



DIAGNOSIS • TREATMENT
EDUCATION & RESEARCH

American Academy of Oral
and Maxillofacial Pathology

ABSTRACTS

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Carl Allen, Presiding

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57th Annual Meeting
&
Continuing Education Program

May 17 – May 21, 2003
The Rimrock Resort
Banff, Alberta
Canada

ESSAY PROGRAM I

Monday, May 19, 2003

#1 8:00 a.m.

LICHEN PLANUS PEMPHIGOIDES IN A HEPATITIS C PATIENT. Y-S L. Cheng and T. D. Rees. Baylor College of Dentistry-TAMUSHSC, Dallas, Texas. Chronic hepatitis C has been associated with oral lichen planus and some autoimmune diseases such as autoimmune thyroid disease and autoimmune thrombocytopenic purpura. Mucous membrane pemphigoid has not been documented to occur in patients with hepatitis C. We report a case of lichen planus pemphigoides, based on the clinical, histologic and direct immunofluorescent findings, in a chronic hepatitis C patient. A sixty-two year old female with a past medical history of epilepsy, hepatitis C and hypothyroidism was referred to our clinic with a two-year history of swelling and bleeding gums. Her current medications included phenytoin sodium, phenobarbital and levothyroxine sodium. Oral examination revealed generalized gingival hyperplasia in the maxilla, palatal redness under a maxillary partial denture and ulcerations with white plaques bilaterally on the buccal mucosa. Our clinical diagnoses included phenytoin-induced gingival overgrowth, candidiasis and lichen planus. Laboratory tests revealed high levels of alkaline phosphatase, SGOT, folic acid and phenytoin and a low platelet count. Yeast culture was positive. Incisional biopsies of buccal lesions revealed lichenoid mucositis on histology and linear deposition of IgG and C3 at the basement membrane zone on direct immunofluorescence. The diagnosis of lichen planus pemphigoides was hence established. Treatment was initiated with nystatin oral suspension and 0.05% fluocinonide gel. The clinical signs of candidiasis greatly improved but the ulcerative lesions on the buccal mucosa remained unresolved after three months of treatment. The patient is currently being treated with nystatin for candidiasis prophylaxis and 0.05% betamethasone gel. Her response to therapy is being closely monitored and the gingival enlargement will be further managed after resolution of the mucocutaneous condition.

#2 8:12 a.m.

ACTINIC CHEILITIS: CLINICAL AND PATHOLOGICAL CHARACTERISTICS IN 65 CASES.

A. Markopoulos, E. Albanidou-Farmaki, I. Kayavis. Aristotle U. Thessaloniki, Greece

Objective: The purpose of this study was to determine the clinical and histopathologic variables in lesions of actinic cheilitis.

Study design: The study group comprised 65 patients with actinic cheilitis. For inclusion in the study, the following criteria were required: (1) a lesion clinically located on the lip; (2) epithelial change equal to or greater than mild epithelial dysplasia and (3) certain changes of the connective tissue. Demographic data, clinical features and histopathologic characteristics were recorded and evaluated in each case.

Results: The mean age at the time of diagnosis for the 65 patients was 52.3 years. Thirty-nine patients (60%) used tobacco in any form. An outdoor occupation was indicated for 43 (66.2%) patients. The location of the lesions of actinic cheilitis was in all cases in the lower lip. Actinic cheilitis appeared in 19 patients (29.2%) with the form of white non-ulcerated lesions. In thirty-one patients (47.7%) it was manifested with erosions or ulcers of the lip, while in 15 cases (23.1%) erosions and ulcers co-existed with white lesions or atrophic areas of the lower lip. The main histopathologic characteristics of actinic cheilitis lesions included increased thickness of keratin layer, alterations of the thickness of spinous cell layer, epithelial dysplasia, connective tissue changes, perivascular inflammation and basophilic changes of connective tissue. In 11 cases (16.9%) the presence of squamous cell carcinoma was observed.

Conclusions: The presence of any of the aforementioned clinical and histopathologic changes are suggestive for actinic cheilitis and should prompt the clinician for a close evaluation and follow-up of the patient for the presence or future development of squamous cell carcinoma.

ESSAY PROGRAM I

Monday, May 19, 2003

#3 8:24 a.m.

SQUAMOUS CELL CARCINOMA ARISING IN AN INVERTED PAPILOMA: A REPORT OF THREE CASES. V. Woo, J. Wu. Long Island Jewish Medical Center, New Hyde Park, New York.

Background: Papillomas of the sinonasal tract, termed Schneiderian papillomas, are subcategorized into three types: inverted papilloma, fungiform papilloma, and oncocytic Schneiderian (cylindrical cell) papilloma. The potential for an inverted papilloma to develop a synchronous or metachronous carcinoma, particularly squamous cell carcinoma, has long been recognized.

Objective: We report the clinical and histopathologic findings of three cases of carcinoma arising in an inverted papilloma. **Methods:** A retrospective search and review of Schneiderian papillomas accessioned at our institution from 1989 to 2002 was performed.

Findings: A total of sixty-three Schneiderian papillomas were identified: 53 inverted papillomas, 7 fungiform papillomas, and 3 oncocytic Schneiderian papillomas. Forty-five of 53 inverted papillomas were benign, 5 of 53 exhibited varying grades of dysplasia, and 3 of 53 demonstrated squamous cell carcinoma arising from the inverted papilloma.

Conclusion: The association of inverted papillomas with carcinomas is an important one and impacts on treatment and prognosis. Identifying features that predict the malignant potential of an inverted papilloma are of interest. Studies linking HPV to inverted papillomas with carcinoma have not been conclusive. p53 overexpression or gene mutation in inverted papillomas has been suggested as a promising predictor of malignant transformation.

#4 8:36 a.m.

OSTEOPETROSIS OF THE MANDIBLE IN A 14 YEAR OLD MALE. N. Said-Al-Naief, J. Holmes, P. Louis, and A. Shipp. UAB at Birmingham and Children's Hospital, Birmingham, Alabama.

A 14 year old male was diagnosed with osteopetrosis in 1987 shortly after birth after having uncontrolled seizures. He was treated with bone marrow transplantation at 4 months of age in December of 1987. He was doing well until the year 2000 when he began bleeding from his nose and ears and started experiencing headaches with decrease in vision, for which, he underwent orbital decompression in January of 2000. He also developed osteomyelitis in his right mandible in September of 2002, which was managed by bone debridement and antibiotics, followed by reconstruction of the osseous defect with a tongue flap. He had a relapse with disease progression and it was decided that he would need another bone transplantation, which was delayed until his jaw infection had completely cleared. He underwent a second bone marrow transplant and continues to do well to date. Osteopetrosis is a group of rare hereditary disorders of varying severity, characterized by osteoclast dysfunction, resulting in diffuse and symmetric increase in skeletal density. Infantile osteopetrosis (often referred to as malignant osteopetrosis), diagnosed at birth or shortly after, is a severe disease characterized by marrow failure, bone fractures, multiple infections, and cranial nerve entrapment that may lead to proptosis, blindness, deafness, facial paralysis, and seizures. Osteomyelitis is also common due to an abnormal blood supply. If untreated, infantile osteopetrosis usually results in death by the first decade of life. Bone marrow transplantation is the only complete cure available for malignant infantile osteopetrosis, with approximately 40 to 70 % survival rate. Bone marrow transplantation have initially yielded favorable results in the present case but relapse occurred after a prolonged period of remission and a second transplantation was necessary to maintain his livelihood, further demonstrating the severity of this disease. The etiology and clinicopathological features and various treatment methods of osteopetrosis are reviewed.

ESSAY PROGRAM I

Monday, May 19, 2003

#5 8:48 a.m.

CONGENITAL CARTILAGINOUS REST OF THE NECK: A CASE REPORT AND REVIEW OF THE LITERATURE. D.Wells. Department of Oral and Maxillofacial Pathology, Naval Postgraduate Dental School, Bethesda, Maryland. The congenital cartilaginous rest of the neck (CCRN) is a rare developmental abnormality that appears as a firm nodule in the lower anterior neck near the insertions of the sternocleidomastoid muscle. The lesions may be unilateral or bilateral and are always present at birth. Clinically, two variations are evident: a firm, subcutaneous nodule, or a pedunculated soft tissue mass. CCRN's are known by several other names including elastic cartilage choristoma of the neck, Meckel's cartilaginous remnant, cervical tab, cervical auricle, and wattle.

Histologically, CCRN's are composed of lobules of mature cartilage in a dense, fibroconnective tissue background. Pedunculated CCRN's have a stalk of normal skin with a central connective tissue core. The specific type of cartilage has been described by some authors as hyaline and others as elastic. The skin overlying the CCRN is usually described as having numerous vellus hair follicles. Some authors note the presence of epithelial rests or pacinian corpuscles bordering the cartilage.

The present case describes a 39-year-old male who presented to the dermatology clinic for removal of a presumed skin tag or nevus on the anterior neck. The lesion had been present since birth with no significant change. The lesion was described as a nodule appearing in the lower anteriolateral neck.

The treatment for CCRN is purely cosmetic and consists of simple excision. CCRN's are superficial to the platysma muscle and not attached to deeper structures so the lesion is easily dissected from the surrounding skin and connective tissue. Malignant transformation has not been reported

#6 9:00 a.m.

REGIONAL ODONTODYSPLASIA. A REVIEW OF THE LITERATURE AND A REPORT OF THREE CASES. T.Gibson, R. Kelsch, S. Sokoloff and C.Pillar. Long Island Jewish Medical Center, New Hyde Park, New York.

Background: Regional odontodysplasia is a rare condition characterized by unique clinical, radiographic and histologic findings. It is presumed to be the result of a developmental abnormality of the mesodermally and ectodermally derived tissues of the odontogenic apparatus. **Objective:** The literature was reviewed and demographic, clinical, radiographic, and histologic data was analyzed. Three additional cases of regional odontodysplasia are presented. **Methods:** A comprehensive search of the 1966-2002 Medline database, review of the reference lists of relevant articles and departmental archives from 1990-2002 formed the basis for analysis. **Results:** One-hundred-seven reported cases of regional odontodysplasia were analyzed. In general, regional odontodysplasia affects females more commonly, and there is a slight predilection for the anterior maxilla. Radiographically, the affected teeth have a thin shell of enamel and dentin covering an enlarged pulp chamber, yielding the pathognomonic "ghost teeth" features. Abnormal enamel matrix and dentin are identified. The stroma tissue contains scattered islands of odontogenic epithelium and enamel-like calcifications surrounded by whorls of odontogenic mesenchyme. Pulp tissue appears normal. **Conclusion:** The etiology of regional odontodysplasia remains unknown. Treatment usually involves extraction of affected teeth with fabrication of a dental prosthesis for cosmetic and functional purposes.

ESSAY PROGRAM I

Monday, May 19, 2003

#7 9:12 a.m.

