American Academy of Oral
and Maxillofacial Pathology

ABSTRACTS

Essay Program I
Monday, April 22, 2002
8:00 a.m. – 12 noon
Abstracts 1-20
Doug Damm, Presiding

Essay Program II
Monday, April 22, 2002
8:00 a.m. – 12 noon
Abstracts 21-40
Carl Allen, Presiding

56th Annual Meeting
&
Continuing Education Program

April 20 – April 24, 2002
Hotel Inter-Continental
New Orleans, LA
USA
EPITHELIOID ANGIOSARCOMA PRESENTING IN THE GINGIVA OF AN ADOLESCENT. C. Penner, W. Grist and S. Müller. Emory University, Atlanta, GA.

Angiosarcoma is a relatively rare neoplasm, most commonly occurring in the skin and underlying superficial soft tissues. There is a peak incidence in the seventh decade of life, although a wide age range may be afflicted. Reported cases of angiosarcoma arising in the oral mucosa have all occurred in older patients, typical with the age of peak incidence. Epithelioid angiosarcoma has been viewed as an aggressive, poorly differentiated neoplasm that has a poor long-term prognosis and should be included in the differential diagnosis of almost any epithelioid malignant neoplasm.

We describe a 16 year old female that presented to her periodontist because she noticed asymptomatic swelling and discoloration of the right mandibular gingiva. Her past medical history was unremarkable. A small biopsy was taken at that time, which was inconclusive. The patient returned several months later because the lesion had recurred. Clinical examination revealed a blue discoloration of the gingiva involving both the buccal and lingual surfaces. This pigmented lesion extended from tooth #29-31, and was approximately 5 cm in length. At this time a gingivectomy was done and the histologic diagnosis was high-grade epithelioid angiosarcoma. The patient underwent an en-bloc resection with positive margins; further resection revealed no residual tumor. Three months later, she noted a swelling of a lymph node under the right mandible. FNA confirmed metastatic angiosarcoma and the patient underwent a right neck dissection. Four of 24 lymph nodes were positive with extra-capsular extension. Bimodal chemotherapy and radiation treatment were performed. The patient is alive with no evidence of recurrent disease at 12 months.

LIMITED WEGENER’S GRANULOMATOSIS X. Zornosa and S. Müller, Emory U., Atlanta, GA.

Wegener’s granulomatosis can involve any organ system, and symptoms may be limited to one or two organs especially the upper and/or lower respiratory tract. Diagnosis is based on two out of three histologic features (vasculitis, necrosis or granulomas) plus involvement of at least one organ system (upper airway, lungs or kidneys). Diagnosis is further supported by elevated serum antineutrophil cytoplasmic autoantibodies (cANCA). Carrington and Liebow in 1966 and Cassan et al in 1976 described a group of patients with a limited form of Wegener’s granulomatosis. These patients did not present with the entire classic clinicopathological triad. Limited and generalized Wegener’s granulomatosis represent a spectrum of clinical manifestations of a single disease. We report two cases of Wegener’s granulomatosis limited to the head and neck and upper respiratory tract. One patient, a 54 year old female, presented with bilateral chronic otitis media and hearing loss, ocular and cutaneous ulcerations, a severe saddle nose deformity and an oral antral fistula. The second patient was a 40 year old female with a history of chronic sinusitis with nasal involvement and hearing loss. The patient presented with a cutaneous ulcer and a focal granular gingival hyperplasia (strawberry gingivitis). The histological findings on both patients were consistent but not diagnostic of Wegener’s granulomatosis. The diagnosis for both cases was supported by elevated serum antineutrophil cytoplasmic autoantibodies (cANCA). Patient one was treated with prednisone and Cytoxan and patient two with prednisone and Methotrexate. Both patients are responding to treatment and continue to be monitored.
INTRAOSSEOUS SCHWANNOMA OF THE MANDIBLE: A CASE REPORT AND REVIEW OF THE LITERATURE. A. Chi, J. Carey and S. Muller. Emory U. Hospital, Atlanta, GA.

Schwannomas are slow growing, benign tumors of Schwann cell origin. These tumors exhibit a predilection for the soft tissues of the head and neck, as well as the flexor surfaces of the upper and lower extremities. Intraosseous schwannomas, however, are rare neoplasms accounting for less than 0.2% of primary bone neoplasms. The most common intraosseous site is the mandible; other sites reported include the sacrum, vertebrae, ilium, femur, patella, tibia, ulna, humerus, and small bones of the hand. A review of the literature reveals 40 reported cases of intramandibular schwannomas with an average age of 28 years and a 1.6:1 female: male ratio. Two of the reported cases were described as the cellular variant, and the rest were consistent with the classic type. All of the reported lesions were solitary, and none was associated with neurofibromatosis type I or neurilemmomatosis. No cases of malignant transformation or recurrence following conservative surgical excision have been reported. We report a case of a 16-year-old female with a well circumscribed, unilocular radiolucent lesion impeding the eruption of a mandibular canine. Histologic examination showed a well-defined lesion with a predominance of Antoni A areas. The patient has had no post-operative complications or signs of recurrence.

A FATAL CASE OF CERVICOFACIAL NECROTIZING FASCIITIS SECONDARY TO MAXILLARY SINUSITIS. J. Lamphier, H. Kim and T. Najjar. UMDNJ, University Hospital, Newark, NJ and Staten Island Hospital, New York

Necrotizing fasciitis is a life-threatening infection usually affecting the perineum, trunk and extremities. It is relatively uncommon in the head and neck region and when it occurs it is usually confused with extensive periorbital and odontogenic infections. The aim of this unusual case presentation is to familiarize other clinicians with the rare existence of this lesion and its origin from the maxillary sinus. In fact a review of current literature revealed only one other case of cervicofacial necrotizing fasciitis originating from the sinus which also led to the patient’s death.

The patient was a 65-year-old female who presented to the ER with a five-day history of sinus pain after being seen at another facility the previous day and placed on Claritin. Over a 24-hour period she developed bilateral cervicofacial edema, purulent exudates from both nares and necrotic tissue in the right maxillary labial vestibule. Despite aggressive surgical debridement, airway protection and broad-spectrum antibiotics, sepsis and multi-organ failure ensued and the patient died nine days after admission. This occurred in spite of accurate differential diagnosis, proper diagnostic tests and intensive medical and surgical management.

In conclusion, this case report revealed that even with close surveillance between the Oral and Maxillofacial surgeon and pathologist and proper diagnosis and treatment, the grave prognosis of this lesion was not avoided.

This is a case report of a rare keratinizing variant of primitive neuroectodermal tumor presenting as a radiolucency displacing teeth in the maxilla of an eleven year old boy. The clinician's impression was that of an adenomatoid odontogenic tumor and he submitted an excisional biopsy specimen for evaluation at the TUSDM oral and maxillofacial pathology biopsy service. The specimen demonstrated infiltrative islands or round blue tumor cells in an eosinophilic fibrillary stroma. Keratin pearl formation was observed in the tumor nests. A comprehensive immunohistochemical panel disclosed strong positivity of the tumor cells for keratin, vimentin, neuron-specific enolase, CD99, synaptophysin and neurofilament protein. Weak positivity was observed for chromogranin. The tumor stained negative for CD45, desmin and muscle-specific actin. The immunohistochemical profile of this lesion places it in the PNET/Ewing's sarcoma category where expression of synaptophysin, neurofilament protein and neuron-specific enolase present strong presumptive evidence towards a diagnosis of PNET. A bone and CT scan as well as a MRI showed absence of any other lesions in the patient's body. Subsequently, a segmental maxillectomy was performed, followed by local radiation treatment. The surgical margins were free of tumor and the patient is currently free of disease. Ewing's sarcoma and PNET are distinctly rare in the oral and maxillofacial area. Current treatment modalities have improved the prognosis considerably, but there is too small a number of cases available in the literature from which to draw reliable prognostic conclusions.


A variety of oral cavity lesions may mimic condyloma acuminatum, both histopathologically and clinically. Since oral condyloma is a sexually transmitted disease induced by human papillomavirus (HPV), it is important to be able to differentiate it from its mimics. The purpose of this study was to determine which histologic features could distinguish oral condyloma, as defined by the detection of HPV DNA by in situ hybridization, from its mimics. Thirty-two paraffin-embedded specimens, clinically and histologically suggestive of condyloma, were analyzed. HPV DNA was detected in 17/32 (53%) of the lesions; no additional positive cases were detected after PCR amplification. Only 5 of the 17 viral positive cases were considered to be histopathologically unequivocal for condyloma. The histologic features significantly associated with HPV detection were non-uniform perinuclear halos, often in association with epithelial crevices (p = 0.02), and papillomatosis (p = 0.02). Each of the 17 HPV positive cases contained either HPV 6 or 11, which is equivalent to condyloma of the penis and vulva/vagina. It is concluded that the differentiation between oral condyloma and its mimics is best accomplished using histologic, clinical, and in situ viral studies.
EVALUATION OF ORAL INVERTED DUCTAL PAPILLOMAS FOR HUMAN PAPILLOMAVIRUS USING IN SITU HYBRIDIZATION. C. Haberland-Carrodeguas, M. Fornatora, R.F. Reich, D. Trochesset, and P. Freedman. Temple U. Philadelphia, PA; New York Hospital Medical Center of Queens, NY.

