Essay Abstracts

EVALUATION OF CELL PROLIFERATION AND ANGIOGENESIS IN TONGUE SQUAMOUS CELL CARCINOMA AND THEIR RELATION TO HISTOLOGIC GRADE. M. Khalili, F. Baghaee, R. Beheshti, Tehran University Medical Sciences, Iran.

Background. Squamous cell carcinoma (SCC) is the most common type of oral cancer and has been identified as a significant public health threat. It has been suggested that angiogenesis and cell proliferation are important factors in tumor progression and metastasis, and it is possible that angiogenesis may influence or be influenced by cell proliferation. Also, the clinical significance of histologic grading is still controversial.

Objective. The aim of this study was to evaluate cell proliferation and angiogenesis in tongue SCC and their relation to histologic grade.

Methods. A total of 24 cases of tongue SCC were selected after applying inclusion and exclusion criteria. Sections were obtained from formalin-fixed and paraffin-embedded blocks, and immunohistochemical staining was performed using antibodies against CD105 (endoglin) and Ki-67. Angiogenesis was assessed by CD105 microvessel density (MVD). Positively stained microvessels were counted for each specimen in a predominantly vascular area (hot spot) at x400 magnification. The proliferation index was expressed by Ki-67 labeling index (LI). Tumor histologic grade was defined as low, intermediate, or high. Data were analyzed with the use of t test and Pearson correlation coefficient.

Results. Both CD105 MVD and Ki67 LI were significantly related to histologic grade (P = .045 and P = .047, respectively). Low-grade tumors had higher MVD and lower proliferation index compared with intermediate and high-grade tumors. No significant correlation was observed between CD105 MVD and Ki67 LI (P = .86).

Conclusions. Our findings suggest that angiogenesis and cell proliferation are separate and independent factors that are both related to tumor differentiation in tongue SCC.

HIGH P63, CD147, AND KI-67 EXPRESSIONS CORRELATE INVERSELY WITH SURVIVAL IN ORAL TONGUE SQUAMOUS CELL CARCINOMA (OTCSS): A TISSUE MICROARRAY STUDY. J. Morales, M. Macaden, L. Feng, A. El-Nagger, J. Lee, N. Vigneswaran, University of Puerto Rico School of Dental Medicine, San Juan, University of Texas School of Dentistry, and University of Texas M. D. Anderson Cancer Center, Houston.

Background. Oral tongue squamous cell carcinoma (OTSCC), despite being diagnosed early, has poor survival rate. Therefore, a biomarker that predicts prognosis in OTSCC is critical for therapeutic decision making. CD147 and CD44v6 promote maintenance of cancer stem cells, tumor invasion, and metastatic progression. GLUT-1 expression in tumors is associated with rapid growth and hypoxia. P63 is implicated in tumor cell survival.

Objective. The aim of this study was to determine the prognostic significance of these biomarkers in OTSCC.

Methods. We used a tissue microarray consisting of OTSCC from 32 patients for this study. These patients were treated at the M. D. Anderson Cancer Center from 1995 to 2008. Biomarker expression levels were examined by immunohistochemistry and graded semiquantitatively. Regression models using generalized estimating equations were used to evaluate the association between histology grade and marker expressions.

Results. Overall, nodal recurrence and distant metastasis–free survivals were assessed by the Kaplan-Meier method. Expression levels of p63 and Ki-67 correlated positively (P < .05) with tumor stage and poor histologic grade. Tumor stage correlated significantly with CD147 (P < .05) and marginally with GLUT-1 (P = .06) expression levels. Increased p63 expression strongly correlated with elevated levels of CD147 and GLUT-1 (P < .05). Nodal metastases and extracapsular spread statuses were the best predictors of overall survival (P < .01). The effect of p63 on overall nodal recurrence–free survival and distant metastasis–free survival was significant (P < .05). Increased risk for nodal recurrence, distant metastasis, and death was associated strongly with p63 and Ki-67 (P < .05) and marginally with CD147 (P < .10) expression. Ki-67, p63, and CD147 expression in OTSCC are inversely
correlated with patient survival and serve as important prognostic markers.