NASAL GLIAL HETEROTOPIA: A CLINICOPATHOLOGIC STUDY OF NINE PATIENTS

C.R. Penner and L.D.R. Thompson. AFIP, Washington DC. Nasal glial heterotopia (also known as “nasal glioma”), is a rare developmental abnormality seen in a wide age group but typically presenting at birth or in early childhood. Failure to recognize the entity is the principle difficulty in diagnosis. Nine cases of nasal glial heterotopia diagnosed between 1970 and 2000 were identified in the files of the AFIP. Histologic and immunohistochemical features were evaluated and patient follow-up was obtained. The patients included 5 females and 4 males with a mean age at presentation of 9.6 years (range, birth to 44 years). Most patients presented clinically with a polypoid mass in the nasal cavity, although 2 patients had a mass on the nasal bridge. Symptoms were present for 2-3 months. A connection to the central nervous system was identified in 1 case. The masses ranged in size from 1 to 7 cm in greatest dimension (mean, 2.8 cm). Histologically, the masses were composed of astrocytes (including gemistocytic type) and neuroglial fibers intermixed with a fibrovascular connective tissue stroma. Neurons and ependymal cells were noted in 2 cases. Focal calcifications and inflammatory cells were identified occasionally. The Masson trichrome stains the collagen intensely blue, while the neural population stains magenta. Immunohistochemical reactivity with GFAP and S-100 protein will help to confirm the histologic diagnosis, while collagen type IV and laminin can highlight the reactive fibrosis. All cases were managed by surgery. All patients were alive without complications at last follow-up (mean, 26.8 years), except for the single fetus included in the study. Nasal glial heterotopia typically involves the nasal cavity and usually presents perinatally, although 3 patients presented in adulthood. The subtle glial component on routine microscopy can be accentuated with a trichrome stain or by immunoreactivity with GFAP and S-100 protein. Imaging studies must be performed before surgery to exclude an encephalocele, which requires different surgery. Complete surgical excision of nasal glial heterotopias is curative.

#8 9:24 a.m.

SCLEROTIC FIBROMA OF THE ORAL MUCOSA. F. Alawi, J. Ghannoum, and P. Freedman. University of Pennsylvania, Philadelphia, and New York Hospital Medical Center of Queens, Flushing, New York.

Sclerotic fibroma (SF) is an uncommon, benign, fibrous neoplasm that may present either as a sporadic, small, solitary cutaneous mass, in an otherwise healthy individual, or as multiple, discrete skin nodules in patients with Cowden’s syndrome. Oral SF has been reported in patients with Cowden’s syndrome, however, to our knowledge, we now report the first documented series of sporadic SF originating in the oral mucosa. We describe 5 cases of SF arising in 3 men and 2 women with an age range of 43-66 years. The buccal mucosa was involved in 4 patients and the lower lip in one case. In all cases, the tumors were slow-growing, asymptomatic, sessile growths ranging in size from 0.4-1.2 cm. None of the patients reported any history of trauma to the affected area. Follow-ups ranged from 8-26 months, with no evidence of recurrence. Microscopically, each of the tumors was characterized by an unencapsulated, well-circumscribed, hypocellular submucosal nodule that was sharply demarcated from the surrounding tissues. The neoplasms were primarily composed of thick collagen bundles that were occasionally arranged in a storiform pattern. Prominent clefts separated many of the collagen bundles. In all cases, a sparse number of spindle cells containing fusiform-shaped nuclei and inconspicuous nucleoli were found scattered throughout the lesion. Occasional stellate-shaped, multinucleated cells were also seen. Some of the cells also exhibited long dendritic cytoplasmic processes that were only observed following immunohistochemistry. The tumor cells strongly expressed CD34 and vimentin but were negative for markers of myofibroblastic, neural or melanocytic differentiation. These findings confirm that oral SF represents a unique entity and should be differentiated from the more commonly occurring traumatic fibroma and giant cell fibroma.

ESSAY PROGRAM I

Monday, May 19, 2003

#9 9:36 a.m.

INTRAORAL MYXOID LIPOMA: REPORT OF A CASE AND REVIEW OF LITERATURE. D. Antoniadis, A. Epivatianos, S. Iordanidis, Th. Zaraboukas. Aristotle U., Thessaloniki, Greece.

Background: Lipomas are benign neoplasms of normal fat cells. Although they represent the most common mesenchymal neoplasms, lipomas of the oral and maxillofacial region are uncommon. Oral lipomas are rare, accounting for only 1% to 2% of all benign tumors in this site. Among the different variants of lipomas the myxoid lipoma is extremely rare in the oral cavity. Review of the literature revealed only 6 reported cases.

Methods: In the present study, we present a case of myxoid lipoma that was located in the buccal mucosa of a 73-year-old man. Analysis of the literature showed that myxoid lipoma of the oral soft tissues occurred in patients older than the second decade of life. The age of reported patients ranged from 30-73 years, with a peak prevalence in the sixth decade (42.8%) and a mean age of 54 years. The tumor affected more men than women (2,5:1) and was located in the tongue and buccal mucosa almost equally. Myxoid lipoma should be histopathologically differentiated from the spindle cell, atypical and pleomorphic lipomas, lipoblastomatosis, soft tissue myxoma and myxoid liposarcoma, because all of these tumors contain fat cells and/or myxoid component.

#10 9:48 a.m.

EPITHELIOID BLUE NEVUS OF THE ORAL MUCOSA: A RARE HISTOLOGIC VARIANT. A. Pinto, S. Raghavendra, R. Lee, S. DeRossi, and F. Alawi. University of Pennsylvania, Philadelphia.

An unusual histologic variant of blue nevus, known as the epithelioid blue nevus (EBN), was originally identified in patients with the Carney complex – an autosomal dominant disease characterized by spotty skin pigmentation, cardiac myxomas, endocrine overactivity and schwannomas. However, recent reports have now identified sporadic cases of EBN in patients without any evidence of the Carney complex. Clinically, EBN typically presents as a single, asymptomatic, small, darkly-pigmented, dome-shaped cutaneous nodule. Unlike other variants of blue nevus, which are primarily composed of spindled, pigmented melanocytes, EBN is characterized by a poorly circumscribed, dermal mass composed of large, well-defined, heavily pigmented, polygonal or epithelioid-shaped melanocytes, intermixed with less-densely pigmented epithelioid melanocytes and poorly-defined, fusiform-shaped melanocytes. Moreover, in contrast to other benign melanocytic proliferations, the lesional cells in EBN exhibit little or no maturation as they extend deeper into the underlying tissue. A recent report detailed four cases of EBN that arose on the genital mucosa, however all of the other documented cases of EBN have been identified on the skin. Furthermore, only five examples of EBN, including one sporadic EBN, have been identified in the head and neck. Although blue nevi are the second most common form of nevus in the oral cavity, to our knowledge, the epithelioid variant has not been previously recognized in the oral cavity. We now report the first documented case of EBN involving the oral mucosa. The current report is of a male patient who presented with EBN of the buccal mucosa. A brief review of the clinical and histopathologic features of the previously reported cutaneous cases of EBN is also presented.

ESSAY PROGRAM I

Monday, May 19, 2003

#11 10:00 a.m.

KERATOACANTHOMA OF THE LOWER LIP. REPORT OF TWO CASES.

D.Antoniades, A.Markopoulos, P.Papanayotou. Aristotle U., Thessaloniki, Greece

Background: Keratoacanthoma is a relatively common low-grade epidermal tumor of the skin that originates in the pilosebaceous glands and closely resembles squamous cell carcinoma pathologically. However cases of lesions of this type are seldom seen on the oral mucosa and lips. Keratoacanthoma is characterized by rapid growth over a few weeks to months, followed by spontaneous resolution over 4-6 months in most cases.

Methods: We report two cases of keratoacanthoma of the lower lip. The first case was a 47-year-old farmer presenting with a rather rapidly growing tumor of the vermilion border of the lower lip, just to the right of the midline of the lip. The tumor was excised and a pathologic diagnosis of keratoacanthoma was established. One year later another rather peculiar horn-like lesion appeared in a different location of the lower lip, this time more to the right. The histopathologic diagnosis again was keratoacanthoma. The second case was a 58-year-old office clerk appearing with a giant tumor on the vermilion border of the lower lip. The tumor was surgically excised and the histopathologic diagnosis was keratoacanthoma.

Conclusion: Keratoacanthomas represent epithelial tumors, which are characterized by a keratin-filled crater, rapid growth in the proliferation stage, and the potential for spontaneous regression. Histopathologically, keratoacanthomas display distinct features that must be differentiated from squamous cell carcinomas. In the regression stage, verruca vulgaris must also be considered in the histopathologic differential diagnosis.

#12 10:12 a.m.

AMELOBLASTIC CARCINOMA; ANALYSIS OF 11 CASES. J. Hall, K. Unni, D. Weathers. Mayo Clinic, Rochester, MN and Emory U, Atlanta, GA. The treatment files of the Mayo Clinic were searched for all ameloblastic tumors (adamantinoma of the jaws). Approximately 200 tumors were reviewed by 3 pathologists, and 11 (.05%) were diagnosed as ameloblastic carcinoma. The mean age at diagnosis was 39 years, 73% were found in men and swelling was the most common sign. There were 5 maxillary tumors and 6 mandibular. Follow-up time averaged 15.5 years. The criteria for diagnosis of ameloblastic carcinoma included cellularity, lack of differentiation, high mitotic index, vascular or perineural invasion and significant numbers of clear cells. All tumors exhibited the histologic criteria necessary for the diagnosis of ameloblastoma. Each patient's tumor contained a variety of patterns however the dominant characteristic was a lack of differentiation, with sheets of monotonous epithelial cells showing no evidence of peripheral palisading, reverse polarization or stellate reticulum. Hypercellularity and hyperchromatism were seen to some degree in all. A pseudosarcomatous pattern with spindled cells in a storiform configuration was seen in 3 tumors (27.3%). Mitoses were evident in 9 of the 11 tumors and 4 (36.4%) exhibited mitoses in almost every medium power field; atypical mitoses were seen in only 2 cases. Clear cells were present in 6 tumors (54.5%) and in 2 cases formed pseudoglandular aggregates. Three of the 4 patients that died with tumor were found to have notable numbers of clear cells. Treatments included curettage, with or without electrocautery, radiation and resection. Those patients with seeming cure were those with the fewest recurrences and the ones who received radical surgery early in the course of their disease. All treatments other than surgery were met with recurrence. The 7 patients who recovered from their disease had an average of 0.875 recurrences (range 0-3). The 4 patients who died with tumor averaged 6.25 recurrences (range 4-9). The average time between recurrences was 16.32 months (range 1-48 months).

ESSAY PROGRAM I

Monday, May 19, 2003

#13 10:24 a.m.

