+RT+Chemo) survived for >1yr; of those, 14 had NED and 3 died of unrelated causes. Out of 28 patients who survived >3yr, 13 DOD and 15 were alive w^ or w/o disease. These data, in keeping with the nature of pluripotential histology and rapidly growing biology, suggest that the combination of aggressive therapeutic approaches may improve treatment outcome.

#31 10:12 a.m.

Rap1GAP induces secretion of MMP-9 and promotes invasion in human oropharyngeal squamous cell carcinoma N.J. D'Silva, R.S. Mitra, S. Palit, D. Maldonado, K. Cordell, Q. Pan, D. Chepeha, B. Henson. U. of Michigan, Ann Arbor.

Rap1GAP functions by switching off rap1, the ras-like protein that has been associated with carcinogenesis. Previous findings suggest that rap1GAP acts as a tumor suppressor protein in squamous cell carcinoma (SCC) by delaying the G1/S transition of the cell cycle. The objective of the current study was to investigate the role of rap1GAP in invasion and migration of SCC cells and in secretion of matrix metalloproteinase -9 (MMP-9), which degrades extracellular matrix. Using SCC cells transfected with empty vector or rap1GAP, cell invasion and migration were determined by matrigel, wounding and motility assays. Cells transfected with rap1GAP exhibited a more invasive and motile phenotype than corresponding control cells. Consistent with these findings, rap1GAP-dependent secretion of MMP-9, was observed on zymograms. Furthermore, chemical inhibition of MMP-9 secretion, inhibited migration of rap1GAP transfected cells. Cell proliferation, as determined by the trypan blue enumeration assay, was inhibited by rap1GAP. Immunohistochemical staining of a SCC tissue microarray from 90 tumors, showed variable expression of rap1GAP in different tumors. In conclusion, rap1GAP inhibits tumor growth but induces MMP-9 mediated SCC invasion and migration in vitro, suggesting a role for this protein as a biomarker for small (early stage) but aggressive SCCs.

Essay Program 2

Tuesday, April 25, 2006

#32 10:24 a.m.

ALTERATIONS OF INTEGRINS AND EPIDERMAL GROWTH FACTOR RECEPTOR EXPRESSION IN ORAL PRECANCEROUS AND CANCEROUS LESIONS. M. El-Abany, T. Ibrahim, G. -ELTaweel, A. Medra, A.El-Murtadi, Alexandria U. Egypt. The examination of molecular alternation in the oral precancerous and cancerous lesions may lead to better understanding of their pathogenesis Alpha v and beta 1 integrin subunit and epidermal gross factor receptor EGFR have been suggested to play a role in epithelial malignancies. This study has been carried out to examine the distribution and evaluate semi quantitatively the expression of alpha v and beta 1 integrins and the EGFR immunohistochemically in 23 oral precancerous lesions (10 leukoplakias, 4 verrucous leukoplakias and 9 lichen planus) and 35 oral cancerous lesions (30 squamous cell carcinomas, 5 verrucous carcinomas) and 5 control samples of oral mucosa using avidin-biotin complex (ABC) method. We also evaluated the expression of these cell surface receptors in relation to the degree of epithelial dysplasia and the grade of tumor differentiation. The results have demonstrated that Alpha v integrin expression was seen in leukoplakia lesions that showed severe epithelial dysplasia and in all erosive lichen planus cases. There was an alteration in the expression of beta 1 integrin in oral precancerous and oral cancerous lesions. There was an alteration of EGFR in oral precancerous and cancerous lesions. Reduced or loss of expression of alpha v, beta 1 and EGFR was a feature of poorly differentiated squamous cell carcinoma. In this study it was suggested that alpha v, beta 1 integrins and EGFR play a significant role in the pathogenesis of oral precancerous and cancerous oral lesions. These findings suggest that the identification of these cell surface receptors by this method may be valuable in the early diagnosis of high risk lesions for malignant transformation.

#33 10:36 a.m.