Oral inverted ductal papillomas (IDP) are rare benign minor salivary tumors. Unlike sinonasal IDPs which have been shown repeatedly to be infected with human papillomavirus (HPV), the association of oral IDP and HPV has never been shown. Review of the literature reveals two case reports of oral IDPs that have been probed for HPV DNA and found to be negative. Six cases were found which fulfilled the criteria for oral IDP, but also showed histopathologic features of HPV infection on routine microscopy, including koilocytosis and increased mitotic activity. Five of these cases also presented with a papillary exophytic surface component. All cases were analysed for HPV DNA using in situ hybridization. The results are as follows:

<table>
<thead>
<tr>
<th>Case #</th>
<th>Sex</th>
<th>Age</th>
<th>Location</th>
<th>HPV WSS* Probe</th>
<th>HPV 6/11</th>
<th>HPV 16/18</th>
<th>HPV 31/33</th>
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<tr>
<td>1</td>
<td>F</td>
<td>27</td>
<td>Soft palate</td>
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<tr>
<td>2</td>
<td>F</td>
<td>57</td>
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<td>-</td>
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<td>-</td>
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<td>39</td>
<td>Right buccal mucosa</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>39</td>
<td>Floor of mouth</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>41</td>
<td>Floor of mouth</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>54</td>
<td>Right buccal mucosa</td>
<td>+</td>
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Classifications of benign salivary gland neoplasms contain a wide array of entities with varied clinicopathologic features. Within the salivary gland nosology are ductal papillomas, of which there are three distinct varieties currently, sialadenoma papilliferum, inverted ductal papilloma and intraductal papilloma. In recent years, it has been noted that some papillomatous lesions of ductal epithelium do not fulfill the criteria of any of the previously mentioned papillomas. The purpose of this study is to introduce a fourth form of salivary ductal proliferation, the everted ductal papilloma, and catalogue its clinical and histopathologic characteristics. From the archives of Indiana University Oral & Maxillofacial Pathology 22 everted ductal papillomas were identified. The histologic criteria fulfilled by this group include: non-keratinized surface, exophytic, papillary growth pattern, increased nuclear/cytoplasmic ratios (basaloid) and ductal differentiation with or without mucous cells. Of the 22 cases reported, 7 occurred on the buccal mucosa, 6 on the lower lip, 2 on the hard palate, floor of mouth and lower lip, and 1 each on the retromolar pad, parotid papilla, and tonsillar pillar. The lesions were most frequently described clinically as small pink to red, soft, papillary growths and were observed in an exclusively adult population (average age – 64.7), with 21 of 22 occurring over the age of 50. A slight female predilection was noted (1.44/1). One recurrence among the cases was noted. Because of its distinctive clinicopathologic profile, the everted ductal papilloma should be added to the diagnostic possibilities of papillary lesions involving the oral cavity.

Mucinous adenocarcinoma of salivary gland origin is extremely rare. The purpose of this study is to report a case of this tumor in the buccal minor salivary gland and the immunohistochemical features of this tumor. The patient was a 65-year-old male. The lesion appeared as a red, raised, ulcerated, and painful mass on the left anterior buccal mucosa. The clinical impression was a fibroma with an abnormal appearance. Microscopic examination revealed mucus-producing cells and small cell clusters floating in mucous pools, which were compartmentalized by thin fibrovascular septa. The cytoplasm of the tumor cells was vacuolated and the nuclei were hyperchromatic with some pleomorphism and prominent nucleoli. Perineural invasion was noted. Immunostains showed tumor cells positive for AE1/AE3, Cam5.2, EMA, CEA, and sialosyl TN and negative for vimentin. Some cells were S-100 positive. Cytoplasmic vacuoles and the surrounding mucous substance were positive for mucicarmine, PAS with and without diastase digestion, and alcian blue at pH 5.2, but negative for alcian blue at pH 1.0. In conclusion, mucinous adenocarcinoma has unique histological features and myoepithelial cells may participate in the tumorigenesis.

IMMUNOHISTOCHEMICAL PROFILE OF SALIVARY DUCT CARCINOMA V.C. Araújo, S.V.L. Loducca, L.P. Kowalski, and N.S. Araújo. Oral Pathology Department, U São Paulo, SP, Brazil.

Salivary duct carcinoma (SDC) is an uncommon and highly aggressive adenocarcinoma of the major salivary glands, occurring more frequently in elderly men, and affecting predominantly the parotid gland. Histopathologically, it has a striking resemblance to the ductal type of breast carcinoma, which exhibits intraductal and invasive components. A low-grade form of salivary duct carcinoma has been proposed as a distinctive variant with a low-grade histopathology and a predominant intraductal growth pattern considered as an in situ process. In order to differentiate intraductal growth from invasive growth, a panel of antibodies was applied to five cases of salivary duct carcinoma that were retrieved from the archives of the AC Camargo Cancer Hospital. This investigation demonstrated that all tumor cells were positive for cytokeratins 7 and 8. Occasional positivity was observed to cytokeratin 14. This positivity was noted in the peripheral basal cells of the tumor islands. This pattern of reactivity to cytokeratin 14 is thought to denote in situ intraductal growth and delineate the low-grade variant of this neoplasm.
ESSAY PROGRAM I
Monday, April 22, 2002

#11 10:00 a.m.

GLIAL FIBRILLARY ACIDIC PROTEIN (GFAP) EXPRESSION IN BASAL CELL AND CANALICULAR ADENOMAS (BCA/CNA) VS. POLYMORPHOUS LOW GRADE ADENOCARCINOMAS AS AN ADJUNCT IN DIAGNOSIS OF MORPHOLOGICALLY SIMILAR CASES. A. Curran, C. Allen, F. Beck, and V. Murrah. U. of Mississippi, Jackson; Ohio State U., Columbus; U. of North Carolina, Chapel Hill.

GFAP, an intermediate filament, is expressed by a number of cells in the mature nervous system. Tumors not generally considered to be of glial origin also express GFAP. In a previous large sample study, pleomorphic adenoma (PA) of minor salivary glands strongly expressed GFAP, unlike polymorphous low grade adenocarcinoma (PLGA). This finding can be helpful to the pathologist when attempting to differentiate between fragmented lesions with equivocal morphologic features. Some BCA/CNAs of minor glands also can present as a diagnostic dilemma when incisionally biopsied or curetted specimens show PLGA-like features. The objective of this study was to determine if GFAP could be an aid in these cases. One hundred seven formalin-fixed, paraffin-embedded specimens (50 PLGAs, 37 BCA/CNAs and 20 PAs) were immunostained with rabbit polyclonal antibodies to GFAP. CNS tissue was used as a positive control. Using the scoring system of Regezi et al, the median scores were PLGA = 0.0, BCA/CNA = 1.0 and PA = 3.0 (kappa = 0.81). This study confirms the previous finding that GFAP reactivity is a reliable marker to differentiate PLGA and PA. BCA/CNAs that were positive showed moderately intense linear reactivity at the tumor/ connective tissue interface while PLGAs showed only occasional faint positivity of luminal cells. Therefore, any morphologically equivocal tumor that shows more than occasional faint GFAP staining may be considered a BCA/CNA or PA depending on the matrix present.

#12 10:12 a.m.

C-KIT EXPRESSION IN BENIGN AND MALIGNANT SALIVARY GLAND TUMORS. P. Edwards, T. Bhuiya, and R. Kelsch. Long Island Jewish Medical Center, New Hyde Park, NY.

Background: C-kit proto-oncogene expression is identified in normal cellular development such as hematopoiesis and organogenesis. Overexpression of this tyrosine kinase receptor protein has been identified in a subset of malignant neoplasms such as gastrointestinal stromal tumors, myeloid leukemias as well as adenoid cystic carcinoma. There is a question as to whether this protein is expressed in other salivary gland neoplasms.

Objectives: To determine c-kit expression in adenoid cystic carcinoma (ACC), polymorphous low-grade adenocarcinoma (PLGA) and monomorphic adenoma. Design: Forty nine formalin-fixed paraffin-embedded salivary gland neoplasms (17 monomorphic adenomas, 17 PLGA and 15 ACC) obtained between 1989 and 2002 were retrieved from the pathology files of the Long Island Jewish Medical Center. Sections from each tumor were reacted with the antibody against c-kit (CD117). Results: Reactivity was considered positive if >5% of tumor cells stained. C-kit expression was uniformly positive in the cytoplasm of luminal neoplastic cells in ACC (15/15, 100%). Positive reactivity also was identified in the majority of PLGA (16/17, 94%), with at least 25% of the tumor cells being positive; a similar prevalence of reactivity was seen in the monomorphic adenomas (16/17, 94%). In the normal surrounding salivary gland, c-kit reactivity was identified focally in ductal epithelium. Conclusion: C-kit expression was not restricted to malignant salivary gland neoplasms but is expressed in all three tumor types evaluated. Therefore, c-kit immunoreactivity may not distinguish between the specific types of salivary gland neoplasia tested.
ESSAY PROGRAM I
Monday, April 22, 2002

#13  10:24 a.m.