CENTRAL MUCOEPIDERMOID CARCINOMA ARISING IN AN ODONTOGENIC CYST. G.Pringle, D.Loggi Jr., S-Y.Chen. Temple University and Cape May Court House, NJ. Central mucoepidermoid carcinoma (MEC) is a rare neoplasm. It occurs most commonly in middle-aged adults in the posterior mandible and has a non-specific radiographic appearance. Most cases are low grade malignancies and typically present with cortical swelling. High grade lesions can cause bone perforation, paresthesia and nodal metastasis with recurrence or death. Pathogenetic origin from ectopic, enclaved salivary gland tissue or from the multipotential epithelial cells of odontogenic cysts are the two principal hypotheses to explain the histogenesis of central MEC. Many reported cases provide circumstantial evidence of an odontogenic epithelial origin, but few reports demonstrate this histologically. We report a case of a 79-year-old female with a large, multilocular radiolucency across the midline of the anterior mandible that was diagnosed as glandular odontogenic cyst following incisional biopsy. Tissue submitted following enucleation with peripheral ostectomy confirmed glandular odontogenic cyst. However, cyst lining epithelium was thickened focally and composed of clear cells with a luminal layer of mucous cells. In adjacent areas, invading strands of cyst lining epithelium and separate cystic islands of low grade MEC composed of mucous cells, clear cells and some epidermoid cells in the connective tissue wall is strongly suggestive of an odontogenic origin. The relationship between mucoepidermoid carcinoma and glandular odontogenic cyst will be reviewed.

#14 10:36 a.m.

OSTEOSARCOMA EX FLORID OSSEOUS DYSPLASIA: REPORT OF A CASE

R. Melrose, J. Handlers; Oral Pathology Assoc., Inc. Los Angeles, CA

History: A 36-year-old African-American woman presented to the Los Angeles County/USC General Hospital Dental Service complaining of increasing pain and rapid swelling of the left face and jaw. Two mandibular molars had been extracted elsewhere several weeks prior because of pain but the symptoms worsened. Clinically, marked swelling of the left face was observed. There was no evidence of redness, heat or drainage. Intraorally, marked non-tender, lobular expansion of the left mandible was present. There was no paresthesia. Radiographs of the area showed a diffuse, ill-defined radiopacity with buccal and lingual expansion. Radiographs taken three years earlier (1997) showed bilateral radiopacities in the alveolar processes of the maxilla and mandible consistent with florid osseous dysplasia (FOD). There was no evidence of hypercementosis. Comparison of an earlier film of the affected area with current films showed a distinct change in a large, lobular opacity seen in 1997. Biopsy was performed and a diagnosis of high grade osteosarcoma was made. Metastatic workup was within normal limits. A core biopsy of the right mandible displayed histology compatible with cemento-osseous dysplasia. Resection was performed and the original diagnosis was confirmed. Following discharge the patient was lost to follow-up. Comment: This case represents the second instance of sarcoma arising in florid osseous dysplasia. A case of osteosarcoma arising in Paget's disease of the mandible has recently been reported and there was microscopic evidence of cemento-osseous dysplasia adjacent to the tumor but the authors concluded that the tumor arose in pagetic bone. It has now been established that, in addition to osteomyelitis, sarcomas can complicate the course of FOD. It seems prudent then to recommend continuing follow-up for patients with FOD.

ESSAY PROGRAM I

Monday, May 19, 2003

#15 10:48 a.m.

POST-IRRADIATION LEIOMYOSARCOMA OF THE MAXILLA: REPORT OF A CASE IN A PATIENT WITH PRIOR TREATMENT FOR RETINOBLASTOMA. P. Sedghizadeh, F. Angiero, C. Allen, Y. Rawal, E. Albright. The Ohio State U., Columbus.

Post-irradiation sarcoma is a well-defined entity; however, only a few case reports document such lesions in the head and neck region. A 30-year-old man presented for evaluation of a painful mass of his left posterior maxilla. His medical history was significant for unilateral retinoblastoma of the eye, diagnosed when he was an infant and treated with a combination of surgical exenteration of the eye and radiation therapy. Biopsy of his maxillary mass demonstrated a spindle cell malignancy that, with immunohistochemical findings, was most consistent with a diagnosis of leiomyosarcoma. Further investigation also revealed that the patient had three children, each of whom developed unilateral retinoblastoma in infancy. The role of the retinoblastoma (RB1) gene in the pathogenesis of retinoblastoma and post-radiation sarcoma is discussed.

#16 11:00 a.m.

LANGERHANS CELL HISTIOCYTOSIS OF THE HEAD AND NECK IN CHILDHOOD: IMMUNOCYTOCHEMICAL AND ULTRASTRUCTURAL STUDY. J Hicks, C Flaitz, E Friedman. TX Children's Hosp, Baylor Coll Med, U Texas at Houston Dental Br, Houston Tx. **Purpose:** This study evaluated the clinicopathologic, immunocytochemical and ultrastructural features of Langerhans cell histiocytosis (LCH) of the head and neck (H&N) region in children. **Design:** The anatomic pathology files at Texas Children's Hospital were searched for LCH cases spanning a 15 year period. Demographic information, clinical history, paraffin tissue blocks, microscopic slides and electron microscopic files were available for review. Immunocytochemistry for CD1a and CD207 (Langerin, type II transmembrane protein restricted to Langerhans cells) was performed on cases. 134 cases of LCH were identified with 69 cases involving the H&N region. **Results:** With H&N LCH, the mean age was 3.9 years (range 3mos-15yrs) with the majority being \leq 4yrs of age. The gender ratio was 1.2M:1.0F. H&N LCH sites were: skull 42%; skin 22%; lymph nodes 13%; orbit 9%; auditory canal 4%; mandible 3%; gingiva 3%; vertebra 1%; and thyroid 1%. CD1a and CD207 immunoreactivity occurred in 87% (60/69) and 91% (63/69) of H&N LCH cases, respectively. Electron microscopy identified pentalaminar structures in all cases examined (42/42). Other EM findings included multivesicular bodies, tubuloreticular inclusions and curvilinear membrane formations. Laminated dense bodies, pathognomonic for congenital self-healing LCH, were not identified. **Conclusion:** The H&N region is the most common site for LCH in children. Either CD1a or CD207 immunocytochemistry confirms the diagnosis in almost 90% of LCH cases. Ultrastructural studies are necessary in at least 10-15% of H&N cases, and should be performed in children under 1 year of age to eliminate congenital self-healing LCH as a diagnostic consideration.

ESSAY PROGRAM I

Monday, May 19, 2003

#17 11:12 a.m.

LYMPHOMA OF THE HEAD AND NECK: A RETROSPECTIVE STUDY

X. Zornosa, S. Budnick, S. Li, Emory U., Atlanta, GA A retrospective study of lymphomas presenting initially in the head and neck, particularly the oral cavity was performed to analyze clinicopathologic features as well as patient follow-up. In addition, we compared the phenotype at presentation with that in recurrent cases. Fifty-six cases of lymphoma diagnosed at the Emory University Oral, Head and Neck Pathology biopsy service were analyzed retrospectively from 1985 to 2002. Thirty-six cases were males and 21 females. The ages ranged from 12 to 87, (mean age-58). The sites involved included the palate, gingiva, buccal mucosa, tonsils, tongue, nasopharynx, sinus, lip and floor of mouth. The most common sites involved were the palate, gingiva, buccal mucosa and tonsils. The cases were reclassified according to the Revised European American Lymphoma classification system. The phenotypes involved included diffuse large B cell lymphoma (50%), follicular lymphoma (16%), extranodal maltoma (16%), peripheral T cell lymphoma (7%), nasal type NK/T lymphoma (3.5%), mantle cell lymphoma (3.5%), anaplastic large cell lymphoma (1.7%), and lymphoblastic lymphoma (1.7%). Out of the 56 cases, 12 patients had a previous history of lymphoma. Follow-up was obtained in 29 of the cases. Thirteen patients received treatment consisting of radiation, chemotherapy or both. Of the 29 cases with follow-up, 14 demonstrated extraoral recurrent disease. The sites of recurrence included lung, uterus, jejunum, bone marrow, skin, pharynx, breast, hilar, inguinal and cervical nodes. All fourteen cases showing recurrent disease demonstrated the same phenotype as the initial oral site with 57% of these being diffuse large B cell, 14% mantle cell, 14% extranodal maltoma, 7% follicular and 7% anaplastic large cell. These results are consistent with previous studies in that B cell lymphomas are the predominant type in the oral cavity.

#18 11:24 a.m.

OROFACIAL AND SINONASAL LYMPHOMAS IN GUATEMALA: CLINICAL, EPIDEMIOLOGICAL AND MOLECULAR FEATURES. R Carlos, E Contreras. Centro de Medicina Oral de Guatemala, Guatemala City, Guatemala.

Orofacial and sinonasal lymphomas of T or NK phenotype represent a frequent subset of extranodal head and neck lymphomas in Guatemala. This phenotype has been described in other geographic regions, mainly Asian countries and Peru. The frequency of this type of lymphoma is dependent on the geographic location, having a relatively low prevalence in Europe and North America, and a relatively high prevalence in Asia, Peru and Guatemala. 100% of the cases presented were positive for Epstein Barr virus, in contrast to 30% positivity in B-cell lymphomas in the same region. In addition, most of T/NK lymphomas in our series expressed CD3 and CD56. While sinonasal lymphomas in Western countries represent only 0.17% of all lymphomas, in Guatemala they represent approximately 4%, and in Asian countries it ranges between 2.6% to 6.7% of all lymphomas. All of our patients were of Mayan descent, which we feel is an interesting finding because the Mayans are thought to be descendents of people migrating from Asia across the Bering land bridge during the last ice age, approximately 6000 BC. T/NK lymphomas are high grade tumors with poor prognosis.

ESSAY PROGRAM I

Monday, May 19, 2003

#19 11:36 a.m.

ANGIOFOLLICULAR LYMPH NODE HYPERPLASIA (CASTLEMAN'S DISEASE) OF THE HEAD AND NECK IN CHILDREN. C Flaitz, V Gresik, J Hicks. UT Dental Branch at Houston, TX Children's Hosp, Baylor College Medicine, Houston TX.

Purpose: The purpose of this study was to evaluate the clinicopathologic features of Castleman's disease (CD) involving the head and neck region (H&N) in children over a 10 year period. **Design:** Anatomic pathology files from Texas Children's Hospital were searched for CD cases over a 10-year period (1992-2002). The demographics, clinical history, ancillary tests (serology, viral cultures, polymerase chain reaction [PCR], flow cytometry, cytogenetics), microscopic slides and paraffin blocks were available for all cases. 8 CD cases were identified, with 5 presenting in the H&N region. **Results:** Mean age for H&N CD was 11 yrs (range 5-16yrs, 3 males, 2 females). Presentation sites were: cervical lymph nodes (3), submandibular and parotid lymph nodes (1), and cervical and submandibular lymph nodes (1). Signs and symptoms at diagnosis included: lymphadenopathy (5), fever (3), weight loss (2), splenomegaly (2), hepatomegaly (1), bone pain (1), respiratory distress (1), anemia (1), coagulopathy (1), and immunodeficiency with prior history of lymphoma (1). The clinical suspicion was lymphoma/leukemia (5). CD types were localized hyaline-vascular CD (2) and multicentric plasma cell CD (3). Multicentric CD involved the spleen (2), numerous lymph nodes (2), bone (1) and lung (1). HHV-8 was detected by serology (4/5) and PCR (4/5). Histopathology, flow cytometry and cytogenetics were negative for malignancy. **Conclusions:** H&N region presentation of multicentric plasma cell CD is more common in children. HHV-8 in pediatric CD may be readily identified in serum and lesional tissue. Because CD may be associated with rheumatologic diseases, autoimmune states, immunodeficiency, viral etiology and lymphoid malignancy, a thorough evaluation at diagnosis and long-term follow-up are necessary.