THE DKC1 GENE IN SPORADIC ORAL SQUAMOUS CELL CARCINOMA. F. Alawi. U. of Pennsylvania, Philadelphia. Dyskeratosis congenita (DC) is a rare syndrome that is characteristically associated with oral leukoplakia which may eventuate in oral squamous cell carcinoma (OSCC). Mutations in the dyskeratosis congenita 1 gene (DKC1) give rise to X-linked DC. DKC1 is an integral component of the telomerase ribonucleoprotein complex; and is also required for normal rRNA processing. Since germline DKC1 mutations elevate the risk for OSCC, we sought to evaluate the status of the gene in sporadic OSCCs. Methods: Genomic DNA and RNA was extracted from 9 OSCCs and patient-matched normal controls; and 4 primary oral keratinocyte and OSCC cell lines, respectively. PCR and DNA sequencing were used to screen for DKC1 mutations. Using standard and real-time RT-PCR, we also measured DKC1 mRNA levels. Finally, we overexpressed DKC1 in two OSCC cell lines that exhibited high and low levels of telomerase activity, respectively. Using a commercially available TRAP assay, we measured the consequent effect on telomerase activity. Results: DKC1 mutations were not identified in any of the tumors or OSCC cell lines (0/13). Instead, wild-type DKC1 was upregulated in 6/9 (66%) OSCCs in relation to their matched normal controls ($p = 0.002$). Three of four OSCC cell lines also demonstrated a 40-100 fold increase in DKC1 expression relative to the primary cells. Overexpression of DKC1 in low or highly telomerase-positive cell lines did not precipitate any further increases in telomerase activity. Conclusions: This represents the first known study investigating DKC1 in OSCC. DKC1 is significantly upregulated, and not mutated, in OSCC without a concomitant increase in telomerase activity. This suggests that DKC1 expression is not a primary determinant of telomerase upregulation. Investigations are underway to determine the role of DKC1 in the pathogenesis of sporadic OSCC.

Essay Program 2

Tuesday, April 25, 2006

#34 10:48 a.m.

MELANOCYTIC MATRICOMA: A DISTINCTIVE CLINICOPATHOLOGICAL ENTITY. N. Islam, I. Bhattacharyya, J. Vega, S. Proper, S. Glanz, A. Hassanein. U. of Florida, Gainesville.

Melanocytic matricoma is a rare recently reported entity. It was first reported and described by Carlson et al in 1999. It usually presents as pigmented, dark papular, crusted lesion on sun-damaged skin of adult patients. Histopathologically these lesions consist of well-circumscribed nodules with, groups of "shadow cells" or "ghost cells"(matrical / supramatrical cells), and prominent pigmented, dendritic melanocytes. It differs from matricomas and pilomatricomas by its lack of calcification, cyst formation, granulomas, and connections to the epidermis and other adnexal structures. The clinical differential diagnosis includes hemangioma, pigmented basal cell carcinoma, and melanoma. Melanocytic matricoma presumably is the representation of an epithelial-melanocytic interaction in the anagen phase of the hair cycle and the melanization is due to normal melanocytes colonizing a neoplastic proliferation. A extensive search of the medical literature revealed five reports of benign melanocytic matricomas and two malignant counterparts. We present two additional cases of melanocytic matricoma with clinicopathologic correlation. The first case is from the dorsum of the hand of a 70 y/o white male and the second from the preauricular area of an 82 y/o white male, both with prior history of skin cancer. The small size, well circumscribed appearance and the asymptomatic nature signifies benignity. However, if cytologic atypia is present, it is indicative of malignant behavior. Correct interpretation of melanocytic matricoma is extremely important, due to, its clinical and histopathological overlap with other more ominous lesions.

#35 11:00 a.m.

LYMPH NODE MELANOPHAGES MIMICKING METASTATIC MELANOMA. E. Philipone, R. Kelsch, J. Wu, J. Fantasia. Long Island Jewish Medical Center, New Hyde Park, NY.

Differentiating melanin containing histiocytes (melanophages) from melanoma cells can cause interpretive difficulty in the assessment of lymph nodes exhibiting pigmentation. Immuno-histochemical stains are frequently employed to aid in the distinction between the neoplastic and reactive cell types. However, several commonly used histiocytic markers such as CD-68, α -1-antitrypsin, α -1-antichymotrypsin and lysozyme may be immunoreactive in melanomas. In addition, HMB-45 immunoreactivity has been reported in melanophages. The immunohistochemical chromogen 3-amino-9-ethylcarbazole is typically substituted for the chromogen diaminobenzidine to avoid further interpretive difficulties. **Purpose:** Provide a diagnostic algorithm to help differentiate melanophages from metastatic melanoma cells identified in dissected cervical lymph nodes removed from a patient with cutaneous melanoma. **Methods:** Case report. **Results:** A panel of melanocytic and histiocytic markers were used to assess lymph nodes for metastatic disease. Positive staining with CD-68 coupled with negative staining with Melan A and non-specific staining with HMB 45 and S-100 protein in conjunction with cytologic features resulted in an interpretation that many lymph nodes contained only melanophages. **Conclusion:** Histologic examination, multiple immunohistochemical stains, and the recognition of possible interpretive pitfalls are sometimes required to differentiate melanophages from metastatic melanoma cells.