Neoplasms arising from the minor salivary glands are relatively common. 209 cases of minor salivary gland tumors in the oral cavity (117 benign and 92 malignant) were studied clinically and microscopically. Pleomorphic adenoma (PA) is the most common benign tumor in our series (91 of 117). PA occurred between ages 17 to 88 years (average age: 46); PAs in females were more common than males with a ratio of 1.9:1. Fifty cases of PA occurred in the hard palate. Canalicular adenoma (CA) is the second most common benign tumor in our series (25 cases). Labial PAs and CAs only occurred in the upper lip. Two Warthin tumor-like lesions were seen. Microscopically, the intraoral lesions showed the diagnostic criteria consistent with Warthin tumors of the parotid gland. The question of the true neoplastic nature of these tumors is raised because similar features can be seen in sialocyst with lymphoid tissue response. 92 cases were malignant (44%) with mucoepidermoid carcinoma (MEC) (39/92) and adenoid cystic carcinoma (ACC)(20/92) most common. Most MECs were low-grade. Seventeen tumors were diagnosed as polymorphous low-grade adenocarcinoma (PLGA). Seven cases of PLGA were recognized in cases previously diagnosed as PAs, particularly before 1984. PLGAs were usually slow growing and carry a relatively good prognosis. Distinction of PLGA from ACC is sometimes difficult but important due to the fact that there is a significant difference in clinical behavior between the two. Our study confirms previous reports that PA is the most common benign tumor and MEC is the most common malignant tumor of minor salivary glands.

#14  10:36 a.m.

PERiapical ACTINOMYCOSIS ASSOCIATED WITH RADICULAR CYSTS: A CLINICO-PATHOLOGIC STUDY. A. Hirshberg, I. Tsesis, Z. Metzger, and I. Kaplan. School of Dental Medicine, Tel-Aviv U, Israel.

The objective of the study was to examine the incidence of accidental finding of actinomycotic colonies in periapical lesions submitted for histologic examination, and to establish its correlation with radicular cysts. All periapical biopsy specimens submitted between 1997 and 2000 were included. Sections of paraffin embedded tissues were stained with Hematoxylin and Eosin, PAS and Gram stain. The identification of Actinomyces was done by the presence of typical branching colonies of filamentous bacteria stained positive with PAS and Gram stain. Actinomycotic colonies were observed in 17 out of 963 cases of periapical biopsy specimens (1.8%). Mean age was 42 with a male predilection (65%). The maxilla was the preferred site (65%), with equal distribution between the anterior and posterior areas. Radiographically, most cases presented as well demarcated radiolucent lesions. Three cases were clinically suspected for malignancy. Radicular cyst was the histologic diagnosis in 15 cases (88%), residual cyst in one case, and periapical granuloma in only one case. Treatment included surgical curettage and a short course of antibiotic therapy. Healing was uneventful in all cases. In conclusion, periapical actinomycosis is not common and is associated with cyst formation in a majority of the cases. Outcome is favorable, following surgical curettage, supplemented by a short-term antibiotic treatment. The relationship of periapical actinomycosis with the more serious cervicofacial actinomycosis should be questioned.
SQUAMOUS CELL CARCINOMA EX ODONTOGENIC KERATOCYST: A REVIEW OF CASES FROM THE ARMED FORCES INSTITUTE OF PATHOLOGY. D.W. Nunez, S.B. Williams, and C.W. Pemble. Armed Forces Institute of Pathology, Washington, DC.

Squamous cell carcinoma arising from odontogenic keratocyst (OKC) is extremely rare and the histologic requirements for this diagnosis are very specific. Consideration must be given to the possibility of cystic degeneration of a primary or metastatic carcinoma, as well as to invasion of an OKC by an adjacent primary intraosseous carcinoma. Dysplastic or malignant transformation of squamous epithelium within an OKC is therefore essential for the diagnosis of squamous cell carcinoma ex odontogenic keratocyst. There is some discrepancy in the literature as to the numbers of reported cases, due in part to controversy over the definition of odontogenic keratocyst versus keratinizing odontogenic cyst. Five cases signed out as carcinoma arising in an odontogenic keratocyst are reviewed from the files of the Armed Forces Institute of Pathology. One of these cases is believed to represent radiation-induced proliferation of an OKC and is therefore excluded from this group. Of the remaining 4 cases, the ages ranged from 15 to 72 years old, with an average age of 52. Two of these were located in the maxilla and two were located in the mandible.

GLANDULAR ODONTOGENIC CYST: ANALYSIS OF 7 CASES AND REVIEW OF THE LITERATURE. C. Fowler and R. Brannon. Lackland AFB, TX, and Louisiana State University School of Dentistry, New Orleans.

The glandular odontogenic cyst (GOC) is a relatively recently described odontogenic cyst which displays a unique histomorphology and tendency for recurrence. As outlined by the W.H.O., the GOC exhibits a cyst lining of nonkeratinized squamous epithelium with surface eosinophilic cuboidal cells, which also line intraepithelial crypts or cystlike spaces of mucicarmine-positive material. Other features variably present are mucous goblet cells, hyperchromatic or vacuolated basal cells, epithelial spheres, and mural calcifications. Information tabulated from 7 new cases and 51 cases selected from the English literature reveals that these cysts occur over a wide age range with a peak in the 6th decade, an average age of 51.9 years, and equal gender distribution. There is a marked predilection for the anterior jaws (77.5%) with the anterior mandible accounting for 60.3% of all cases. Pain and swelling were identified in 34% and 75%, respectively. Most of the cysts were located periapically to several teeth; however, 3 presented as globulomaxillary radiolucencies, 3 as dentigerous cysts, and 1 as a lateral periodontal cyst. Slightly more than half presented as multilocular radiolucencies. Lesion size varied from 0.5 cm to 10 cm with several cysts involving large portions of the mandible. Most cases were treated initially with enucleation or curettage. Recurrences were recorded in 14 of 47 cases with available follow-up for a recurrence rate of 29.8%. Three lesions recurred twice. The average interval from initial treatment to recurrence was 46 months. Results of Ki-67, PCNA, and p53 analysis in one of our cases may explain, in part, the tendency for the local destructive growth and recurrence observed in the GOC.
ORAL NON-HODGKIN’S LYMPHOMAS: AN ANALYSIS OF 46 CASES.  S. Sousa, R. Mesquita, N. Araújo, and V. Araújo.  U. of São Paulo, Brazil.

Extranodal non-Hodgkin’s lymphoma (NHL) of the oral tissues is relatively rare. We studied 46 cases of NHLs of the oral mucosa and diagnosed them according to the WHO 2001 classification of lymphoid neoplasms. Clinical and histopathological aspects, immunophenotype, genotype and expression of EBV were analysed. Forty-two cases represented B-Cell lymphomas; being 23 diffuse large B-cell lymphomas (DLBC-CD20 and CD79a+), 10 of the subtype plasmablastic, HIV-associated (DLBCP-CD20 and CD79a-, plasma cell +); 16 Burkitt’s lymphomas, (BL, CDs 10, 19, 20, 22 and 79a+, plus BCL-6, IgM and κ or λ +), 1 HIV-associated; 2 MALT lymphoma (CDs 20 and 79a+ and also ½ cases λ +), and 1 mantle cell lymphoma (MCL, CDs 5, 20 and 79a+, plus cyclinD1). The remaining 4 cases were T-cell lymphomas, 3 extranodal NK/T-cell lymphoma, nasal type (CDs 2, 3, 45RO, 16, and 56+), and 1 peripheral T-cell lymphoma, unspecified type (CDs 3 and 45RO+). Clinical aspects as sex, age, race, and lesion locations were similar to what is shown in the literature for each lymphoma subtype. EBV was detected using in situ hybridization in all 10 cases of DLBCP-HIV-associated lymphomas, 13/15 cases of BL and in 2/3 cases of NK/T-cell lymphomas. Monoclonality was investigated using PCR, in DNA extracted from formalin fixed, paraffin embedded tissue of B-cell lymphomas. A monoclonal band in immunoglobulin heavy chain gene (IgH) was present in 12/14 cases of the B-cell lymphomas analysed. These included 3 DLBC, 3 DLBCP HIV-associated, 4 BL, including the HIV-associated and 1 MALT and 1 MCL. The analysis of clinical aspects, morphology, immunophenotype, genotype and EBV presence are important for appropriately diagnosing oral lymphomas. Supported by FAPESP 01/06351-2


Objective: High grade B-cell lineage lymphomas are a recognized complication of human immunodeficiency virus infection. A recently reported AIDS related lymphoma derived from B-cells, and with morphologic and immunophenotypic features of plasma cells has been defined as plasmablastic lymphoma. This lesion has a predilection for the oral cavity. We report two cases of plasmablastic lymphoma presenting respectively as an exophytic mass of the right maxillary alveolus in a fifty-nine year old man and as a diffuse mass involving the left posterior mandible and mandibular vestibule in a thirty-five year old man. Findings: These tumors exhibited a CD56-, CD138+, and CD45+ immunohistochemical immunphenotype. Flow cytometry confirmed a monoclonal cell population and consistent expression of CD38+, cytoplasmic immunoglobulin G, and CD45+. Each case was CD20-, and one of the cases demonstrated CD10+ expression. Histologically, both cases were characterized by a diffuse infiltrate of large plasmacytoid cells. These cells had eccentrically placed round to oval nuclei with prominent nucleoli. Mitoses were also noted. Bone marrow biopsy, plasma protein and urine immunoglobulin analyses were unremarkable. Conclusion: Absent expression of CD56 (neural cell adhesion molecule, a natural killer cell marker) in association with CD38+, CD45+ and CD20- markers characterizes the entity plasmablastic lymphoma.
ESSAY PROGRAM I
Monday, April 22, 2002

#19 11:36 a.m.