#20 11:48 a.m.

CERUMINAL GLAND ADENOMAS: A CLINICOPATHOLOGIC STUDY OF 41 CASES.

BL Nelson, §L Barnes, LDR Thompson. Otorhinolaryngic Pathology, AFIP, Washington, DC and §Department of Pathology, Presbyterian University Hospital, Pittsburgh, PA

Ceruminal gland neoplasms are rare neoplasms. To date, a large clinicopathologic study of benign ceruminal gland neoplasms has not been reported. Forty-one cases of ceruminal gland adenomas diagnosed between 1970 and 2000 were retrieved from the files of the AFIP. Histologic features were reviewed, immunohistochemical analysis was performed (n=21), and patient follow-up was obtained (n=40). The patients included 22 men and 19 women, aged 24-85 years (mean, 54.2 years). Patients presented clinically with a painless mass of the outer half of the external auditory canal (n=33) or with hearing changes (n=11), present for an average of 16.3 months. The polypoid masses affected the external auditory canal only with a mean size of 1.1 cm. Histologically, the tumors were cystic, with a tubuloglandular proliferation of inner apocrine cells (cerumen-secreting epithelium with decapitation secretion) subtended by a myoepithelial layer. A hyalinized stroma created an infiltrative pattern of growth. Most tumors were ceruminal adenoma (n=36) although ceruminal pleomorphic adenomas were also seen. The luminal cells were CK7 and CD117 positive, while the basal cells were S-100 protein reactive. Surgical excision was used in all patients. Four patients developed a recurrence due to incomplete excision. All patients were without evidence of disease at last follow-up: mean, 14.9 years. Ceruminal gland adenomas are the most common external auditory canal tumors that demonstrate a dual cell population of basal myoepithelial-type cells and luminal apocrine (ceruminal) cells. Complete surgical excision results in an excellent long term clinical outcome.

ESSAY PROGRAM I

Monday, May 19, 2003

#21 12:00

THE FREQUENCY OF ORAL TUMORS AND PSEUDOTUMORS IN THE CENTRO MÉDICO NACIONAL “20 DE NOVIEMBRE” MEDICAL PUBLIC SERVICE FROM 1997 TO 2002 B. Cruz, G. Meza, C. Páez, B. Aldape, Faculty of Dentistry of the UNAM, National Medical Center “20 de Noviembre”.

Objective: to document the frequency of tumors and pseudotumors in the oral cavity during the last five years in a tertiary care hospital in México. Methods: a file review in the Anatomic Pathology Department was done, looking for oral tumors and pseudotumors. Results: from a total of 49,615 reports, 504 (1.01%) cases were found to be oral tumors and pseudotumors, of which 166 (32.9%) were classified as pseudotumors, 89 (17.79%) were benign tumors and 249 (48%) malignant tumors. From the 78 different lesions found, the 10 most frequent were: squamous cell carcinoma, 149 (29.56%); pleomorphic adenoma, 45 (8.93%); epithelial hyperplasia, 39 (7.74%); squamous papilloma, 33 (6.55%); fibrous hyperplasia 27 (6.36%); hemangioma, 21 (4.17%); adenoid cystic carcinoma, 18 (3.57%); non-Hodgkin’s lymphoma and pyogenic granuloma, 15 cases each (2.97%); and adenocarcinoma 11(2.18%). The lesions were grouped by age, gender and site. In the 504 samples, women were predominantly affected; for malignancies, however, males were affected more frequently. The average age was 53.2 years (median-55 years; mode-46 years). The most frequent site was the tongue. Conclusion: It is important to know the frequency of these types of oral lesions in a tertiary care hospital; however, it is necessary to compare these results with other hospitals in Mexico in order to estimate the frequency of oral lesions in the country. In this hospital, malignant tumors were most commonly seen, probably because it is a referral center for these lesions.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#22 1:00 p.m.

GENE-ENHANCED BONE REGENERATION IN A RABBIT MODEL USING GENETICALLY-ENGINEERED GINGIVAL FIBROBLASTS, PERIOSTEAL-DERIVED CELLS, AND FAT-DERIVED STEM CELLS EXPRESSING THE SONIC HEDGEHOG GENE. P. Edwards, S. Ruggiero, J. Fantasia, D. Grande and J. Mason. Long Island Jewish Medical Center, New Hyde Park and North Shore U. Hospital, Manhasset, NY. **Objectives:** The development of novel and improved methodologies for the regeneration of bone is desirable in many clinical situations, especially in dental and craniofacial reconstruction. Several studies suggest that Sonic Hedgehog (SHH), a key protein involved in craniofacial morphogenesis, has the potential for increasing the commitment of pluripotential mesenchymal cells into the osteoblastic lineage. We are employing a gene-enhanced tissue engineering approach using SHH-expressing cells in a novel osteoconductive matrix to stimulate repair of bone defects in an *in vivo* model. **Study Design:** Allogenic gingival fibroblast, periosteal and fat-derived cells transduced with a replication incompetent SHH retroviral vector and control vector were combined with an absorbable alginate-collagen matrix carrier and inserted into 8 mm full thickness calvarial defects in adult New Zealand white rabbits. Additional controls include alginate-collagen matrix alone and empty defect (N=6 for each group). **Results:** RT-PCR demonstrated that the transfected cell lines express SHH at the RNA level. SHH protein production was confirmed by ELISA. To assess the viability of cells in this composite bone graft material, composites were prepared and submitted for histological sectioning immediately after assembly and after 7 days in culture. The cells were healthy and had expanded in clusters throughout the graft after one week in culture, demonstrating the suitability of this graft material. The bone regenerative potential of these three SHH-expressing engineered matrices are examined *in vivo*.

#23 1:12 p.m.

PARATHYROID HORMONE-RELATED PROTEIN (PTHrP) EXPRESSION IN AMELOBLASTOMA. Abdelsayed RA†, Vartanian RK†, and Ibrahim NA*. Department of Pathology, Medical College of Georgia† & Department of Business Administration, Augusta State University, * Augusta, Georgia. **Background:** PTHrP production has been demonstrated in a variety of tumor subtypes. Local production of PTHrP by metastatic tumor cells in bone has been linked with bone destruction & tumor growth. Ameloblastoma (AB) is a relatively common epithelial odontogenic neoplasm that manifests local expansile and destructive intraosseous growth. AB recapitulates the developing enamel epithelium, in which PTHrP has been recently demonstrated (*Proc Natl Acad Sci 1998; 95:11846-51*). Yet, PTHrP expression in a series of ABs has not been studied to date. **Design:** Formalin-fixed, paraffin-embedded AB tissue sections (n=30; 24 conventional, 4 unicystic & 2 AB arising in cyst) were immunostained with the highly specific anti-PTHrP antibody (N1-34; Peninsula Labs, San Carols, CA) using the multi-step streptavidin-peroxidase technique (positive control: hyperplastic parathyroid gland; negative control: omission of 1^o antibody). Semiquantitative scoring of immunopositivity was assessed as follows; mild, moderate and intense. **Results:** All cases (100%) demonstrated immunoreactivity with anti-PTHrP, as follows: mild in 3 conventional AB, 1 unicystic and 1 AB arising in cyst; and moderate in 12 conventional AB, 3 unicystic and 1 AB arising in cyst. Intense reaction is seen in only 9 conventional AB cases. This difference in immunostaining was not statistically significant ($\chi^2=4.41, p=0.358$). **Conclusion:** This study demonstrates consistent PTHrP expression in AB. These results may explain, at least in part, the mechanism of the local destructive behavior and growth potential of AB. Thus, adjuvant therapeutic modalities directed against local PTHrP-mediated bone resorption, e.g., (amino)bisphosphonates, may prove efficacious in management of AB.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#24 1:24 p.m.

CELL CYCLE ALTERATIONS IN CENTRAL GIANT CELL GRANULOMA OF THE JAWS: A COMPARISON WITH GIANT CELL TUMOR OF BONE. A. Kauzman, S. Li, G. Bradley, R. Bell, J. Wunder, and R. Kandel. U. of Toronto, Ontario. Several studies have attempted to differentiate between central giant cell granuloma (CGCG) of the jaw and giant cell tumor (GCT) of long bone based on histomorphometric criteria and found a considerable overlap between these lesions. We have previously demonstrated cyclin D1 overexpression in GCT and it is not known whether similar changes occur in CGCG. **Objectives:** to determine whether cyclin D1 gene amplification and protein overexpression occurs in CGCG and whether these changes are similar to those observed in GCT. **Materials and Methods:** H&E-stained slides from 29 cases of CGCG and 32 cases of GCT were reviewed and 7 histologic parameters were evaluated. All cases were stained with monoclonal antibodies reactive with cyclin D1, cyclin B1, and Ki-67. The percentage of giant cells (GCs) and mononuclear cells (MCs) reactive with each antibody was assessed semiquantitatively. Genomic DNA was extracted from microdissected tissue sections to assess for cyclin D1 gene amplification using differential PCR (DPCR). **Results:** Histologically, the diffuse distribution of the GCs in GCT and their tendency to accumulate in areas of hemorrhage in CGCG allowed differentiation between the 2 lesions in 70% of the cases. DPCR showed that 9 cases (31%) of CGCG showed low level cyclin D1 gene amplification, compared to 19 cases (61%) of GCT. Of these 9 cases, 3 were histologically similar to GCT. Cyclin D1 expression was detected predominantly in the GCs while cyclin B1 and Ki-67 staining was restricted to the MCs. The pattern of immunoreactivity was identical in both conditions. **Conclusions:** CGCG and GCT show similar abnormalities in cyclin D1 suggesting that they may represent a continuum of the same disease process. High levels of cyclin D1 protein in the GCs, without associated cell proliferation, might play a role in the pathogenesis of both lesions.

#25 1:36 p.m.

IMMUNOHISTOPATHOLOGIC STUDY OF EPIDERMAL GROWTH FACTOR, EPIDERMAL GROWTH FACTOR RECEPTOR, a FGF, b FGF, AND FGFR IN RADICULAR CYSTS IN KOREANS .

J. Cho, K. Ma, Kyung Hee Univ., Seoul, Korea

The purpose of this study was to evaluate the role of EGF, EGFR, aFGF(FGF-1), bFGF(FGF-2), FGFR in the development of radicular cysts in Koreans. For this study 37 lesions diagnosed as radicular cysts were used as the experimental group. For the control group, 2 samples of normal oral mucosa without any inflammatory changes were used. All tissues were formalin-fixed and paraffin-embedded. Serial tissue sections were made at 5 μ and processed in the standard way for immunohistochemical methods, using primary antibodies against EGF, EGFR, aFGF, bFGF, FGFR, followed by the application of the streptavidin - horseradish peroxidase technique, and counter stained. The sections were examined and the intensity of the immunohistochemical reaction was graded 0, +, ++, to +++ for the all tissues. EGF, EGFR, aFGF, bFGF, FGFR showed more intense staining in radicular cysts compare to that seen in association with normal mucosa. EGF, EGFR, aFGF, bFGF, FGFR stained in mucosa and submucosa of the control group and also stained the lining epithelium and connective tissue of the cyst wall. EGF, EGFR, aFGF, bFGF, FGFR may play a part in the development of the radicular cyst.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#26 1:48 p.m.