Essay Program 2

Tuesday, April 25, 2006

#36 11:12 a.m.

DEEP PENETRATING NEVUS IN A COMBINED NEVUS. Y. Cheng, H. Kessler, D. Watkins, S. Watson. Baylor College of Dentistry-TAMHSC, Baylor University Medical Center and private practice, Dallas, Texas. A 46-year-old female presented with a pigmented lesion on left cheek that was removed by shave biopsy. The provisional clinical diagnosis was hemangioma. Histologic examination revealed round to spindle cells with poorly defined cell borders in the superficial dermis. The cells tended to group in a thèque-like arrangement in some areas and melanin pigment was found associated with these cells. Nevus giant cells were occasionally seen. The shave biopsy was signed out as an intradermal nevus. A wider and deeper excision was performed for esthetic purposes and the histopathology revealed sheets of round to spindle epithelioid cells surrounding adnexal structures and penetrating through the entire thickness of the dermis and into the subcutaneous fat. A vague nest-like growth pattern of these epithelioid cells was seen in some areas and numerous large melanin-containing cells were identified. Nuclear pseudo-inclusions were seen in many of these epithelioid cells. Mitotic figures were rare and no inflammation was seen. A diagnosis of deep penetrating nevus was rendered. The differential diagnosis and current knowledge on combined nevi will be discussed.

#37 Read by Title

EPITHELIOID ANGIOSARCOMA OF THE ORAL CAVITY. E.T. Stoopler, F. Alawi, G. Salazar, T. Tanaka, A. Sareli, T.P. Sollecito. Hospital of the University of Pennsylvania, Philadelphia. A 59 year old male presented with persistent hemoptysis and radiographic evidence of bilateral, well-defined pulmonary masses. Over a period of three months, multiple diagnostic procedures were performed; however, a definitive diagnosis for the lung lesions could not be made despite the persistence of his symptoms. In all cases, the retrieved material exhibited hemorrhage and fibrinoid deposits, with few benign cells. A thoracotomy for more definitive diagnosis was not advised due to difficult access to the lung masses. While the radiographic appearance of the lung lesions remained unchanged, the patient began to experience spontaneous gingival hemorrhage; and he reported the development of a painless, intraoral mass. Examination revealed a 1.5 cm, ulcerated, irregular mass involving the right posterior mandibular gingiva. A panoramic radiograph revealed no evidence of bony involvement. An incisional biopsy revealed inflamed mucosa containing a small cluster of malignant epithelioid-appearing cells. The tumor cells were enlarged, contained hyperchromatic, pleomorphic nuclei with prominent nucleoli, and abundant cytoplasm. Numerous mitoses were identified. Large aggregates of fibrinous material and extravasated hemorrhage were also noted, with only focally scattered malignant cells. There was no morphologic evidence of any vascular differentiation. Nonetheless, immunohistochemical studies demonstrated diffuse reactivity of the neoplastic cells with CD31 and Ulex europaeus I agglutinin, and focal reactivity with CD34, Factor VIIIa and pan-cytokeratin. Based on these findings, a diagnosis of epithelioid angiosarcoma was rendered. Since the lung masses and hemoptysis preceded the development of the oral lesion, it was presumed that the lung was the primary site of the tumor, with the gingival lesion representing a metastatic deposit.

Essay Program 2

Tuesday, April 25, 2006

#38 Read by Title

SARCOMA EX PLEOMORPHIC ADENOMA. A CASE REPORT OF A UNIQUE ENTITY. N Said-Al-Naief, C. Moran, & M. Luna. The University of Alabama at Birmingham & U. of Texas-MD Anderson, Houston TX. Various types of non-lymphoid sarcomas have been documented to arise primarily in the salivary glands representing about 0.3 - 0.5 percent of all benign and malignant salivary gland tumors. The criteria for establishing this diagnosis have been clearly identified, including the exclusion of carcinosarcoma (true malignant mixed tumor), histologically. We present a unique case of left parotid gland sarcoma that involved a 59 year old white man who was referred by his primary physician in February of 2000 to a local ENT physician for further investigation of a several weeks history of an enlarging left, parotid gland swelling. Medical history was positive of 30+ years of 5ppd smoking, hypertension cardiovascular disease, bypass surgery, asthma and asbestosis of the lung. Fine needle aspiration was performed and showed features suggestive of benign mixed tumor. CT scans demonstrated a 3Cm lobulated mass with focal areas of calcification and necrosis, accompanied by lymph node involvement. A parotidectomy was performed in August of 2000. The tumor showed high grade sarcoma, exhibiting metaplastic bone, with evidence of vascular invasion and capsular invasion and disruption identified a background of an otherwise typical being mixed tumor. Examination of additional sections demonstrated the same. The histomorphological features were verified by consultation, independently, at the U. of Texas and UAB. The patient received chemotherapy after further workup demonstrated a recurrent and progressive disease with lung metastasis. The patient expired, with complications, in January of 2002. The clinicopathological and radiographical features of this rare, and probably the first case report, of this entity are presented.