**P38 MEDIATES CYTOKINE SECRETION VIA INACTIVATION OF TRISTETRAPROLIN IN SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK.** R. van der Broek, E. van Tubergen, K. Kirkwood, N. d’Silva, University of Michigan School Dentistry, Ann Arbor, and Medical University of South Carolina, Charleston.

**Background.** Proinflammatory cytokines enhance tumor progression in squamous cell carcinoma of the head and neck (SCCHN). RNA-binding proteins, such as tristetraprolin (TTP), bind to and induce decay of cytokine mRNA transcripts, thereby reducing cytokine secretion. Previously, we showed that TTP down-regulation in SCCHN leads to increased IL-6 secretion, which is correlated with poor disease-specific survival. However, the role of the p38/mitogen-activated protein kinase pathway in TTP-regulated cytokine secretion has not been investigated in any cancer.

**Objective.** The goal of this project was to investigate the role of p38 in TTP-mediated cytokine secretion in SCCHN.

**Methods.** Phospho-p38, total p38, and TTP expression were detected by immunoblot analysis. Experiments were performed in 3 different cell lines. Cell lysates were generated from control or IL-12 activated cells. Knockdown and inhibition of p38 were performed by small interfering RNA and SB203580, a p38 inhibitor, respectively. To generate control shRNA. Cytokines were quantified by enzyme-linked immunosorbent assay.

**Results.** Phospho-p38 activity is increased in SCCHN compared with normal keratinocytes. IL-12 induces p38 activation, which was abrogated by p38 inhibitor in a dose-dependent manner. Knockdown of p38 decreased IL-6, vascular endothelial growth factor, and prostaglandin E2 secretion, even in the presence of p38 inhibitor, respectively. To generate control shRNA. Cytokines were quantified by enzyme-linked immunosorbent assay.

**Conclusions.** These findings suggest that targeting upstream regulators of cytokine secretion, such as p38 and TTP, may improve responsiveness of SCCHN to treatment via inhibition of cytokines.


Calcifying epithelial odontogenic tumors (CEOT) are uncommon locally aggressive odontogenic tumors characterized by a peculiar amyloid matrix. The nature of this matrix has been debated, and though CEOT are generally regarded as odontogenic tumors, few authors have reported myoepithelial differentiation in CEOT. We performed a clinicopathologic and immunohistochemical survey of 19 cases of CEOT in 12 patients to address these issues. Of the cases with known demographics, a 1:1 female-to-male ratio was seen with a mean age of 48.6 (range 21-78) years. Eight cases involved the maxillary sinus and 2 the gingiva. One case was associated with a complex odontoma, and another case had features of an adenomatoid odontogenic tumor. Two cases exhibited aggressive features, such as angiolymphatic invasion. One of these cases showed malignant transformation, recurring at 2 years with tumor extending from the condyle and zygomatic arch to base of the skull. In all cases, tumor cells were positive for P63 (100%), but negative for smooth muscle actin (0%) and calponin (0%) as well as calretinin (0%), and lymphoid enhanced factor 1 (0%). Using fluorescent immunohistochemical techniques we demonstrated that the tumoral cells of CEOT contain and secrete the enamel protein amelogenin and that amelogenin is a component of the amyloid stroma (100%). In conclusion, our findings indicate that amelogenin is a component of the amyloid stroma secreted by tumoral cells. Furthermore, CEOT are low-grade tumors capable of malignant transformation. Immunophenotypic evidence is suggestive of an odontogenic phenotype and shows no evidence for myoepithelial differentiation.


**Background.** Sarcomatoid carcinoma (SC) is a biphasic tumor with a conventional epithelial squamous component and a sarcomatoid spindle cell component. Conclusive determination of epithelial differentiation may be difficult under light microscopy. The degree and intensity of reactivity to epithelial and keratin markers is variable and creates a significant diagnostic challenge when reporting on limited biopsy material and considering the cost of immunohistochemistry.