CORRELATION BETWEEN PROLIFERATION AND INFLAMMATION IN ODONTOGENIC KERATOCYST. I Kaplan, A Hirshberg. School of Dental Medicine, Tel-Aviv U., Israel. Inflammation may alter the proliferative potential of the epithelial lining of the odontogenic keratocyst (OKC). The objectives of the study were to analyze the proliferative potential of OKC in relation to inflammation using Ki-67 and PCNA as markers of proliferation. The study included 45 cases of OKC retrieved from the files of the Department of Oral Pathology. In each 5u slide 10 high power fields (HPF) were observed, with the type of epithelial lining recorded separately for each field (metaplastic squamous or classic parakeratinized OKC lining). Labeling indices for Ki-67 and PCNA were separately calculated for each field, and the inflammatory infiltrate in the depth of 1 HPF adjacent to the basement membrane was scored. Comparison of parameters was performed between fields. In addition, for each case the average inflammatory score and average labeling indices were calculated, and comparisons between cases performed. In 24.5% of cases inflammation was not observed, in 30.5% mild inflammation was seen, and in 45% moderate to severe inflammation was present. In 64% of cases foci of metaplastic non-keratinizing epithelial lining were observed. This finding was twice as common in inflamed cysts (90%) than in non-inflamed cysts (44%). The average labeling index for both PCNA and Ki-67 did not differ between inflamed and non-inflamed cysts. However, when compared between HPFs, there was an increase in the Ki-67 labeling index in metaplastic squamous epithelium adjacent to moderate and severe inflammation ($p=0.036$). The same tendency was seen in the classic OKC epithelium; however significance was not reached. The PCNA labeling index was not affected by inflammation. The results of the present study demonstrate an increase in expression of Ki67 only in metaplastic epithelial lining of OKC adjacent to moderate and severe inflammation, without a significant effect on the overall proliferation activity of the cysts.

#27 2:00 p.m.

IMMUNOHISTOCHEMICAL EXPRESSION OF ANGIOGENESIS-RELATED MARKERS IN SALIVARY GLAND NEOPLASMS. VS Papanikolaou, NG Nikitakis, D Tiniakos, D Anteriotis, M Arnaouti, N Apostolikas, H Siavash, OB Ioffe, and JJ Sauk. St. Savvas Hospital and U. Athens, Greece, and U. Maryland, Baltimore. Salivary gland neoplasms (SGN) comprise a wide group of tumors with diverse histology and broad biologic behavior, often presenting difficulties in their definitive diagnosis and treatment. In the last decades, the prominent role of angiogenesis in the neoplastic process has been recognized, and alterations of its promoters and inhibitors have been investigated in most human tumors. However, angiogenesis in SGN has not been thoroughly studied. We evaluated the immunohistochemical expression of the angiogenesis-promoter vascular endothelial growth factor (VEGF), the angiogenesis-inhibitor endostatin and the related molecules collagen XVIII and HSP47 in 9 benign (6 mixed tumors, and 3 Warthin tumors) and 36 malignant SGN (10 adenoid cystic Ca, 9 mucoepidermoid Ca, 9 polymorphous low grade adenoCa, 3 adenoCa NOS, 3 Ca ex-mixed tumor, and 2 salivary duct Ca). VEGF was expressed in all benign and 34 of 36 (94.4%) malignant tumors. All benign and 33 of 36 (91.6%) malignant tumors were positive for endostatin. All cases were positive for collagen XVIII. All benign tumors, but only 27 out of 36 (75%) malignant tumors, showed HSP47 immunoreactivity. All markers predominantly showed a diffuse pattern of immunostaining (more than 50% positive cells). In contrast, the immunostaining intensity for all markers varied widely among cases, ranging from weak to strong. Interestingly, the intensity of immunoreactivity for endostatin and collagen XVIII was significantly higher in benign compared to malignant tumors ($p=0.001$ and $p=0.011$, respectively). There was no correlation between immunostaining and patients' demographic data or tumor histologic type. Our results show that malignant SGN express low levels of endostatin and collagen XVIII, which correspond to an increase in the ratio of angiogenic to angiostatic elements and suggest that enhanced angiogenesis may contribute to salivary gland carcinogenesis.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#28 2:12 p.m.

AMELOBLASTOMA: COMPARISON OF HISTOPATHOLOGICAL AND IMMUNOSTOCHEMICAL FEATURES BETWEEN YOUNG AND OLD CASES. ESPECIALLY CELL PROLIFERATION AND INTRATUMOR MICROVESSEL RATE. Y. Koizumi., A. Kauzman., K. Kuvama., H. Okada., J. McComb, H. Yamamoto. Department of Pathology, Nihon U. School of Dentistry at Matsudo, Chiba, Japan and Department of Oral Pathology, Faculty of Dentistry, University of Toronto, Canada **Objectives:** The aim of this study was to compare young and old cases of ameloblastoma in terms of proliferative activity and intratumor microvessel density (IMVD) and area (IMVA) and to identify factors that could be implicated in determining the growth pattern (plexiform vs. follicular) of ameloblastoma.

Materials and Methods: A total of 23 cases were included in the study. Cases were divided into 2 groups according to age: group A ≤ 15 years (12 cases), and group B ≥ 60 years (11 cases). Each case was assessed for the predominant histological pattern (plexiform vs. follicular) and for immunoreactivity with 2 monoclonal antibodies: Ki-67 and CD-31. Ki-67 labeling index (LI), IMVD and IMVA were calculated in each case.

Results: Plexiform pattern was more common in group A, while follicular pattern was more frequently seen in group B. Ki-67 LI, IMVD and IMVA were significantly higher in group A. When the 2 histological patterns of ameloblastoma were compared, only IMVD and IMVA showed statistically significant differences.

Conclusions: Ameloblastomas in the young tend to be of the plexiform pattern and generally have a higher Ki-67 LI than those seen in older patients. Similarly, our results suggest that angiogenesis as determined by intratumor IMVD and IMVA might play an important role in determining the growth pattern of ameloblastoma.

#29 2:24 p.m.

DETECTION OF MOLECULAR CHANGES IN CLINICALLY 'NORMAL' MUCOSA BY MICROSATELLITE ANALYSIS. L. Zhang, M. Williams, A. Hovan, R. Priddy, Laronde D, C. Poh and M.P. Rosin. U. of British Columbia, and British Columbia Cancer Agency, Vancouver, B.C., Canada.

At present, the diagnosis of high-risk premalignant lesions and early squamous cell carcinomas (SCCs) relies upon histology of biopsies. The availability of biopsies is determined by two major factors: first, the lesion is clinically identifiable and second, the clinical presentation (e.g., appearance) of the lesion is regarded high-risk. There is increasing evidence that these lesions may not always be clinically apparent or have a 'high-risk' appearance. This may account for the fact that patients with a history of SCC or dysplasia can have cancer 'pop-up' at the treated site despite close follow-up. **Objective:** To determine whether microsatellite analysis of exfoliated cells can be used to detect re-emergence of molecular clones and predict cancer risk. **Method:** Exfoliative samples were collected at the sites of previous SCC (n = 37) or dysplasia from 43 patients. These sites either had no apparent clinical lesion (65%) or innocuous-looking lesions that did not warrant biopsy at the time of sampling. 15 (35%) patients developed a cancer at the sampling site (progressing cases). 10 microsatellite markers were used to evaluate loss of heterozygosity (LOH) on 3 chromosome regions: 3p14, 9p21 and 17p13. **Results:** LOH was significantly more frequent in exfoliative samples from progressing cases compared to nonprogressing cases for any LOH (87% vs. 46%, $P = 0.02$), multiple LOH (33% vs. 7%, $P = 0.04$), and LOH at 3p &/or 9p with or without LOH at 17p (80% vs. 36%, $P = 0.01$). **Conclusion:** These data indicate that molecular changes precede clinical changes and support the use of microsatellite analysis in exfoliated cell samples to predict cancer progression at former cancer or dysplasia sites. (Research supported by NIDCR grant R01DE13124).

ESSAY PROGRAM II

Tuesday, May 20, 2003

#30 2:36 p.m.

ID PROTEIN EXPRESSION IN ORAL EPITHELIAL DYSPLASIA AND SQUAMOUS CELL CARCINOMA. A. Chi and S. Muller. Emory U., Atlanta, GA. The recently described Id proteins antagonize basic helix-loop-helix transcription factors, which play a key role in cell development, proliferation, and differentiation. Thus, Id overexpression correlates with cell proliferation and arrested differentiation. Although Id expression has been observed in normal skin and overexpression in a variety of carcinomas, no studies have examined its expression in the oral cavity. To evaluate Id's possible role in oral carcinogenesis, we examined immunohistochemical staining patterns for Id-1, 2 and 3 on sections of oral normal mucosa (n=5), mild/moderate dysplasia (n=5), severe dysplasia/carcinoma-in-situ (CIS) (n=5), well/moderately differentiated squamous cell carcinoma (SCC)(n=5) and poorly differentiated SCC (n=5). Presence of staining was evaluated for each epithelial cell layer (basal/parabasal or B/PB, lower spinous or LS, upper spinous or US, and stratum corneum). Within each cell layer, staining was considered focal if <50% and diffuse if >50% of cells stained. Staining intensity was graded on a scale of 0 to 3. Id-1 staining was cytoplasmic and in all 5 cases of normal epithelium was diffusely present in the B/PB layer (av. intensity=2). 2 cases of normal epithelium also showed focal LS staining (av. intensity=0.8). Among cases of mild/moderate dysplasia, all 5 showed diffuse B/PB (av. intensity=2.6), 3 diffuse and 2 focal LS (av. intensity =3), and 2 focal US staining (av. intensity=0.4). Among cases of severe dysplasia/CIS, all 5 showed diffuse B/PB and LS staining, and 4 showed diffuse US staining (av. intensity=2.4, 2.2 and 1.6, respectively). No trends were seen for Id-2 and Id-3, which stained all but the stratum corneum in both normal and dysplastic epithelium. In 7 of 10 cases of oral SCC, Id-1, 2 and 3 stained over 67% of tumor cells with an av. intensity range of 1.75-2.80. In conclusion, Id -1 expression generally increases in upper levels of oral epithelium as the degree of dysplasia increases, and Id-1, 2 and 3 overexpression is seen in oral SCC. Future studies will examine Id expression as a potential prognostic indicator in oral dysplasia/SCC.

#31 2:48 p.m.