The diffuse infiltrative lymphocytosis syndrome (DILS) is a symptom complex in HIV patients, characterized by the persistence of CD8 circulating lymphocytes and lymphocytic infiltration predominantly in salivary glands. There also may be an extraglandular involvement mainly in the lungs, kidneys and gastrointestinal tract. The aim of this work was to study the histopathologic changes and the viral association in patients affected with DILS. We examined seven HIV positive patients with bilateral parotid enlargement and sicca symptoms. Minor labial salivary gland biopsies were performed in all patients and submitted for histopathologic analysis, according to Chisholm and Mason criteria, and for immunohistochemistry for CD4, CD8, CMV, EBV emp protein, and p-24 (HIV protein). Histopathologic analysis revealed lymphocytic infiltration of the minor salivary glands, mainly periductal, in all cases; the lymphocytic focus score was ≥2 in all cases and ≥4 in 3 cases. Acinar atrophy, ductal ectasia and mild ductal epithelial atypia were also observed. The immunohistochemical findings showed strong positive reaction for EBV emp and p-24 in ductal cells in all cases, while CMV was consistently negative. Also, the lymphocytes were positive for CD8, but consistently negative for CD4, confirming the CD8 nature of the lymphocytic infiltrate. Our results support that minor labial salivary gland biopsy is a very useful diagnostic tool in establishing the diagnosis of DILS. A role of EBV and HIV, but not CMV, in the pathogenesis of DILS is suggested by our immunohistochemical findings.

#20 11:48 a.m.


This study evaluated the prevalence of post-transplantation lymphoproliferative disease (PTLD) in the head and neck region (H&N) of children. 34 children with PTLD were identified (mean age 6.7y, 1.1M:1.0F). 17 children presented with H&N PTLD. The children had undergone solid organ (liver, lung, heart) transplantation. 50 biopsies were performed (1.6/child). PTLD sites were: H&N [n=19]; lungs [n=13]; non-cervical lymph nodes; liver [n=3]; heart [n=3]; bone marrow [n=1]; spleen [n=1]; kidney [n=1]. H&N PTLD sites were: tonsils/adenoids [n=9]; cervical lymph nodes [n=8]; parotid gland [n=1]; suboccipital area [n=1]. PTLD diagnosis was based upon histopathologic features and EBV detection by in situ hybridization (EBER-1) or PCR. Immunocytochemistry (CD20, CD3, kappa, lambda), cell surface marker flow cytometry, and B-cell gene rearrangement were performed to rule out clonality and malignant transformation. Malignant transformation with EBV-associated H&N lymphomas (nasopharynx, cervical lymph node) occurred in 2 cases. Prior PTLD treatment consisted of reducing immunosuppression therapy and steroids. Current therapy employs a CD20 antibody that markedly depletes the B-cell population to eliminate EBV-infected B-cells. PTLD commonly presents in the H&N region of children (50% of cases; 38% of biopsy sites). With increasing numbers of children undergoing solid organ transplantation requiring long-term immunosuppression, PTLD is becoming a more common entity that requires extensive evaluation to detect an EBV-driven malignant process.
SPECTRUM OF ORAL CONDITIONS SUBMITTED FOR MICROSCOPIC AND DIRECT IMMUNOFLOUORESCENCE ANALYSIS. J. Rinaggio, A. Aguirre, M. Neiders, and V. Kumar. U. of Medicine and Dentistry of New Jersey, Newark, SUNY at Buffalo School of Dental Medicine, and IMMCO Diagnostics Inc., Buffalo, NY.

The clinical and/or histopathological findings of vesiculobullous diseases of the oral cavity are rarely pathognomonic. Direct immunofluorescence (DIF) is a valuable ancillary test that enhances the segregation of these conditions. The goal of this study was to determine the spectrum of oral conditions that prompted a microscopic and DIF examination to rule out vesiculobullous disease. We reviewed 270 consecutive oral biopsies submitted by private practitioners to our laboratory for H&E and DIF testing. One hundred twenty-nine (48%) cases showed positive DIF findings. This group consisted of lichen planus (n=99), pemphigoid (n=21), pemphigus (n=6), linear IgA disease (n=2), and chronic ulcerative stomatitis (n=1). One hundred forty-one cases (52%) showed negative DIF findings. This group was comprised largely of nonspecific ulcerative, vesicular, and/or inflammatory diseases. In addition, actinic keratosis, granulomatous inflammation, foreign body granulomatous inflammation and a cyst, were diagnosed. More importantly, there were two cases of squamous cell carcinoma and six cases of epithelial dysplasia, which accounted for 2.9% of the total sample. Our data revealed that only approximately half of the cases examined yielded positive immunofluorescence findings, emphasizing that a wide variety of conditions of diverse pathogenesis may share a common clinical presentation.

IDENTIFICATION OF SALIVARY GLAND HYPOFUNCTION IN THE MANAGEMENT OF ORAL MUCOSAL DISEASE
Zunt, SL, Indiana University School of Dentistry, Indianapolis, Indiana, USA; Lee, L, Princess Margaret Hospital, Toronto, Ontario, Canada; Woo, S-B, Harvard School of Dental Medicine & Brigham and Women's Hospital.

Oral and maxillofacial pathologists manage many chronic mucosal diseases with immune-modulating therapies such as corticosteroids. The response to these therapies may be less than ideal if salivary gland hypofunction also is present. Salivary gland hypofunction may not be apparent upon clinical examination. Commercially available Schirmer tear test strips (Eagle Vision, TN, USA, 1-800-222-7584) have been reported to be an easy method to quickly measure unstimulated and stimulated salivary flow in a quantitative manner. The Modified Schirmer Test (MST) requires placement of the dye-containing calibrated paper test strip in the floor of the mouth for three minutes. The MST can be used to measure the stimulated salivary flow rate after sialogogue therapy, either pilocarpine (Salagen, MGI Pharma) or cevimeline (Evoxac, Daiichi). The MST is a quantitative method which requires three minutes, is easy to read, and facilitates patient education. 339 consecutive new patients referred for oral and maxillofacial pathology consultation had their unstimulated salivary flow rate measured using the MST. Of these patients, 159 (47%) exhibited normal salivary flow rates ≥ 28 mm/3 min and 179 (53%) patients had clinical diagnosis of xerostomia (subjective) or salivary gland hypofunction (objective MST measurement). Of the patients with clinical diagnoses of xerostomia or salivary gland hypofunction, 30 (17%) had mild dry mouth with MST 24-27 mm/3 min., 47 (26%) had moderate dry mouth with MST 11-23 mm/3 min., 92 (51%) had severe dry mouth with MST ≤ 10 mm/3 min, and 10 (6%) of the patients had a sensation of dry mouth with MST ≥28 mm/3 min. Identification of salivary gland hypofunction may have a significant impact on the management of oral disease.
HIDDEN CANCERS – FREQUENCY OF MALIGNANCY IN 17,372 PERIAPIICAL AND NON-APICAL RADIOLUCENCIES. J. Bouquot. The Maxillofacial Center, Morgantown, WV.

**Background:** The need for microscopic interpretation of apical tissues, i.e. the risk of missing a malignancy, is unclear, and the risk for non-apical radiolucencies has never been estimated. **Objective:** To review the histopathology of a large number of lesions presenting as either periapical pathosis or areas of focal osteoporotic radiographic change, none of which were suspected clinically of being malignant. **Methods:** Clinical presentation and microscopic interpretation of consecutively accessioned periapical and non-apical alveolar bone lesions submitted to a national mail-in biopsy service were reviewed. Lesions clinically suspected of malignancy were excluded, as were radiopaque lesions and non-apical cystic or other well-demarcated radiolucencies. **Results:** Of 8,263 routine periapical granulomas and cysts, 3 (0.04%; 1/2,500) proved at biopsy to be malignant, all metastatic carcinomas from below the clavicles. Of 9,109 poorly demarcated and ill-defined radiolucencies, 14 (0.15%;1/714) proved to be malignant (5 primary lymphomas of bone, 5 multiple myelomas, 2 fibrosarcomas, 1 osteosarcoma, 1 malignant fibrous histiocytoma). **Conclusions:** The estimated risk of malignancy in poorly defined jawbone radiolucencies is 1/714 biopsied samples, while the estimated risk in routine periapical lesions is 1/2,500 biopsied samples. The unknown and unknowable case-selection biases inherent to all biopsy services are assumed to be present here as well. Hence, these numbers represent only relative frequency rates for a large biopsy service; they are not population prevalence rates.

THROUGH-TRANSMISSION ALVEOLAR SONOGRAPHY (TTAS) – A NEW TECHNOLOGY FOR EVALUATION OF MEDULLARY DISEASES. CORRELATION WITH HISTOPATHOLOGY OF 285 SCANNED JAW SITES. J. Bouquot, M. Margolis, W. Shankland II, and J. Imbeau. The Maxillofacial Center, Morgantown, WV; Mesa, AZ; Columbus, OH; Tauranga, NZ.