**Objective.** The aim of this study was to determine the most effective epithelial markers when SC is suspected.

**Methods.** Eleven archival cases of SC were obtained and screened with pankeratin AE1/3. If AE1/3 was negative or if no evidence of surface epithelial involve-
ment was found, immunohistochemical staining with other epithelial markers was done, including 34BE12, EMA, p63, MAK-6, CAM5.2, and pancytokeratin.

Results. Seven cases displayed evidence of dysplasia or carcinoma involving the surface epithelium. The remaining 4 showed positivity to ≥1 marker for keratin. Two cases were negative for all markers except MAK-6, despite evidence of surface epithelial neoplasia. Our findings demonstrated that MAK-6 was the most reliable marker, with positive reactivity in 86% and positive in 3 of the cases with negative AE1/3. CAM5.2 was positive in 4/8 cases including 2 where AE1/3 was negative. EMA, 34BE12, and pancytokeratin were the least useful and negative when used.

Conclusions. Our results substantiate that SCs demonstrate highly variable reactivity to keratin and epithelial markers. MAK-6 and CAM 5.2 were the most reliable markers when either AE1/3 was negative or no histologic evidence of epithelial neoplasia was noted.


The buccal bifurcation cyst (BBC) is an uncommon inflammatory odontogenic cyst arising at the bifurcation of mandibular molars in children. Although there has been much debate as to the pathogenesis of the BBC, it appears that the BBC and the paradental cyst, affecting mandibular third molars, share common pathogenic mechanisms and histopathologic features, lending credence to the proposal that the BBC and paradental cysts are variants of the same lesion. We review a series of 5 cases of BBC collected over 1 year by the authors from the archives of the Oral and Maxillofacial Pathology Laboratory at the University of Florida and examine the clinical, radiographic, and histologic findings along with theories regarding etiology and appropriate treatment.


Bizarre periosteal osteochondromatous proliferation (BPOP), also called Nora’s lesion, is a rare benign reactive bone lesion first reported 1983 as occurring on the bones of the hands. BPOP has since been reported in the hands, feet, and long bones and is reported to have a high rate of recurrence. This lesion can easily be confused both clinically and microscopically with other benign and malignant lesions of bone, including osteochondroma, parosteal osteosarcoma, myositis ossificans, and reactive periostitis. We present a rare case of BPOP of the mandible in a 10-year-old African-American boy with a well defined knob-like 2 × 1–cm extension arising from the right premolar region of the mandible. Microscopically a fibrocartilaginous cap giving rise to a proliferation of variably mineralized osteophytic finger-like projections of bone was seen. Multiple trabeculae of “blue bone” were noted as well as numerous atypical-appearing chondrocytes. The lesion recurred within 4 months after the initial excision but had not recurred after the second local excision at the time of writing. To the best of our knowledge, this is the first report of BPOP arising in the mandible. There has been 1 case reported in the maxilla and 2 others in the head and neck region. Clinical, microscopic, and prognostic considerations of this rare entity are discussed.


Rosai-Dorfman disease (RDD) is a rare benign non-Langerhans cell histiocytic disorder of unknown etiology classically associated with significant lymphadenopathy. Rare examples of RDD without clinical or radiographic evidence of concomitant lymph node involvement have been reported; however, only 5 cases thus far have been reported of extranodal RDD localized to the oral cavity. We report only the sixth such case. Our patient was a 20-year-old woman with no significant past medical history who initially presented with mobile but vital teeth #7 and #8 with overlying discomfort. A radiolucent lesion was noted on x-ray, and initial biopsy of the lesion was reported as granulation tissue. Given her ongoing discomfort, she then underwent root canal therapy and 3 curettage procedures on both teeth without improvement in her symptoms, but rather with enlargement in size of the lesion. She then presented to our institution, where we reviewed the biopsy slides, which showed sheets of larger histiocytes with areas of emperipolesis, which is highly characteristic of RDD. Immunohistochemical staining revealed these large histiocytes to be S-100 positive and CD1a negative, helping to confirm a diagnosis of RDD.