PROGNOSTIC SIGNIFICANCE OF SYNDECAN-1 (CD 138) IN ORAL MUCOSAL DYSPLASIA. N. Narayana, M. Fornatora, R. Reich, P.D.Freedman Oral Pathology Lab Inc, NY & Temple University School of Dentistry, Philadelphia, PA. The histological grading of dysplasia has remained subjective with poor intra/inter examiner reliability. The need for an objective marker to help standardize grading of dysplasia cannot be over emphasized. Syndecan 1(S1) originally discovered as a cell surface receptor assisting in cell surface interactions & differentiation has been extensively studied. S1 expression has been related to the histological differentiation of epithelial cells with a positive expression associated with favorable prognosis of squamous cell carcinoma (SCC). A pilot study was undertaken to identify the prognostic significance of S1 in oral mucosal dysplasia. Methods: 5 cases (mean age 71.8yrs) diagnosed as epithelial dysplasia that recurred as SCC (mean age 76.6yrs), and 4 cases (mean age 73.5yrs) of mild/moderate epithelial dysplasia recurring as severe dysplasia (mean age 78.5yrs), were included in the study. Controls for staining pattern & intensity of S1 consisted of 2 cases each (mean age 64yrs) of normal mucosa and poorly differentiated SCC (mean age 73.5yrs). Immunohistochemical staining for S1, Clone B-B4, (Serotec, Raleigh NC) was performed on formalin-fixed tissue. Results: The staining of normal mucosa in the present study was similar to that reported in the literature with increasing intensity from basal cells to spinous cells, with no staining of the keratin layer. Poorly differentiated SCC also demonstrated cytoplasmic & cell membrane staining of all epithelial cells. This pilot study showed no appreciable difference in the pattern and intensity of S1 staining of basal and spinous cells between normal mucosa, varied dysplasias and SCC. Due to maturational abnormalities in dysplastic epithelium, we expected an altered pattern of S1 staining which could not be demonstrated. In view of these results it can be concluded that S1 does not seem to have a prognostic significance in the grading of oral mucosal dysplasia.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#32 3:00 p.m.

USE OF PROTEOMICS FOR IDENTIFYING MOLECULAR MARKERS OF ORAL CANCER. R. King, B. Herr, M. Fekete, M. Lingen. U. of Chicago, Chicago, IL.

The criteria for diagnosing and grading dysplasia are subjective and open to a wide range of interpretation. In addition, no genotypic/phenotypic based criteria currently exist for predicting the risk of cancerous transformation of a given dysplastic lesion. Therefore, the histological findings can only be used to indicate that a given lesion has a malignant potential, and cannot be used for the prediction of malignant change. Diagnostic protocols that can more readily identify the lesions that are likely to progress to HNSCC are required. Whole cell protein extracts were isolated from normal keratinocytes, the immortalized but non-tumorigenic HaCat cell line, and the tumor cell lines SCC-4, SCC-9, SCC-25 and OSCC-3. Extracts were then separated on the basis of pI (Isoelectric point) and then molecular weight using 2-dimensional gel electrophoresis in order to develop a "protein map" specific to each cell type. The individual protein expression patterns were then analyzed using computer based image analysis and comparisons among cells were performed. The comparisons of normal, HaCat and four tumor cell lines revealed changes in protein expression in a total of 122 proteins. Of these, 57 proteins showed a consistent alteration in expression when comparing normal to immortalized keratinocytes, with 34 proteins being increased and 23 proteins being decreased in the HaCat cell line. In addition, 65 proteins demonstrated a consistent change in expression in the tumor cell lines, with 47 proteins showing increased and 18 proteins demonstrating decreased expression. These data demonstrate that proteomic profiling can be used to identify potential genotypic/phenotypic biomarkers that may be predictive of oral cancer progression. This work was supported in part by the NIH grants: DE12322 and DE00470 (MWL).

#33 3:12 p.m.

EPITHELIAL PROLIFERATION MARKERS IN DYSPLASIAS AND CARCINOMAS ASSOCIATED WITH HUMAN PAPILLOMAVIRUS. V. Murrah and E. Gilchrist. The Univ. of North Carolina, Chapel Hill.

Proliferative verrucous leukoplakia (PVL) is a clinical condition characterized by the hallmark of progressive development of epithelial dysplasias eventuating in carcinoma. The majority of these lesions have been associated with human papillomavirus (HPV). The purpose of this study was to evaluate two epithelial proliferation markers in HPV-associated oral dysplasias and carcinomas in order to determine the level of epithelial activation and the possibility of predicting prognosis for patients with PVL using such markers. Forty archival cases of paraffin-embedded HPV positive lesions diagnosed as epithelial dysplasia, verrucous hyperplasia, verrucous carcinoma and squamous cell carcinoma from patients with a clinical picture of PVL were retrieved from the files of the Univ. of North Carolina Oral & Maxillofacial Pathology Laboratory. Controls consisted of epithelium surfacing irritation fibromas. Immunostaining using primary antibodies to epidermal growth factor (EGFr) and proliferating cell nuclear antigen (PCNA) was performed using the avidin-biotin peroxidase technique with diaminobenzidine as chromogen. EGFr positivity was graded subjectively on a scale from 0 to 3+, whereas PCNA positivity was evaluated by examining sections under 100X oil immersion and determining the ratio of labeled to unlabeled cells from a count of 1000 cells per section. Results showed a mean of .53 PCNA labeling in controls and a mean of .72 in all experimental groups combined. (t-test: $p < .0001$). EGFr staining showed similar staining elevation over controls. We conclude that these proliferation markers have potential as prognostic indicators for the progression of PVL. (Supported by USPHS R03 DE13855-02)

ESSAY PROGRAM II

Tuesday, May 20, 2003

#34 3:24 p.m.

HUMAN PAPILOMAVIRUS IN ORAL EXFOLIATED CELLS AND RISK OF HEAD AND NECK CANCER. E. Smith, J. Ritchie, K Summersgill, H. Hoffman, D. Wang, T. Haugen, and L. Turek. U. of Iowa and Veterans Affairs Medical Center, Iowa City and U. of Pittsburgh, PA.

Objectives: The role of human papillomavirus (HPV) infection in head and neck cancer (HNC) is becoming clearer. This case-control study evaluated whether risk factors were different between HPV-infected and uninfected cases and controls, and whether HPV DNA found in exfoliated oral cells was an independent predictor of risk of head and neck cancer.

Methods: HPV DNA was evaluated from exfoliated oral cells in 201 oral and oropharyngeal cancer cases and 333 age-gender frequency matched controls using PCR and DNA sequencing to type HPV infection.

Findings: High-risk (HR) oncogenic HPV types were detected in 23% of cases and 11% of controls. After adjusting for age, tobacco, and alcohol use, the risk of malignancy was significantly greater for those with HPV-HR types (adj.OR=2.6, 95% CI:1.5-4.2), but not in those with low-risk HPV types, compared to uninfected patients. Furthermore, HPV-HR positivity in oral exfoliated cells was predictive of HR viral detection in biopsies of cancer cases. There was a significant synergistic effect between HR-infected heavy alcohol users compared to uninfected never users, whereas HPV-HR-associated risk with tobacco appeared to be additive.

Conclusions: HPV oncogenic infection is a significant risk factor for HNCs independent of alcohol and tobacco and acts synergistically with alcohol. High-risk types detected in oral exfoliated cells appear to be a significant predictor of oncogenic infection in HNCs, suggesting that an oral rinse may provide an early biomarker of cancer at a site noted for its low survival and significant morbidity.

#35 3:36 p.m.

SANGUINARINE'S EFFECT ON HUMAN ORAL EPITHELIUM. S. Mallery, A. Bookwalter, J. Andersen, J. Karp, K. Rodrigo. Ohio State University., Columbus.

While sanguinarine structurally resembles the established oral carcinogens, polycyclic aromatic hydrocarbons (PAH), no studies have shown human oral keratinocytes can metabolize sanguinarine. This study used cultured human oral keratinocytes, which have been shown to retain expression and function of carcinogen metabolizing enzymes, to assess sanguinarine's effects on: 1) cell proliferation (MTT mitochondrial reduction assay), 2) carcinogen metabolism [effects on bioactivation of the tobacco associated PAH, benzo-a-pyrene (BaP), 3) activation status of the aryl hydrocarbon receptor (AhR) via EMSAs, 4) expression of the carcinogen metabolizing AhR responsive genes (RT-PCR). Dose response studies show: 1)IC50s of approximately 0.75 mM in all cell lines (n=5), 2) 0.5 mM sanguinarine resulted in comparable cell numbers and viabilities as controls (n=5). Isolated CYP 1A1 and 1B1 human enzyme metabolism studies (0.1, 1, 10 mM sanguinarine) showed a dose-dependent inhibition of BaP bioactivation. All sanguinarine doses inhibited 1A1 BaP bioactivation, while only the 10 mM dose inhibited 1B1 BaP metabolism (P<0.05, Neuman-Keuls Multiple Comparison test, n=3 for each group). EMSA results show sanguinarine causes nuclear translocation of the AhR. Preliminary RT-PCR studies show sanguinarine upregulates expression of the potential carcinogen bioactivating enzymes CYP 1A1 and 1B1. Our data suggest that sanguinarine functions: i) as a competitive substrate for CYP 1A1 and 1B1 enzymes, and therefore is potentially capable of being bioactivated by these enzymes, ii) as a ligand for the AhR that increases expression of the AhR responsive enzymes.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#36 3:48 p.m.

SANGUINARINE-ORAL MUCOSAL INTERACTIONS. K. Anderson, M. Dohar, B. Gregg, S. Mallery. The Ohio State U. Columbus.

Recent epidemiological studies have shown an association between the use of sanguinarine, the active ingredient in Viadent[®] oral health care products, and oral premalignant lesions. Archived oral mucosal specimens, consisting of normal, dysplasia (prior to Viadent[®] availability), and epithelial atypia (known Viadent[®] users) were stained for markers associated dysregulation of the cell cycle, dysplasia, and malignancy. These markers consisted of the tumor suppressor genes p16 and p53, the proliferative markers cyclin D1 and Ki-67, and the apoptosis protein Bcl-x. In addition, in an effort to show "proof of principle," sanguinarine was topically applied to the cheek pouch of 19 Syrian Golden Hamsters, with staining conducted for these same markers. Ongoing analyses show: 1) Predominantly nuclear staining for all. 2) Ki-67: cells exclusively located in the basal and parabasal layers, with greater variability in dysplastic and Viadent[®]-related specimens. 3) p16: spinous layer staining. 4) p53: increased basal and parabasal expression in dysplastic and Viadent[®]-related specimens. 5) Bcl-x: no notable trends. 6) Hyperplasia and hyperkeratosis of treated hamster cheek pouch specimens. Quantitative image analyses (Simple PCI[®] image analysis software) for the Ki-67, cyclin D1, and p16 antibodies showed trends towards intermediate staining in Viadent[®]-related specimens, and lowest in dysplasias (Ki-67: normal: 18.12 ± 2.15 , Viadent[®]: 16.11 ± 2.16 , dysplasia: 14.53 ± 2.04 ; cyclin D1: normal: 15.65 ± 3.68 , Viadent[®]: 12.52 ± 3.57 , dysplasia: 1.94 ± 3.93 ; p16: normal: 55.04 ± 4.16 , Viadent[®]: 49.74 ± 4.16 , dysplasia: 45.03 ± 4.45 ; $p > 0.05$, Kruskal-Wallis). Our Viadent[®] staining profiles, which are intermediate between normal and dysplasia, support a preneoplastic diagnosis for Viadent[®] lesions.