**Background:** New sonography technology assesses sound wave attenuation across bone and may improve our ability to find poorly demarcated alveolar lesions. **Objective:** To correlate TTAS scans with medullary histopathology. **Study Design:** 285 alveolar sites with pain or localized osteoporotic change on radiographs were biopsied after TTAS imaging. Diagnoses were categorized into 5 broad disease types, which were then correlated with graded (4-point scale) TTAS images. **Results:** Average patient age was 53 years; 60% were 40-59 years of age; 69% were female. 76% of lesions occurred in the molar/retromolar region; there was a slight predilection for the maxilla. For 88 osteoporotic lesions, the mean grade was 3.4 (median = 4; 95% CI = 3.29-3.56). For 83 ischemically damaged bone samples, the mean grade was 3.4 (median = 4; 95% CI = 3.20-3.55). For 52 chronic osteomyelitis lesions, the mean grade was 3.0 (median = 3; 95% CI = 2.73-3.24). For 14 cases of osteosclerosis, the mean grade was 3.1 (median = 3; 95% CI = 2.65-3.50). For 39 odontogenic lesions, the mean grade was 2.0 (median = 2; 95% CI = 1.61-2.39). 74% of osteoporotic/ischemic lesions had high-grade (Grade III or IV) TTAS images. The level of false positive TTAS scans was less than 3%. **Conclusion:** TTAS imaging appears to be very effective in identifying low bone density and ischemically compromised bone, but is less effective in identifying odontogenic inflammatory and cystic lesions.
FOCAL OSTEOPOOROTIC MARROW DEFECT – AN ISCHEMIC OR POST-ISCHEMIC PHENOMENON?
LITERATURE REVIEW AND EVALUATION OF 596 NEW CASES. J. Bouquot, M. Rohrer, R. McMahon, M. Makek, and T. Boc. The Maxillofacial Center, Morgantown, WV; U. Minnesota, Minneapolis; Valparaiso, IN; U. Zurich, Zurich, Switzerland; Atlanta, GA.

Background: FOMD presents as a localized, poorly-demarcated radiolucency of unknown etiology; 300 cases have been reported. Examples of a similar lesion, ischemia-induced regional osteoporosis, have been recently described in long bones. Objective: To review a large number of FOMD lesions and determine the proportion showing histopathologic evidence of ischemic marrow disease. Methods: 596 cases of microscopically diagnosed FOMD were reviewed for features of regional ischemic osteoporosis and other ischemic change. Microscopic criteria were from the orthopedic literature; international experts on long bone ischemic disease were visited and consulted prior to this review. Results: 74% of patients were female; average age at diagnosis was 49 years. Lesions were evenly distributed between the jaws; 79% were in the retromolar/third molar region, 92% were in edentulous bone (77% in old extraction sites); 3% of cases were bilateral; 30% were tender or painful. Average lesion size was 1.2 cm (range: 0.5-2.8 cm.); no lesion showed cortical expansion. 76% of lesions were comprised primarily of fatty marrow; 88% showed microscopic features of ischemic marrow damage; 9% demonstrated intravascular thrombi. Fatty lesions were much more likely to be in the maxilla, to be in males, and to be associated with pain. Conclusions: FOMD appears to be the jawbone variant of regional osteoporosis of long bones and the 2 subtypes are associated with clinical differences.

SOLITARY FIBROUS TUMOR INVOLVING THE SPHENOID SINUS, CAVERNOUS SINUS AND PITUITARY FOSSA: A CLINICOPATHOLOGIC CASE STUDY D. Cassarino, A. Auerbach and P.Duray Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, MD.

Solitary fibrous tumor (SFT) is a spindle cell tumor which was described first in the pleura, but also has been described in multiple extrathoracic sites including the meninges, orbit, and nasal and paranasal sinuses. There have not been any reported cases involving the sphenoid sinus, cavernous sinus or pituitary fossa. We report a case of a 54 year old female who presented with progressive amaurosis and headache. Imaging studies showed an infiltrative and destructive lesion involving the sphenoid sinus, cavernous sinus and pituitary fossa, and invading the medial temporal bone, ethmoid and pterygoid bones, with extension into the posterior nasopharynx. At surgery, the tumor was found to abut but not invade the pituitary gland, and was only partially resectable due to its bony invasion and encasement of the carotid artery. Histopathology showed a proliferation of spindle-shaped cells in a dense, hyalinized collagenous stroma, with frequent interspersed slit-like vascular spaces. Some of the vascular spaces showed a branching appearance. There was cellular pleomorphism but few mitoses were identified. The tumor reacted intensely with CD34, factor XIIIa, neuron-specific enolase, CD99, and the proto-oncogene Bcl-2. Markers for muscle, neural, epithelial, vascular, and melanocytic derivation were negative. The histopathologic and immunohistochemical profiles fit the diagnosis of SFT. Given the tumor’s impressive size, extensive invasion and bony destruction, it most likely was a malignant SFT. This is the first report of a SFT, benign or malignant, involving the sphenoid sinus, cavernous sinus or pituitary fossa. The occurrence of SFTs in the sinus is rare but should be considered in the differential diagnosis of lesions arising in the soft tissue and sinuses of the head and neck.
PALATAL MUCOSAL CALCIFIED NODULE: CASE REPORT AND REVIEW OF THE LITERATURE.
W. J. Demsar and S. B. Williams.  Armed Forces Institute of Pathology, Washington D.C.

The mucosal calcified nodule (MCN) is a rare lesion with only three other cases being reported in the literature, all of which describe a single oral mucosal nodule found on the palate, gingiva, and tongue in children, aged 5 months, 1 year, and 5 years respectively. This is a report of a MCN on the anterior palate of a 6 year old male. The MCN is the oral counterpart of the subepidermal calcified nodule (SCN), which is one of the four forms of calcinosis cutis (metastatic calcinosis, dystrophic calcinosis cutis, idiopathic calcinosis cutis, and SCN). Metastatic calcinosis cutis is found in patients with hypercalcemia or hypophosphatemia, and more commonly involves the arteries and kidneys, and when subcutaneous tissues are involved, multiple nodules are found in the vicinity of large joints. Dystrophic calcinosis cutis occurs in individuals with normal serum calcium and phosphorus who have previously damaged tissue usually due to an underlying connective tissue disease, with large calcium deposits occurring in subcutaneous tissues, often within muscles and tendons. Idiopathic calcinosis cutis resembles dystrophic calcinosis cutis, but there is not an underlying connective tissue disease or previous tissue injury. An example of this type of calcinosis cutis is tumoral calcinosis, which is usually familial and associated with hyperphosphatemia. The SCN most commonly occurs as a single nodule on the face of children, is sometimes present at birth, and these patients have normal serum calcium and phosphate levels with no history of connective tissue disease. As with the SCN, the MCN is a rare oral lesion, which appears to show a predilection for pediatric patients.


Vitamin D dependent rickets is subdivided into Type I and Type II; the two types are inherited as an autosomal recessive trait. The disorders result in a deficiency or an abnormality in the enzyme renal 1-alpha-hydroxylase. The gene for Type I has been mapped to the long arm of chromosome 12 bands 12 to 14 (12q12-14). Patients with the syndrome have growth failure, hypotonia, weakness, rachitic rosary, convulsions, tetany, open fontanels and pathologic fractures. The enamel is markedly hypoplastic, similar to that seen in the pitted type of enamel hypoplasia. Patients also demonstrate a marked anterior open-bite. Type II is similar to Type I but is accompanied by total absence of scalp hair (alopecia totalis). A 10 year old girl with tubular renal acidosis and short stature will be presented. The patient also had malposed teeth with yellow to brownish enamel, chronic generalized marginal gingivitis and chronic localized periodontitis. Hand radiographs revealed decreased bone density with osteoporotic changes. Panoramic and periapical x-rays showed improper root formation in posterior teeth, taurodontic pulp chambers and pulp horns. Histopathologic examination of dental hard tissue showed atypical enamel matrix and different degrees of dentinal calcification, areas of globular and interglobular dentin, osteodentin and a wide predentin layer.
ORAL-FACIAL-DIGITAL SYNDROME TYPE I: A LONG TERM FOLLOW-UP.  B. Nelson, S. Williams and S. Norton.  Armed Forces Institute of Pathology, Walter Reed Army Medical Center, Washington, D.C.

Oral-facial-digital syndrome I (OFDI) is characterized by malformations of the face, oral cavity and digits. Mental retardation and polycystic kidney disease also can be features of the condition. The syndrome is a dominant condition and has been mapped to a region on the short arm of the X chromosome (Xp22.2-Xp22.3). The trait is lethal in males. A female patient with OFDI was followed from birth to age nine. Frontal bossing and a hypoplastic upper lip are responsible for the typical facial features of OFDI. The patient demonstrates the oral stigmata of the syndrome including cleft palate, cleft tongue, numerous hamartomas and frenula of the tongue, micrognathia and absence of a deciduous and permanent mandibular lateral incisor. The digits of the hands are mildly affected with progressive weakness of the left arm. The patient also has learning and behavior disorders. Earlier cases have described individuals affected with OFDI at a single point in their lives. The progression of the traits and characteristics of this syndrome have not been reported in long-term follow up. Clinical, radiographic and photographic records depict the ongoing development of an individual with OFDI from the time of diagnosis and over a nine-year period.