LYMPHANGIOMA-LIKE KAPOSI SARCOMA IN THE ORAL CAVITY. P. Pugalagiri, Y. S. L. Cheng, D. Watkins, D. Carlton, J. Wright, Texas A&M University Health Science Center–Baylor College of Dentistry, and Baylor University Medical Center, Dallas, Texas.

Kaposi sarcoma is a malignancy of vascular origin. It usually presents with an increased vascular
proliferation and a spindle cell component which demonstrates slit-like vascular spaces. We present a case of lymphangiomatoid Kaposi sarcoma, a rare variant of Kaposi sarcoma, in the oral cavity. A 45-year-old man presented with a large diffuse red lesion in the left posterior maxillary palate and tuberosity. The clinician’s differential diagnoses included lymphoma or other neoplasms. Histologically, the lesion showed extensive chronic inflammation and numerous dilated vascular spaces with papillary projections, resembling lymphangioma, in the lamina propria. These vascular spaces and the papillary projections were lined by flat or plump endothelial cells with bland morphology. Mitoses are rarely seen. In the deep lamina propria, there were plump spindle cells in the chronically inflamed fibrous connective tissue. Prominent extravasation of blood was not seen. The endothelial cells as well as the plump spindle cells showed positive immunohistochemical staining for CD31, CD34, and human herpesvirus 8. The clinical presentation, histologic features, and immunohistochemical findings supported the diagnosis of lymphangiomatoid Kaposi sarcoma. The patient did not have a history of AIDS, and the HIV status was unknown at the time of biopsy. Therefore, he was referred to an oncologist for evaluating his HIV status and further treatment for the neoplasm. However, he soon moved and was lost to follow-up.


Although much data has been published regarding the incidence and characteristics of bisphosphonate-related osteonecrosis of the jaws (BRONJ) in the setting of intravenous (IV) and oral bisphosphonate use, little information is available on the prevalence of BRONJ in patients taking a single yearly IV zoledronic acid (Reclast) infusion. The purpose of this article is to document 3 cases of BRONJ arising in patients treated with yearly zoledronic acid with an history of oral bisphosphonate use for osteoporosis or osteopenia. To study the incidence and characteristics of bisphosphonate-related osteonecrosis of the jaws, with funding from Merck and Co. we have established the largest well documented database to date with 35 patients with oral BRON. It appears BRON has a clear twofold pathogenesis, including injury to the mucosa and profound and prolonged inhibition of bone remodeling and healing. The injured tissue becomes contaminated by pathogens, chiefly Actinomyces species, which leads to a challenge in healing that the compromised bone and ineffective inflammatory response cannot meet. To be included in this study, patients had to have sufficient data available to complete our stringent prescribed dataset based on American Society of Bone and Mineral Research task force recommendations for BRON case studies. We followed these patients for 3 years. Oral BRON lesions are usually much less extensive than those seen in patients on the intravenous preparations, and most patients [32/35 (94%)] presented in stage 1 or 2. Twenty-nine out of 35 (83%) were on the drug for >3 years (range 18 to 180 months) before they developed the lesion(s). Oral BRON cases appear to be much more responsive to conservative treatment, with only 6% of patients requiring a resection and 88% completely cured after 2 years of follow-up. Characteristic radiographic features were consistently present in BRON patients and include sclerosis of only the alveolar process, periosteal thickening, sclerosis of the dental lamina, widening of the case resolved in 4 months with no treatment, but the other 2 patients did not heal completely, with one becoming stable after 10 months and one remaining unhealed at 18 months. This case series illustrates the potential risks associated with a single dose of a potent bisphosphonate given to patients with a history of long-term oral bisphosphonate therapy. The patients involved appear to have had a mild clinical course similar to oral BRONJ. However, the onset of symptoms appeared much more rapidly than typically seen in oral BRONJ. In addition, all of the patients had additional risk factors for BRONJ. Clinicians should be aware of the risk of development of BRONJ after the use of Reclast to optimize prevention and treatment.