#37 4:00 p.m.

INHIBITION OF COX-2 ACTIVITY AND EXPRESSION BY *SCUTELLARIA BAICALENSIS* ON HEAD AND NECK SQUAMOUS CELL CARCINOMA. J. Wu, F. Ye, S. Jiang, and D. Zhang. Mount Sinai School of Medicine, NY, NY.

OBJECTIVE: *Scutellaria baicalensis* (SB) is a widely used Chinese herbal medicine that has been used historically in anti-inflammatory and anticancer therapy. The purpose of this study is to evaluate its molecular mechanisms of anticancer activity on head and neck squamous cell carcinoma (HNSCC) and investigate its effect on cyclooxygenase -2 (COX-2) which converts arachidonic acid to prostaglandin E₂ (PGE₂).

METHODS: A HNSCC cell line, SCC-25, was evaluated for COX-2 activity and expression after treatment with SB extract. Its effect on COX-2 activity was evaluated by a time course study of PGE₂ levels compared with celecoxib, a selective COX-2 inhibitor. COX-2 expression was evaluated by mRNA expression by Northern blot and protein expression by immunohistochemistry.

RESULTS: SB demonstrated a strong inhibition of PGE₂ levels in SCC-25 cells. After a 12-hour treatment with SB, suppression of PGE₂ synthesis was similar to that of celecoxib. No significant decrease in COX-2 mRNA expression with SB was observed. However, there was a significant decrease in COX-2 protein expression in SB-treated cells, from 20% in control cells down to 8% in treated cells.

CONCLUSIONS: SB effectively inhibits COX-2 activity and expression and can be an effective chemotherapeutic agent for HNSCC. Inhibition of PGE₂ synthesis via COX-2 protein expression, not mRNA levels may be responsible for its anticancer activity.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#38 4:12 p.m.

IMMUNOHISTOCHEMICAL EXPRESSION OF CYTOKERATIN 7 AND CYTOKERATIN 20 IN MALIGNANT SALIVARY GLAND TUMORS. NG Nikitakis, KI Tosios, VS Papanikolaou, H Rivera, SI Papanicolaou, and OB Ioffe. U. Maryland, Baltimore, U. Athens, Greece, and Central U. Caracas, Venezuela.

On the basis of the heterogeneity of cytokeratin 7 (CK7) and cytokeratin 20 (CK20) expression in various types of malignant epithelial tumors, the CK7/CK20 immunophenotype has served as a useful diagnostic tool for discrimination of primary and/or metastatic carcinomas of unknown origin. However, the expression of these cytokeratins in malignant salivary gland tumors (MSGT) has not been thoroughly studied. Our study material consisted of 84 cases of MSGT of major or minor salivary gland origin. Nine histologic types of carcinoma were represented, including mucoepidermoid (26 cases), adenoid cystic (25), polymorphous low grade (11), salivary duct (8), acinic cell (4), ex-mixed tumor (3), not otherwise specified (3), clear cell (2) and basal cell (2). Thirteen cases of squamous cell carcinoma (SCCa) involving salivary glands were also examined. Immunoreactivity for CK7 was evident in all MSGT; the staining pattern was diffuse and strong in 62 cases, and focal and strong in 22 cases. In contrast, 78 cases were negative for CK20, whereas only 6 cases (2 mucoepidermoid, 1 adenoid cystic, and 3 salivary duct) displayed a focal weak positivity. Overall, 92.9% of MSGT were characterized by a CK7+/CK20- immunoprofile; CK7+/CK20+ phenotype was evident in the remaining 7.1% of cases. CK7+/CK20+ pattern was more common in salivary duct carcinomas than other MSGT ($p < 0.0001$). On the other hand, SCCa were negative for CK20 and focally weakly positive for CK7 in 4 cases (31%), while 9 cases (69%) were CK7-/CK20-; the latter phenotype was only observed in SCCa ($p < 0.0001$). We suggest that assessment of CK7/CK20 immunoprofile may facilitate the differential diagnosis of a) primary MSGT from metastatic tumors to the head and neck; b) metastatic salivary gland neoplasms; c) primary MSGT, especially mucoepidermoid carcinomas, from SCCa, and d) salivary duct carcinomas from other MSGT.

#39 4:24 p.m.

EXPERIMENTAL ORAL CARCINOGENESIS IN RATS: HISTOMORPHOMETRIC STUDY AND GLOBAL GENE EXPRESSION. A Hirshberg, D Dayan, M Vered, Y Yaacob, N Amariglio, G Rechavi, I Kaplan. School of Dental Medicine. and The Haim Sheba Medical Center, Tel-Aviv U, Israel

Oral tumorigenesis involves a field cancerization process that proceeds in a multifocal fashion through multiple events. The study design consisted of 4-nitroquinoline-N-oxide (4NQO) induced oral carcinogenesis in rats. 0.001% 4NQO was administered via drinking water. Rats were sacrificed at 7, 14, 22, 28, 33, and 36 weeks. The tongues were dissected by a longitudinal mid-lingual incision. One half was processed for routine histopathologic examination, while the other half was stored in liquid nitrogen and used for RNA extraction. Examination of the hematoxylin and eosin stained sections revealed progression from simple hyperkeratosis to varying degrees of dysplasia and ultimately to invasive squamous cell carcinoma of the tongue mucosa. Histomorphometry of the lingual salivary glands, showed a decrease in volume fraction of the serous acini with almost no morphological changes in mucous glands. Excretory ducts of serous glands exhibited various degrees of dysplasia. In order to study the global gene expression during 4NQO induced tongue carcinogenesis, RNA samples from the tongues at different times were analyzed, using Affymetrix rat oligonucleotide microarrays. Comparison of gene expression profiles in the treated animals at various time points revealed changes in genes involved in proliferation, apoptosis, adhesion, migration, DNA repair and stress response. Of particular interest was the increase in the expression of genes associated with salivary glands (the common salivary protein 1, rat proline-rich salivary protein, neonatal submandibular gland proacinar cell protein precursor, rat pancreatic amylase and lingual lipase). The results of the present study may indicate a role of salivary glands in the process of oral carcinogenesis.

ESSAY PROGRAM II

Tuesday, May 20, 2003

#40 4:36 p.m.

INTEREST AMONG SENIOR DENTAL STUDENTS IN CHOOSING A CAREER IN ORAL PATHOLOGY.

A. Curran, A. Chattopadhyay, U. North Carolina, Chapel Hill, North Carolina.

Recent discussions about the future of Oral and Maxillofacial Pathology (OMP) have identified the need for recruitment of qualified applicants to advanced training programs to accommodate future OMP faculty vacancies in dental schools. The purpose of this survey was to gather data on the attitudes and interest among senior dental students about choosing OMP as a career and their beliefs about the field of OMP. The data were used to identify barriers as well as positive influences toward considering OMP and to identify misconceptions about the specialty of OMP and its training programs. The 30-question survey was administered to senior dental students at ten US and Canadian dental schools. Based on the first 190 responses, preliminary results showed that 28% of dental students were aware of OMP prior to entering dental school. One fourth would consider OMP as a career choice, with the majority indicating the most significant influence on that choice was they found OMP challenging. The main reason for not considering OMP was an early decision in their dental school experience on post-graduation plans. One third indicated that the option of an MD degree would cause them to be more interested in OMP. 36% reported occasional or regular meetings with their OMP faculty with the most often reported reason to discuss patient management. Preliminary results indicate that while seniors harbor some misconceptions about OMP, there is some interest in OMP as a career choice. Because OMP is one of the lesser-known specialties in dentistry, dental students may be less aware of it prior to entering dental school than other more well-known clinical specialties. We suggest that OMP faculty may use clinic consult opportunities, earlier introduction of OMP in the curriculum and/or offer internships in OMP departments to increase awareness and interest in OMP.

#41 4:48 p.m.

ORAL AND MAXILLOFACIAL TUMORS OF CHILDREN WITH SPECIAL REFERENCE TO UNDIFFERENTIATED SMALL ROUND CELL TUMORS (USRCT's) .

M. EL-Abany and L . Ismail . Alexandria U. and Mansoura U . Egypt . Two hundred and forty-four oral and maxillofacial tumors in children less or equal to 15 years of age were examined histopathologically at the Oral & General Pathology Departments , Faculties of Dentistry and Medicine , Universities of Alexandria & Mansoura between 1995 -2000 . The present study was done to clarify the characteristics of oral and maxillofacial tumors in children , and to solve the problem of diagnosis and histogenesis of USRCT's . The results showed that the oral cavity was the most commonly affected site in the maxillofacial region (25%), especially the lip (21.3%) .The mandible (n =15) was affected more often than the maxilla (n =10) . Most of the maxillofacial tumors in children were benign (68%). USRCT's) consist of a variety of malignant tumors of differing histogenesis , behavior and prognosis that deserve definite discrimination . The present study included 66 cases of USRCT's) submitted for immunohistochemical study by Strept-Avidin Biotin Complex methods. Lymphoma was diagnosed in 37 cases, rhabdomyosarcoma in 7 cases, neuroblastoma in 14 cases, neuroectodermal tumor of infancy in 3 cases, adenocarcinoma in 3 cases, and alveolar soft part sarcoma in 2 cases. Immunohistochemistry seems to be an available tool for discriminating among the group of USRCT's and providing a precise diagnosis for each.

ABSTRACTS READ BY TITLE

#42

DENDRITIC CELLS IN ORAL NON-HODGKINS' LYMPHOMAS. S. O. M. Sousa, R. A. Mesquita, V. C. Araújo, R. A. P. Paes, N.S. Araújo. U. of São Paulo, Santa Casa School of Medicine, São Paulo, Brazil

Evaluation of immune-accessory cells may provide invaluable information for understanding and classifying malignant lymphomas. Immune-accessory cells are also called dendritic cells (DC), and are known as antigen presenting, non-phagocytic cells. Tew (1993) classified DC under two head groups: those associated to T cells (as interdigitating dendritic cells -IDC and Langerhans' cells-LC) and those related to B cells (follicular dendritic cells-FDC). Usually DC can be identified by their morphology or by specific commercially available antibodies. Thus, in the present study we evaluated the distribution of DC in oral B and T cell lymphomas, in order to help improve immuno-morphologic diagnosis of these tumors. For this purpose, we studied the distribution of DCs in a total of 50 oral lymphomas classified as: diffuse large B cell lymphoma (n=13); diffuse large B cell lymphoma, subtype plasmablastic (n=11); Burkitt's' lymphoma (n=17); MALT lymphoma (n=2); mantle cell lymphoma (n=1); T-cell lymphoma, extranodal NK/T nasal type (n=4), and peripheral T-cell lymphoma, unspecified type (n=2). The antibodies used were: CD21, CD35, S100 protein, caldesmon and CD1a. The results obtained showed that FDC detected by CD21 and CD35 were present in 3 cases of diffuse large B cell lymphoma, 1 MALT lymphoma and in the case of mantle cell lymphoma, only in areas of follicle center formation, and in different patterns of arrangement. FDCs positive to caldesmon were present in all studied cases, seen as an expanded meshwork, and were quantified, with statistically significant smaller amount in Burkitt's lymphomas. IDCs were detected in all the cases studied by the positivity to S100 protein but were negative to CD1a. They were scattered among neoplastic lymphocytic cells. We concluded that FDC and IDC may be detected in lymphomas and may help in their immunophenotyping, since the detection by different antibodies is related to their function in the tumor. (Supported by FAPESP01/06351-2)

#43

A RARE CLINICAL AND HISTOLOGIC PRESENTATION OF ACUTE MYELOGENOUS LEUKEMIA (AML-M0). E. Stoopler, F. Alawi, and T. Sollecito. University of Pennsylvania, Philadelphia.