It is currently unknown whether oral epithelial dysplasia develops clonally from a single mutated cell or is the result of multiple cells undergoing separate genetic mutations. A number of neoplasms have been analyzed for clonality using the HUMARA (human androgen receptor) locus located on chromosome X. We hypothesized that if a lesion of epithelial dysplasia were clonal in origin, the dysplastic cells would also exhibit homozygous expression of this marker. We have employed laser-capture microdissection on paraffin-embedded tissue to separate dysplastic epithelium from adjacent normal epithelial tissue and underlying connective tissue in 12 female patients. The specimens were denatured and the DNA amplified using PCR with a P32–labeled, CAG repeat of the HUMARA locus. Connective tissue and/or adjacent normal epithelium from the same tissue sample were used as a heterozygous control. A difference in allelic expression of ≥ 50% from control was considered consistent with clonality. Results will be presented and discussed.
#31 10:00 a.m.


Proliferative verrucous leukoplakia (PVL) is a clinical condition of the oral mucosa that progresses inexorably through stages of epithelial hyperplasia to dysplasia to frank carcinoma of the oral cavity in affected individuals. Previously published work has indicated an overwhelming predominance of the condition in women. Preliminary work in our laboratory with a transgenic mouse model manifesting this type of progressive epithelial proliferation in the oral cavity suggests that exogenous estrogen appears to enhance the progressive epithelial dysplastic process. The objective of this investigation was to determine whether human archival specimens of oral dysplasias (OD) or carcinomas (CA) from patients with PVL would display estrogen receptors. 18 cases of OD or CA were obtained from the files of UCSF and 20 cases were obtained from UNC. These were subjected to immunostaining utilizing mouse monoclonal antibody to estrogen receptor (Zymed Laboratories, San Francisco). Antigen retrieval procedures were performed with 0.01 M citrate buffer prior to immunostaining. The positive control consisted of breast carcinoma metastatic to the gingiva. Negative controls consisted of sections of the positive control substituting non-immune serum for primary antibody. Results were negative for all specimens tested. We conclude that estrogen receptors are not present on epithelium of ODs and CAs present in patients with PVL. Potentially, however, estrogen could function to exert a proliferative effect on the oral epithelium by increasing circulating levels of various growth hormones via the pituitary. (This study was supported by NIH/NIDCR grant 1-R03-DE13855.)

#32 10:12 a.m.

**ENDOSTATIN MODULATES GENE EXPRESSION AND FUNCTION IN HUMAN ORAL SQUAMOUS CELL CARCINOMA (SCC) CELLS.** S. Mallery, R. Wilson, P. Pei, R. Renner, D. Schuller, M. Morse, and F. Robertson. Ohio State U., Columbus.

Due to endostatin's recognized angiostatic properties, previous investigations focused on endostatin-endothelial cell interactions. However, many of the cellular mechanisms necessary for angiogenesis are also employed by invading SCC cells, including activation of surface receptors and proteolytic enzymes. **Objective:** This study investigated endostatin's effects on SCC tumorigenic functions. The parameters evaluated in this study included transcription factor activation, gene expression of integrins, matrix metalloproteases and their inhibitors, as well as the ability of SCC cell lines to migrate and invade across an artificial basement membrane. **Methods:** Migration and invasion assays were conducted with the BioCoat FluoroBlok systems (Becton Dickinson), EMSAs were employed to determine transcription factor activation, and RT-PCR analyses were performed to assess gene expression. **Results:** Soluble endostatin significantly inhibited SCC cell migration and invasion to epidermal growth factor (EGF) (migration data: p<0.001, n=21, One Way χ2 Classification; invasion data: p=0.002, n=9, Mann Whitney U test). Similar to EGF, endostatin functioned to activate both NF-κB and AP-1, suggesting that endostatin activates SCC signal transduction. In contrast to EGF's induction of gene expression, endostatin challenge caused suppression of many promigratory and proinvasive genes. However, endostatin did not cause a generalized, nonspecific suppressive effect on gene expression as shown by stable levels of the "housekeeping" gene, GADPH. **Conclusions:** Our data imply that endostatin's clinical applications have the potential to extend beyond suppression of tumor-associated angiogenesis to include inhibition of migration and invasion of human oral SCC cells.

There is strong evidence that non-steroidal anti-inflammatory drug (NSAID) sulindac exerts a significant antineoplastic effect. The purpose of this study was to explore sulindac’s effect on human oral squamous carcinoma (SCCa) cells and to elucidate the underlying molecular mechanisms. The changes that sulindac treatment induced on growth, apoptosis and cell cycle distribution of human oral SCCa cell lines were assessed by cell growth and flow cytometry experiments. Both sulfide and sulfone metabolites of sulindac, which differ in the ability to cause COX-2 inhibition, were tested. By quantitative RT-PCR, Western blot and immunocytochemistry, we determined the effects of sulindac on COX-2, PPARγ and Stat3 mRNA and protein levels. To further explore PPARγ-mediated pathways, treatment with PPARγ agonists or PPARγ antisense oligonucleotides were applied. Both sulfide and sulfone induced a significant cell growth reduction accompanied by increases in apoptosis without concomitant cell cycle arrest. Sulindac treatment also caused upregulation of the mRNA and protein levels of COX-2 and PPARγ, while sulfide, but not sulfone, eliminated both phosphorylated and unphosphorylated Stat3. PPARγ agonist treatment was similar to sulfide effects on cell growth, apoptosis and Stat3 levels. Treatment with antisense PPARγ oligonucleotides abolished sulindac’s growth inhibitory effect, but did not affect sulfide’s ability to downmodulate Stat3. Our results support a significant, apoptosis-mediated, growth inhibitory effect of sulindac on human oral SCCa cells. We suggest that upregulation of PPARγ expression and activation and downmodulation of Stat3 expression and phosphorylation may mediate, at least partially, the antineoplastic effect of sulindac.


Tumor progression is dependent in large part on angiogenesis and angiogenesis inhibitors have repeatedly been shown to inhibit tumor growth. The present study sought to determine whether the oral squamous carcinoma cells expressed and produced collagen XVIII, a known precursor of endostatin. Four established cell lines of oral squamous cell carcinoma were employed for these studies. Quantitative Real-Time RT-PCR was used to assess the expression of collagen XVIII and CBP2/Hsp47, an ostensible chaperone for fibrilar and basement membrane collagens. Real-time PCR assessment of collagen XVIII with primers selected to the common region of collagen XVIII revealed variable expression among cell lines of oral squamous cell carcinomas. Comparatively, the long form of collagen XVIII revealed no products. Conversely, the lowest level of expression of CBP2/Hsp47 was observed in SCC4 that also had the lowest level of collagen XVIII. However, there was no direct relationship between the level of CBP2/Hsp47 and Collagen XVIII expression across the four cell lines. Treatment of SCC cells with CBP2/Hsp47 antisense phosphorothioate oligonucleotides modulated the production of collagen XVIII but not its expression. These findings indicate that CBP2/Hsp47 may play a role in tumor progression by mediating the endogenous processing of collagen XVIII in tumor cells. This work was supported in part by grants to J. Sauk from U.S.P.H.S. R01-DE12606 and R01-DE13118.
### MICROARRAY BASED GENE EXPRESSION PROFILING IDENTIFIES UP-REGULATION OF CYSTATIN M EXPRESSION RELATED TO METASTATIC PHENOTYPE IN ORAL CANCER CELLS. N. Vigneswaran, M. Gilcrease, P.G. Sacks and W. Zacharias U.TX-Dental Branch, MD Anderson Cancer Center-Houston, NYU College of Dentistry and U. Louisville.

Tumor metastasis is a leading cause of death in oral cancer patients. Identifying the genetic and molecular mechanisms involved in the oral cancer metastasis may aid in early diagnosis and therapeutic intervention. We compared the gene expression patterns of oral cancer cell lines derived from the primary (686TU) and metastatic tumor (686LN) of the same patient using the HuFL microarrays (Affymetrix) with probes for 6800 known human genes. The 686TU and LN cell lines were established from a 49-year old male patient with a squamous cell carcinoma involving the posterior tongue and oro-pharynx (Tumor stage: T3N3B). Fold-change differential analysis between these two cell lines revealed down-regulation of 181 genes and up-regulation of 83 genes in 686LN cells compared to 686TU by two-fold or more. One of the genes is cystatin M (CyM) which is up-regulated by 40-fold in metastatic cell line. RT-PCR analysis of tumor cells derived RNA demonstrated substantially increased levels of CyM mRNA in 686LN cells. When analyzed by immunoblotting, culture supernatants of 686LN cells displayed high levels of both glycosylated and non-glycosylated forms of CyM whereas it was not detectable in 686TU supernatant. Immunohistochemical and in situ hybridization studies of the archival tumors of these cell lines were conducted using a polyclonal anti-CyM antibody and biotin-labeled antisense RNA probe, respectively, which confirmed the expression of CyM in metastatic tumor but not in the primary tumor. CyM is an endogenous inhibitor of lysosomal enzymes cathepsin B, which was recently identified as a dominant execution protease in tumor cells apoptosis, induced by tumor necrosis factor (TNF). We propose that CyM over expression aids metastasis by blocking cathepsin B activity and thereby rescuing tumor cells from TNF-induced apoptosis.