Because the University of Florida is a major referral center for bisphosphonate-related osteonecrosis (BRON) of the jaws, with funding from Merck and Co. we have established the largest well documented database to date with 35 patients with oral BRON. It appears BRON has a clear twofold pathogenesis, including injury to the mucosa and profound and prolonged inhibition of bone remodeling and healing. The injured tissue becomes contaminated by pathogens, chiefly Actinomyces species, which leads to a challenge in healing that the compromised bone and ineffective inflammatory response cannot meet. To be included in this study, patients had to have sufficient data available to complete our stringent prescribed dataset based on American Society of Bone and Mineral Research task force recommendations for BRON case studies. We followed these patients for 3 years. Oral BRON lesions are usually much less extensive than those seen in patients on the intravenous preparations, and most patients [32/35 (94%)] presented in stage 1 or 2. Twenty-nine out of 35 (83%) were on the drug for >3 years (range 18 to 180 months) before they developed the lesion(s). Oral BRON cases appear to be much more responsive to conservative treatment, with only 6% of patients requiring a resection and 88% completely cured after 2 years of follow-up. Characteristic radiographic features were consistently present in BRON patients and include sclerosis of only the alveolar process, periosteal thickening, sclerosis of the dental lamina, widening of the
PDL, incipient bifurcation involvement, and bony sequestration/expansion. These are especially helpful in identifying most, if not all, cases of BRON.


Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is an uncommon clinical condition in which patients present with exposed necrotic bone in the jaws, which may be painful or infected. Most commonly the condition follows removal of a tooth, but it can also develop spontaneously. Research is being conducted to elucidate the pathogenesis, risk factors and treatment strategies, but evidence-based recommendations are lacking. The ambiguity of the disease pathogenesis, associated risk factors, and possible impact on routine dental procedures is hypothesized to generate a high level of uncertainty for oral health care practitioners. This survey was conducted to determine the methods by which general dentists and dental specialists in the state of Florida first came to know about BRONJ and stay abreast of the current developments, their perceptions and beliefs about BRONJ, and its impact on their daily practice.


**Background.** The physician being the proverbial “healer” remains the first line of defense for detection of most oral conditions. The medical community should be acutely aware of oral lesions, because some malignancies, such as oral squamous cell carcinomas, can easily be misdiagnosed, especially in small biopsies from rare locations, including the maxillary sinus, because of the wide variety of architectural and cytomorphologic features of the tumor cells. We report 2 cases of myoepithelial carcinoma occurring in the maxillary sinus which posed a histologic challenge. One was a woman aged 59 years and the other was a man aged 31 years. Both patients initially presented with a history of facial swelling for 3-4 weeks. The biopsy from the maxillary sinus of the female patient was diagnosed to be sinonasal adenocarcinoma, and the diagnosis of the biopsy specimen from the maxillary dental root of the male patient was odontogenic carcinoma. Both patients underwent unilateral total maxillectomy. The diagnosis of myoepithelial carcinoma was arrived at only after histologic examination of the maxillectomy resection specimens. We describe the salient clinical, histologic, and immunohistochemical features of both cases. Myoepithelial carcinoma can easily be misdiagnosed, especially in small biopsies from locations other than major salivary glands. Awareness of the occurrence of this tumor in rare locations, including the maxillary sinus, and a combination of histomorphologic and immunohisto-
chemical approaches is advisable to arrive at a correct diagnosis.


Objective. The aim of this study was to review the clinicopathologic features of alveolar soft part sarcoma (ASPS) and presentation of a well documented case of the sinonasal region in a middle-aged man.