Acute myelogenous leukemia with minimal differentiation (AML-M0) is a rare subtype of AML that accounts for less than 3% of all AML's. AML-M0 is primarily characterized by myeloid blasts that do not exhibit either the morphology or antigenic phenotype that normally characterizes differentiating or mature myeloid cells. We report an unusual case of a 49-year old male who had been admitted to a hospital complaining of a recent onset of fever, chills, night sweats, weight loss, and debilitating, persistent, oral ulcerations. A routine hematologic evaluation revealed leukopenia with a large number of circulating blasts. A subsequent bone marrow biopsy and aspirate revealed numerous medium to large-sized blasts with prominent nucleoli but with no other discernible morphology. Cyto- and immunohistochemical staining with conventional myeloid and lymphoid markers was negative. However rare cells were positive for the hematopoietic progenitor cell antigen, CD34. Flow cytometric analysis also revealed a population of CD34-positive cells without any other notable evidence of myeloid or lymphoid differentiation, thus confirming the diagnosis of AML-M0. Shortly thereafter, an oral medicine consultation was requested for evaluation of the oral ulcers. The ulcers were large and poorly-defined and involved the lateral tongue and ipsilateral buccal and lower labial mucosae. An incisional biopsy of the labial ulcer revealed microscopic features consistent with AML. There was no evidence of any associated infectious disease. To our knowledge, this case represents only the second documented example of AML-M0 involving the oral mucosa. This report emphasizes that an unusual intraoral presentation and a lack of microscopic and immunophenotypic evidence of myeloid differentiation should not preclude a diagnosis of AML.

ABSTRACTS READ BY TITLE

#44

PERIPHERAL CALCIFYING EPITHELIAL ODONTOGENIC TUMOR AND INCIPIENT AMELOBLASTOMA: ORIGIN FROM PRENEOPLASTIC SURFACE EPITHELIUM? C. Birek, S. Ahing, and J. Perry. U. of Manitoba, Canada.

The peripheral ameloblastoma (PA) is widely believed to arise from either the epithelial remnants of the odontogenic apparatus, or from the basal layer of the surface epithelium, but microscopic evidence for the tissue origin of the peripheral epithelial calcifying tumor (PCEOT, the extraosseous counterpart of the CEOT of Pindborg) is lacking, and preneoplastic epithelial lesions have not been identified. Here we describe three unique cases of peripheral odontogenic tumors with histopathologic evidence of origin from the surface epithelium. The tumors were found in lesions of clinically diverse presentation, in subjects of 10 – 90 years of age. Serial sections were obtained from primary and recurrent lesions. In addition to pathognomonic features, the following appearances were revealed: 1) initial epithelial proliferation of the surface epithelium in the primary lesion with progressively tumor-like appearance in the recurrent lesions, 2) coexistence of hyperplastic and tumor-like features in serial sections, 3) continuity of the tumor with the surface epithelium, and 4) “stromal” changes in the fibrovascular connective tissue adjacent to surface or tumor epithelium reminiscent of epithelial - ectomesenchymal interactions in the initiation of odontogenesis. These histopathologic features are interpreted as evidence of direct origin from the surface epithelium of the oral mucosa. In our previous studies we have demonstrated c-Myc and N-Myc oncogene overexpression, and Myc-associated DHFR gene amplification in a significant number of ameloblastomas (Birek *et al.*, J. Dent. Res.78, Abstr. # 2037, 1999), but not in normal, non-neoplastic epithelium. The current and similar cases are examined further to investigate the possible role of c-/N-Myc deregulation and associated target gene aberrations in the progression of hyperplastic (presumed pre-neoplastic) epithelia to full-fledged tumors.

#45

BOWENOID PAPULOSIS OF THE LABIAL MUCOSA. J. Rinaggio, M. Glick, S. Patrick, M.K. Howett. U. of Medicine and Dentistry, Newark, and Pennsylvania State U. College of Medicine, Hershey.

Bowenoid papulosis typically manifests as numerous pigmented lesions of the anogenital region with a variable clinical course. The disease has been linked to HPV types 16 and 18. Few cases have been described in the oral cavity. A 42-year-old African-American male presented to the Oral Medicine Clinic for evaluation of intermittently symptomatic lesions of his lips of 1.5 years duration. The patient had a past medical history significant for HIV disease of 10 years duration, cryptococcal meningitis in 1994, Kaposi's sarcoma of the right leg, disseminated HSV-2 infection, and polysubstance abuse. His lowest recorded CD4 lymphocyte count was 1. Intraoral examination revealed multiple pink papulonodular lesions of the upper and lower labial mucosae ranging in size from approximately 0.5 – 1.5 cm. Histologic evaluation of one of the lesions revealed acanthotic and bluntly papillary oral mucosa exhibiting cellular atypia throughout the full thickness of the epithelium. This atypia was characterized by nuclear enlargement, multinucleated epithelial cells, scattered abnormal mitoses, and dyskeratotic cells. There was no evidence of stromal invasion. The presence of HPV was confirmed by testing for group specific antigen. Viral typing by polymerase chain reaction followed by restriction analysis and sequencing showed the presence of HPV type 32. Therapy consisted of intralesional and subcutaneous interferon-alpha injections. After approximately 2.5 months of treatment, the lesions had decreased in size, but had not completely resolved.

ABSTRACTS READ BY TITLE

#46

ORAL NEOPLASMS IN DOMESTIC ANIMALS. C. Felizzola, M. Martins, N. Araujo, V. Araujo, S. Sousa. Oral Pathology Department, U. of Sao Paulo, SP, Brazil. Oral neoplasms comprise 5.4% of malignancies in domestic species (canine, bovine, equine, feline), and approximately 1.8% of all neoplasms in dogs. The aim of the present study was to verify the prevalence of neoplastic lesions that affect the oral cavity of dogs, cats, horses and rabbits. One thousand and eighty biopsies were examined in the Oral Pathology Department at the University of Sao Paulo, Brazil, between 1988 and 2002. In our sample, 827 biopsies were neoplasms, while 253 corresponded to cysts, chronic inflammatory lesions, and gingival hyperplasias. Among neoplastic cases, 68.8% were malignancies, and the most frequently found lesions were melanoma (33.9%), squamous cell carcinoma (13.7%), osteosarcoma (6.0%), and lymphoma (2.2%). Benign non-odontogenic neoplasms comprised 7.62% of the cases, and were represented mainly by papillomas (2.3%) and fibromas (1.5%). Odontogenic neoplasms comprised 23.6% of the cases and were most frequently represented by fibrous epulis (18.1%), ossifying epulis (2.7%), acanthomatous epulis (1.5%) and odontoma (0.6%). It could be concluded that: malignant neoplasms were more commonly biopsied, and most of these represented malignant melanoma.

#47

STUDIES OF MITOCHONDRIA DNA ALTERATIONS IN MICRODISSECTED BETEL QUID-RELATED ORAL CANCER AND PRECANCEROUS LESIONS. W. B. Chow, D.B. Shieh, and Y. T. Jin. National Cheng Kung U. Medical Center, Tainan, TAIWAN

Previous studies demonstrated that direct genotoxicity and tissue oxidative damage from the betel quid components were the most likely etiologic factors in carcinogenesis. Reactive oxidative species (ROS) can cause DNA damage both in nuclear and in mitochondrial genomes, but the accumulative effects are greater quantitatively and qualitatively in mitochondrial DNA (mtDNA) due to its deficient DNA repair mechanisms and high genome copy numbers compared with nuclear DNA. The specific aim of this study was to investigate the correlation of betel quid-related oral mucosal lesions, their disease progression and the specific patterns of mtDNA alterations, including the specific 4977 bps deletion. We used a laser microdissection system to isolate specific cellular populations of normal, malignant, and premalignant cells, as well as the adjacent stromal cells in the pathological sections of patients with serial biopsy specimens available from precancerous lesions to advanced oral cancer status. Quantitative polymerase chain reaction (PCR) analysis revealed a significant disease status dependency in the ratio of 4977 bps mtDNA deletions versus total mtDNA. The mtDNA from lymph node had the lowest percentage of the deletion (0.0005%), followed by normal mucosa (0.004%), cancer cells (0.27%) and dysplastic cells (4.6%). The results of all five cases in the study showed consistent profiles, indicating an increase in deletion ratio followed by a slight decline when normal mucosal cells transformed to precancerous status then cancer cells. The stromal cells showed highest degree of mtDNA deletion (4.3%) compared with adjacent epithelial cells (0.40%) in the one case analyzed. This work may contribute the missing link among betel quid exposure, mtDNA alteration pattern, and oral carcinogenesis.

ABSTRACTS READ BY TITLE

#48

IMMUNOHISTOCHEMICAL APPRAISAL OF FAS RECEPTOR, AND CASPASE 8 IN ORAL CANCER:
B. Singh, J. Borke, N. Do, G. Caughman, S. Hsu and R. Abdelsayed. Medical College of Georgia, Augusta,
We have previously reported on the role of Bcl-2 and its congeners in the regulation of programmed cell death (PCD). However, the caspases have been considered to play a central role in terminal execution of PCD (apoptosis). Therefore, the objective of this investigation was to examine the status of Caspase 8 (C-8) and FAS receptor in oral squamous cell carcinomas. For this purpose 5u-thick sections from formalin-fixed archival paraffin blocks were examined using polyclonal antibodies to C-8 (active and inactive form) and FAS receptor (Santa Cruz Biotech, CA). Sections of lymph nodes served as positive controls. C-8 immunoreactivity was observed primarily in the cytoplasm in 75% (n=25) of oral carcinomas. Well and moderately well differentiated tumors revealed varying degrees of zonal reaction, whereas the poorly differentiated tumors showed a diffuse heterogeneous and a focal granular reaction. There was strong immunoreactivity for FAS-receptor in the plasma membrane zone in 80% (n=25) of tumors and a granular cytoplasmic reaction based on the degree of cell differentiation. The upstream C-8 proenzyme associates with death-inducing signal complex (DISC) resulting in pro-enzyme activation to C-8. Activated C-8 transactivates downstream Caspase-3 (C-3), which also is expressed in oral cancer as previously reported by our laboratories. C-3 is also activated by Caspase 9 via an intrinsic pathway involving cytochrome c. C-8 and C-3 are also reported in breast and pancreatic carcinomas; however their role in an epithelial cancers remains as yet unclear. Our investigations demonstrate that FAS receptor, C-8 and C-3 are differentially expressed in oral tumors, suggesting their plausible involvement in oral cancer progression by induction of PCD (apoptosis) and/or cell differentiation.