### IMMUNOHISTOCHEMICAL STUDY OF CELL PROLIFERATION AND APOPTOSIS RELATED PROTEINS IN ORAL GRANULAR CELL TUMORS. E Chrysomali, K Tosios, NG Nikitakis, JJ Sauk, and SI Papanicolaou.


The purpose of this study was to assess the cell proliferation activity as well as to evaluate the immunohistochemical expression of proteins that promote or inhibit apoptosis in granular cell tumors (GCT). The material consisted of 14 cases of GCT of the tongue, 8 in females and 6 in males. The mean age was 39.8 years. Immunohistochemistry was performed on sections of formalin-fixed paraffin-embedded specimens according to a 3-step streptavidin-biotin method. The antibodies used included Ki67, a cell proliferation marker, Bcl-2, an antiapoptotic protein, and caspase 3, a protein implicated in the promotion of apoptosis. In 7 of 14 cases, intense nuclear immunostaining for Ki67 was observed in isolated granular cells (1-2%); in the remaining cases, less than 1% of granular cells were positive for Ki67. In 10 of 14 cases, more than 90% of the granular cells exhibited moderate to intense cytoplasmic immunoreactivity for Bcl-2. The granular cells showed moderate to intense cytoplasmic staining for caspase 3 in 5 cases and was weak in 9 cases; the percentage of caspase 3 positive granular cells ranged from 50 to 100%. The overlying epithelium, which exhibited pseudoepitheliomatous hyperplasia in 10 cases, was consistently negative for Bcl-2; in contrast, caspase 3 immunostaining, limited to the upper layers, and Ki-67 immunoreactivity, limited to the basal and parabasal cells, were seen in all cases. In conclusion, GCT cells display low proliferation activity, consistent with their benign behavior. Although caspase 3 expression suggests an activation of the apoptotic cascade in the granular cells, their persistence in the tissues could be attributed to the expression of the Bcl-2 protein, which functions as a survival factor. *ResCode 70/4/5783

The purpose of this study is to estimate the prevalence of Epstein Barr virus (EBV) in odontogenic cysts. For the detection of EBV DNA (BamC, BNRF1, BMLF1 genes), 51 formalin-fixed paraffin-embedded tissue samples of odontogenic cysts (29 radicular cysts, 12 odontogenic keratocysts, 10 dentigerous cysts) and 32 samples of chronic inflammation were chosen for this study. The patients were enrolled at the Department of Oral Pathology, Chosun University Dental Hospital, from 1996 to 2000.

EBV genes were identified in 46 out of 51 cases (90%) by PCR, and the BNRF1 gene was detected in all 46 of the positive cases. BMLF1 was detected in 10 cases, while BamC was positive in three cases. Simultaneous positive reactivity to BMLF1 and BamC gene was seen in BNRF1 positive patients.

These findings suggested that EBV can be related to the development of odontogenic cysts.


No standard histologic parameters have proven to be markers of local recurrence or distant metastasis for adenoid cystic carcinoma (ACC). The presence of p53 mutation allelic loss has been shown to be an adverse predictor of disease activity in many diffuse forms of human cancer, including ACC. Cortactin is a tyrosine kinase substrate and actin-binding protein that is overexpressed in ~30% of head and neck squamous cell carcinomas (HNSCC). Cortactin overexpression has been correlated directly with increased metastatic potential and poor patient outcome.

Objectives: The current study examined the role of p53 mutations in ACC and Cortactin expression levels in an attempt to determine if positive results might influence the development and natural course of the disease.

Methods: Fourteen formalin-fixed, paraffin-embedded ACCs and fourteen samples of normal salivary gland tissue were evaluated immunohistochemically for the presence of p53 and Cortactin. Immunoreactivity was scored using a 0 to +3 scale in which staining was either negative (0), spotty (+1), weakly positive (+2), or strongly positive (+3).

Results: We were able to demonstrate p53 expression in 9 of 14 tumors and Cortactin overexpression in 11 of 14 tumors. The tumors showed varying degrees of immunopositivity ranging from 0 to +3. Conclusions: These studies suggest that p53 aberrations may be involved in some ACC tumor progression and that Cortactin is overexpressed in tissue samples from ACC and may play a role in ACC development. These findings may be of possible prognostic and therapeutic value in some cases of ACC.

This study was supported by funding from the National Organization for Rare Disorders.

Oral alveolar soft part sarcoma (OASPS) is one of the rare soft tissue sarcomas that involves the oral cavity. Currently, the etiology of this neoplasm still is uncertain. Two cases of OASPS were examined immunohistochemically for the existence of Epstein-Barr virus (EBV), which has been incriminated in certain neoplasms. One of the two examined cases was located in the floor of the mouth, while the other arose in the ventral surface of the tongue. Both cases affected young female patients, 16 and 13 years of age, and involved the right side. Salivary fluids and sera from the two affected patients revealed positivity for EBV antibody by ELISA technique. Immunohistochemical examinations on paraffin-embedded tissues of these lesions were performed by the labeled strept avidin biotin (LSAB) method using the monclonal anti-EBV BZF1 protein, transactivator protein (ZEBRA). Positive expressions for EBV antibody in both cases were observed as cytoplasmic, nuclear and total cell reactivity. Treatment modulation by antiviral agents for EBV may be beneficial as an adjuvant therapy in combination with surgery and radiation for this neoplasm.

COMBINED MEDICAL DEGREE AND ORAL, HEAD & NECK PATHOLOGY RESIDENCY TRAINING PROGRAM AT THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT SAN ANTONIO. H. McGuff and N. Clare. U. Texas Health Science Center at San Antonio.

Background: Traditionally, the practice of oral & maxillofacial pathology has been largely restricted to the dental school academic environment. Continued dependence on this limited and shrinking venue threatens the existence of this sub-specialty area of pathology.

Objective: The proposed goal is to develop a training program that will allow dentists to practice the full scope of oral pathology and surgical head & neck pathology.

Results: A feasibility study is underway to determine the advantages/disadvantages of an integrated 5 year combined training program that will include acceptance into medical school with advanced standing, completion of the second, third and fourth years of medical school, a residency in anatomic pathology and a fellowship in oral, head & neck pathology. Graduates will be awarded a medical degree, a certificate in anatomic pathology and a certificate in oral, head & neck pathology.

Conclusion: This program will increase the options available to dentists who desire advanced training in pathology. Graduates of this program will expand the scope of practice of oral, head & neck pathology into private laboratories, community hospitals and medical centers.

Background: Epithelioid hemangioendothelioma is an unusual vascular neoplasm. Approximately one-fourth of these neoplasms are considered atypical based on histologic features. These tumors occupy an intermediate position, in regards to behavior, between hemangioma and angiosarcoma. They are capable of producing metastasis, though far less frequently than angiosarcoma. They arise in a wide variety of sites, including the head and neck.

Method: We report a case of a 81 year old gentleman presenting with a slow growing, painful tumor of the left parotid. A pathologic diagnosis of epithelioid hemangioendothelioma with atypical features was rendered.

Conclusion: This is the first reported case of an atypical epithelioid hemangioendothelioma of the parotid. These diagnostic features include cytologic atypia, necrosis, spindling and increased mitotic activity. Aggressive behavior and metastases usually occur in the tumors with atypical features.


The objective of this preliminary study was to characterize a series of 10 unusual solitary exostoses, each located adjacent to the apex of an endodontically involved teeth. Contralateral vital teeth did not show a similar presentation. The mean age of affected patients was 45.5 (SD=10.4); no gender predilection was evident. No specific radiographic features were identified with periapical films. Eighty percent of the cases presented in the mucobuccal fold region of the maxillary first molar/bicuspide (7 cases) and the mandibular first molar (1 case). Three of these cases were evident visually as circumscribed, dome-shaped hard swellings about 2-3 mm in diameter and the others were evident, by palpation only, as similar hard, localized exostoses. The remaining 2 cases (20%) presented in the first molar region on lingual mandibular bone and could be discerned only by palpation of lingual alveolar mucosa. In three cases, there was a history correlating lesion development with endodontic involvement. Following successful endodontic treatment, 2 maxillary lesions showed resolution at 2 and 6 months; however, two mandibular lesions were still present after follow-up periods of 2 years and 15 years. One case was biopsied and showed immature bone suggestive of a proliferative periostitis. Thus, these exostoses most likely form as a localized proliferative periostitis initiated by inflammatory stimuli of endodontic origin. Often, they are evident only by palpation and indicate a contiguous non-vital tooth but do not appear to correlate with a clinically successful endodontic result.
APPLICATION OF PARTICLE INDUCED X-RAY EMISSION (PIXE) TO THE STUDY OF INTRAOSSEOUS PATHOLOGIES  U. RODRIGUEZ, J.L. RUBALCAVA, B. ALDAPE, and D. QUEZADA  UNAM Dental School; UNAM Physics Institute; Mexico.

Particle induced X-ray emission (PIXE) is used to examine the chemical composition of all kinds of materials and objects. This technique has even been applied to analyze biological samples. In order to carry out the present study, the chemical composition of a normal bone (control) and three different intraosseous pathoses (central ossifying and cementifying fibroma, fibrous dysplasia and hypercementosis) were analyzed with the use of PIXE. The objective of this research was to determine whether bones presented a different chemical composition in such pathologies. Samples embedded in paraffin were irradiated with an external proton beam. The following results were obtained: 1) On the one hand, fibrous dysplasia showed absence of chlorine. On the other hand, it revealed the presence of four times the iron and ten times the calcium found in the other pathologies. 2) Only hypercementosis revealed the presence of lead. Potassium, manganese and zinc were found in soft tissue, but no sulfur or chlorine was present. Differences in the concentration of chemical elements were found. Results showed that this method can be used to analyze the biological behavior and eventually may assist in the diagnosis of pathoses of the jaws. The present research was supported by CONACYT J32159-U and G0010- E.