Case report. A 46-year-old man presented in 1989 with complaint of blurred vision, ptosis, and intermittent epistaxis from the left nasal cavity. Endoscopic examination revealed a 6 × 5 cm pedunculated polypoid mass in the left nasal cavity. The radiographic features were consistent with a vascular tumor causing significant destruction of the skull base and extension through the cribriform plate. Biopsy revealed organoid nests of polygonal to round cells showing clear to red-blue cytoplasm, separated by wispy fibrovascular septae and showing pseudoalveolar pattern with borders between the lesion and the surrounding mucosa. The principle differential diagnosis from traumatic neuroma was based on the absence of pain in NVH, whereas pain is typical for traumatic neuroma. The colors reported were pink, yellowish, and red-blue. The clinical diagnosis was irritation fibroma, 3 granular cell or other tumor, and 1 mucocele. There were no reported symptoms associated with any of the lesions. Microscopically, all lesions were covered by keratinizing squamous epithelium. The underlying connective tissue was generally hypocellular, with varying degrees of collagen deposition. Within this background there were multiple aggregates of capillaries or small-size blood vessels in close proximity to small–medium-size nerve bundles. There were no clear borders between the lesion and the surrounding mucosa. The principle differential diagnosis from traumatic neuroma was based on the absence of pain in NVH, whereas pain is typical for traumatic neuroma. In addition, the vascular component is not a feature of traumatic neuroma. In comparison with 10 cases of

NEUROVASCULAR HAMARTOMA OF THE ORAL CAVITY. I. Kaplan, D. Allon, S. Calderon, Rabin Medical Center and School of Medicine, Tel-Aviv University, Israel.

Background. Neurovascular hamartoma (NVH) has been reported in the skin, but it is very rarely reported in the oral mucosa.

Objective. The aim of this study was to describe the clinical and pathologic characteristics of neurovascular hamartoma of the oral cavity.

Methods. The archives of our pathology department (1994-2011) were searched for neurovascular hamartoma (NVH) of the oral mucosa. The microscopic and clinical characteristics have been analyzed.

Results. A total of 10 NVHs were retrieved: 5 male, 5 female, 12-76 (mean 45) years old. Seven occurred in the tongue, and 1 each in the lip, uvula, and buccal mucosa. The typical presentation was an exophytic mass, pedunculated or wide-based with a smooth surface. The colors reported were pink, yellowish, and red-blue. The clinical diagnosis was 6 irritation fibroma, 3 granular cell or other tumor, and 1 mucocele. There were no reported symptoms associated with any of the lesions. Microscopically, all lesions were covered by keratinizing squamous epithelium. The underlying connective tissue was generally hypocellular, with varying degrees of collagen deposition. Within this background there were multiple aggregates of capillaries or small-size blood vessels in close proximity to small–medium-size nerve bundles. There were no clear borders between the lesion and the surrounding mucosa. The principle differential diagnosis from traumatic neuroma was based on the absence of pain in NVH, whereas pain is typical for traumatic neuroma. In addition, the vascular component is not a feature of traumatic neuroma. In comparison with 10 cases of
traumatic (irritation) fibroma, NVH presented significantly more nerve bundles.

Conclusions. NVH are not common lesions, but it seems that they may be more frequent in the oral mucosa than expected from the literature.

ORAL INFLAMMATORY MYOFIBROBLASTIC TUMOR, A LESION CLINICALLY AND HISTOLOGICALLY MIMICKING MALIGNANCY: A CASE PRESENTATION. M. Madriz, H. Rivera, M. Cutanda, J. L. Castro, Central University of Venezuela, Caracas.

Background. Inflammatory myofibroblastic tumor (IMT) is considered to be a reactive inflammatory lesion affecting several systemic locations, the lungs being the most common. Only a few cases have been reported in the head and neck area, specifically in the oral cavity. Numerous etiologic factors have been associated with IMT, including the Epstein-Barr virus. Although it is a benign lesion, it behaves clinically in an aggressive manner.

Objective. The purpose of this study was to analyze clinically and histologically an infrequent case of introral IMT with treatment and 1-year follow-up.

Case report. A 58-year-old female patient was examined with an intraoral ulcerated mass measuring 5 × 4 cm in diameter, pedunculated and firm in consistency, located on alveolar mucosa extending to the buccal mucosa. Panoramic x-ray, computerized tomographic scan, and routine laboratory tests were conducted. Incisional biopsy was performed and the sample submitted for histopathologic study. The tumor was composed of spindle cells within a myxoid stroma with numerous inflammatory cells. An immunohistochemical panel of antibodies, including vimentin, desmin, smooth muscle actin, S100 protein, CD68, cytokertan AE1-AE3, ALK, and Ki67, was performed to establish the definitive diagnosis. The tumor cells were immunoreactive with smooth muscle actin, CD68, vimentin, ALK, and Ki67.