#39 Read by Title

CORTISOL AFFECTS mRNA EXPRESSION FOR MATRIX METALLOPROTEINASES AND TISSUE INHIBITORS OF METALLOPROTEINASES IN HUMAN GINGIVAL FIBROBLASTS. P. R. Cury, V. C. Araújo, K. R. M. Leite, C. Furuse, N. S. Araújo. Sao Leopoldo Mandic Dental Research Institute, Campinas, Brazil. A positive correlation between the progressive course of periodontal disease and the psychosocial stress status has been reported. Stress leads to activation of the hypothalamic-pituitary-adrenal axis resulting in the increased release of cortisol. The aim of this study was to evaluate the effect of cortisol, at different concentrations, on mRNA expression of MMPs and TIMPs in cultured, human, gingival fibroblasts. The fibroblasts were stimulated with 10⁻⁷, 10⁻⁹, 10⁻¹² M cortisol for 24 hours; untreated cells served as controls. The cells were lysed and the RNA was extracted. Alterations in the expression of MMP-1, MMP-2, MMP-3, MMP-7, MMP-11, TIMP-1 and TIMP-2 mRNA were evaluated using real-time PCR. -actin mRNA expression was used as a control gene. Comparing higher versus lower concentration of cortisol, a marked reversal effect on MMP-2, MMP-7, MMP-11, TIMP-1 and TIMP-2 gene expression was observed. While higher dose (10⁻⁷ M) induced up-regulation of their expressions, lower doses between 10⁻⁹ and 10⁻¹² M resulted in down-regulation, except for TIMP-2 expression, which was down-regulated at higher concentration and up-regulated at lower concentration. Higher cortisol level induced up-regulation of 7.84 fold in the expression of MMP-1, while the lower doses resulted on up-regulation of 2.39 fold. Lower dose induced up-regulation of 23.18 fold of MMP-3, and the higher dose resulted on lower up-regulation. In conclusion, higher cortisol levels can significantly affect the balance of the mRNA expression for MMPs and TIMPs, which may represent a likely mechanism involved in the increased periodontal breakdown associated with psychosocial stress status.

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STAT-3 EXPRESSION AND ACTIVATION IS DYSREGULATED IN ACTINIC CHEILITIS. V. C. Araujo, P. R. Cury, C. Furuse, N. S. Araújo. Sao Leopoldo Mandic Dental Research Institute, Campinas, Sao Paulo, Brazil. Actinic cheilitis is a widely recognized precancerous lesion of the lip caused by ultraviolet radiation. The aim of this study was to evaluate the signal transducer and activator of transcription (Stat-3) expression in actinic cheilitis and its relationship with the degree of epithelial dysplasia. Twenty-five biopsies from cases diagnosed as actinic cheilitis and biopsies from normal mucosa were analyzed. Lesions were graded as mild dysplasia when up to 2 epithelial changes were present, moderate dysplasia when 2-4 epithelial changes were seen and severe dysplasia when more than 5 epithelial alterations were present. Immunohistochemistry for Stat-3 and Phospho-Stat3 (Stat-3P) was performed. In the sections of normal mucosa obtained from lip, only cytoplasmic expression of the Stat-3 in the basal and parabasal layer was observed. In the actinic cheilitis, STAT-3 was expressed in the cell cytoplasm of all the epithelial layers, except in the parakeratin or orthokeratin layers. A nuclear expression of the Stat-3 in rare cells of the basal and parabasal layers was observed in moderate and severe dysplasia. In the sections of normal mucosa and actinic cheilitis, the nuclear expression of Stat-3P was observed in the entire epithelium, except for the parakeratin or orthokeratin layers, being more intense in the deeper layers. Nevertheless, in severe dysplasia, some epithelial cells presented a loss of Stat-3P expression and the expression was more intense in the superficial layers than in the deeper layers. In conclusion, the expression of Stat-3 is dependent of the dysplasia degree and it is dysregulated in the actinic cheilitis.