DESENSITIZING ACTION OF HOT PEPPER (CAPSAICIN) ON THE TREATMENT OF PATIENTS WITH BURNING MOUTH SYNDROME (BMS) C. TETLAMATZIN, and B. ALDAPE, School of Dentistry, Mexico.

The objective of this research was to determine if Capsaicin is a good desensitizing agent for patients with BMS. Capsaicin is the main compound of hot pepper (chili), a plant originally from America, which has been used as a condiment and preservative. A number of studies have shown that hot pepper has therapeutic properties, which proved effective for the treatment of pain when used for several weeks. The aim of this research project was to assess the effects of hot pepper (Capsaicin) on the symptoms of BMS. The study was carried out with the participation of 14 female patients who had been diagnosed with BMS and suffered no injuries or concomitant systemic diseases. First, all patients underwent psychological tests in order to determine whether they were experiencing periods of depression or anxiety related to the presence of BMS. Forty-eight hours later, Capsaicin placebo effect was discarded. Finally, each day Capsaicin was applied for ten minutes to those subjects who presented no placebo effects. This was spread over the oral mucosa on the specific areas where the patients suffered from pain. Patients were examined weekly in order to rate the quantity of pain / comfort. The main age was 50 years, and the gender was female. Since this pilot study proved the efficacy of Capsaicin on the treatment of patients who have BMS, it is now being used at the School of Dentistry (UNAM). One hundred percent of the patients analyzed were found to suffer from depression related to BMS. Whereas only 10% responded to placebo, 90% showed a positive pain relief following use of Capsaicin.
ABSTRACTS READ BY TITLE

#45


Previously, we reported the status of anti-PCD oncogenes Bcl-2, Bcl-XL, Mcl-1 and Bag-1 as well as Bax and Bak (pro-PCD) in oral neoplasia. The objective of this investigation was to elucidate the status of Caspase 3, an enzyme considered to mediate the final steps leading to PCD (apoptosis). Five micron thick sections of formalin-fixed human oral tumors from archival paraffin blocks were examined immunohistochemically using polyclonal antibodies (3 p20-n19; Santa Cruz Biotech, CA) to Caspase 3. Sections of lymph nodes served as positive controls. Evaluation revealed primarily cytoplasmic staining (occasional intra-nuclear) in 80% (n=25) of Squamous Cell Carcinomas. Well and moderately well differentiated lesions expressed varying degrees of zonal immunoreactivity, primarily in the differentiating cell layers and to a lesser degree in the peripheral cells of keratin pearls. The poorly differentiated lesions displayed a diffuse heterogeneous reaction. The immunoreactive carcinomas also exhibited a focal granular reaction, probably involving apoptotic bodies. Caspases, expressed in proenzyme form, are activated in a cascade-like sequence. Caspase 3 is trans-activated by upstream Caspase 8 or 9 following their own activation by various mechanisms. In addition to their PCD effects, Caspase 3 and other caspases also are involved in epithelial cell differentiation (keratinization). Bcl-2 family members control cytochrome c release from mitochondria which assists activation of Caspase 9. The role of caspases in tumor progression are not yet known. Our results demonstrate that Caspase 3 is differentially expressed in oral tumors, suggesting that caspases plausibly may play a role in oral neoplasia via induction of PCD.

#46


Squamous cell carcinoma is very common in head and neck area and the incidence increases in Koreans. Down-regulation of p27, which is a member of family of CDK inhibitors that bind to cyclin/CDK complexes and arrest cell cycle, has been reported to correlate with poor survival of various cancer patients including oral squamous cell carcinoma. To investigate the relationship of expression of p27 protein with prognosis of Korean oral squamous cell carcinoma patients, we examined 5-year survival rate of 83 OSCC patients who treated at Seoul National University Dental Hospital between 1992 and 1995. 83 paraffin embedded specimens were processed for immunohistochemistry using a streptavidin-biotin method with p27 monoclonal antibody. Association of clinicopathologic factors as age, sex, TNM stage, histologic grade, lymph node metastasis and 5-year survival rate with p27 expression were evaluated. The 5-year survival rate of the p27(+) group was 68%, while that of the p27(-) group was 29%, and the difference between 5-year survival and p27 expression was statistically significant. (p<0.01, log-rank test). There was no significant difference between lymph node metastasis and p27 expression; the presence of lymph node metastasis was higher in p27(-) group (17 of 31, 54.8%) than in p27(+) group (5 of 13, 38.5%). There was no significant difference between age, sex, histologic grades, and p27 expression. But there was a trend that p27 expression increased with differentiation of tumor. From the above results, reduced p27 expression is related with poor prognosis.
ABSTRACTS READ BY TITLE

#47


Telomerase activation plays a central role in the malignant transformation of epithelial tissues and has been observed in a high proportion of cases of oral squamous cell carcinoma (SCC).  The correlation of telomerase expression levels with the histopathologic grade of tumors, however, remains relatively unexplored.  **Objectives:** To determine if there are quantitative differences in the levels of telomerase expression in well differentiated (grade 1) versus moderately differentiated (grade 2) oral SCCs.  **Methods:** Frozen specimens were obtained from the head and neck tumor bank of the Colorado Cancer Center, including eight grade 1 and seven grade 2 SCCs.  Telomerase expression was determined by the TRAPeze assay (Intergen Co., Purchase, NY), and the levels of expression were evaluated by phosphorimager analysis, relative to a standard curve generated from a serial dilution of HeLa cells.  **Results:** Telomerase activity was detected in 13/15 cases.  The levels of telomerase expression in positive cases were higher in grade 1 SCCs (mean 1675, s.d. 1992) than in grade 2 SCCs (mean 856, s.d. 947).  Review of the corresponding histopathologic sections suggested that the differences in telomerase expression were not a result of differences in the proportion of lesional epithelial cells in the tumor biopsy specimens.  **Conclusion:** Telomerase is expressed in most cases of oral SCC, and the levels of expression may correlate with the histopathologic grade of the tumors.  Further evaluation of quantitative differences in telomerase expression in grade 1 versus grade 2 tumors will require the analysis of microdissected specimens in an expanded study population.  Supported by grant 1R-013 from the Colorado Tobacco Research Program.

#48


Leiomyosarcoma (LMS) is a malignant neoplasm of smooth muscle origin prevalent in the gastrointestinal or genitourinary tract and distinctly rare in the oral cavity.  Oral LMS usually presents as a mass or swelling that gradually increases in size.  Dysphagia, bleeding or pain, are common symptoms.  The maxillary area appears to be the most common location, followed by the mandible, buccal mucosa, tongue, lips and floor of the mouth.  We report a case of a 65-year old man who presented with a 2.5 by 3cm mass in the buccal aspect of tooth #17.  The patient was experiencing pain and bleeding in the area.  An excisional biopsy of the lesion was performed.  Histopathological examination disclosed a proliferation of anaplastic spindle cells arranged in fascicles exhibiting large elongated nuclei with prominent nucleoli.  The pattern of proliferation was invasive and extended to the margins of the specimen.  There was abundant mitotic activity noted.  A preliminary diagnosis of malignant spindle cell neoplasm consistent with either spindle cell carcinoma or sarcoma was made and immunohistochemistry was performed.  The tumor was found to be positive for vimentin and smooth muscle actin and negative for S100, HMB45 and keratin.  A diagnosis of leiomyosarcoma was rendered.  At the same time, the patient developed bloody sputum, anemia and weight loss and was hospitalized.  After a thorough medical examination, a diagnosis of well -differentiated squamous cell carcinoma of the lung was rendered.  The patient died within two months of hospitalization of lung cancer and at the time of his death the oral leiomyosarcoma had recurred locally.  Although we considered the possibility that one lesion represented metastatic spread of the other, the two tumors (LMS and SCC of the lung) were found to have distinctly different histopathological features.
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**NECROTIZING SIALOMETAPLASIA. REPORT OF TWO CASES. D. Antoniades, A. Markopoulos, and P. Papanayotou**  Aristotle U. School of Dentistry, Thessaloniki, Greece.

**Background:** Necrotizing sialometaplasia is an uncommon inflammatory condition of the salivary glands, resulting in ischemia of the salivary tissue which finally leads in local infarction, tissue destruction and formation of crater-like ulcer.

**Case reports:** Two cases (two males) with necrotizing sialometaplasia of the soft palate are presented. Both cases were characterized by the presence of deep crater-like asymptomatic ulcers. Diagnosis was based on clinical and histopathologic examination of the lesions. No specific treatment was administered. The lesions in both cases resolved on their own approximately in five weeks.

**Conclusions:** Because of the worrisome clinical appearance of necrotizing sialometaplasia, biopsy is necessary to rule out the possibility of malignancy. Histopathological examination should always be performed carefully because in many instances necrotizing sialometaplasia may be easily misdiagnosed as squamous cell carcinoma or mucoepidermoid carcinoma.