Conclusions. The present case represented an inflammatory myofibroblastic tumor in an infrequent location. It is emphasized that IMT should be recognized as a distinct entity, and a definitive diagnosis of IMT should include a correlation between clinical, histopathologic, and immunohistochemical features, because this lesion simulates a sarcoma histologically and clinically.

GRANULOMATOUS FOREIGN BODY REACTION TO CALCIUM HYDROXYLAPATITE FILLER. REPORT OF THREE CASES. S. Farahani, M. Hein, S. Kabani, R. Konya, J. Sexton, S.-B. Woo, Harvard School of Dental Medicine, Boston, Brockton, Stratas Path Services, Lexington, Massachusetts, Private Prac-
tice, Wellesley, Massachusetts, and Fayetteville, New York.

Dermal fillers are often used to smooth out wrinkles and treat facial fat atrophy. They are classified into biostimulatory, filling, and combined fillers. An example of a combined filler, which has both biostimulatory and space-filling properties, is calcium hydroxylapatite, one of the brands of which is Radiesse (Bioform Medical, San Mateo, CA). This is used for the correction of moderate to severe facial wrinkles and folds and for the treatment of facial fat loss due to human immunodeficiency viral infection. The filler consists of sterile, latex-free, synthetic, injectable calcium hydroxylapatite microspheres (30%) suspended in an aqueous gel carrier (70%). Although this brand of filler is nontoxic, nonirritating, and nonantigenic, nodules and foreign body granulomas have also been described, and this is a report of 3 cases of such an adverse reaction. Patients were women aged 46, 67, and 68 years, all with a history of Radiesse injection to the upper (2) or lower (1) lip for cosmetic reasons. All three developed swellings or nodules, and 2 were painful. Histopathologically, the cases showed foreign material in the form of regularly sized round pale purple-to-beige spherules that were not refractile in polarized light, associated with a nonnecrotizing granulomatous foreign body reaction with many giant cells and fibrosis. The overlying epithelium did not exhibit hyperplasia.

Conclusions. Calcium hydroxylapatite fillers such as Radiesse may induce painful nodules at or near the site of injection which represent foreign body reactions.

OROFACIAL MANIFESTATIONS OF INHERITED SYSTEMIC HYALINOSIS: CASE REPORT AND REVIEW OF THE LITERATURE. C. Haberland, M. Co-pete, S. Dructeinis, J. Persing, Yale–New Haven Hospital, New Haven, Connecticut, and University of Saskatchewan, Saskatoon, Canada.

Inherited systemic hyalinosis is a rare autosomal recessive disorder caused by a mutation in the ANTXR2 gene located on chromosome 4q21 that results in an accumulation of an amorphous hyaline substance in the papillary dermis and submucosal tissue. The clinical manifestations include severe pain with movement, progressive joint contractures, osteolytic lesions, and perianal masses. In the mild form of the disease (previously called juvenile hyaline fibromatosis) patients survive into adulthood, and in the severe form (previously called infantile systemic hyalinosis) there is visceral involvement resulting in death within the first 2 years of life. Head and neck manifestations include coarse facial features, gingival hypertrophy, oral mucosal nodules, and postauricular and perinasal pearly papules. We report a case of a 13-year-old Hispanic girl
with mild systemic hyalinosis. She had a history of multiple surgeries to remove hypertrophic gingival tissue and intraoral nodules. Her mouth opening was limited due to hyaline material accumulation periorally. Dental findings included delayed eruption of teeth. Histologic examination of the gingivectomy material showed hypocellular hyalinized areas that contained spindle-shaped cells and dilated capillaries. The hyaline material was periodic acid–Schiff positive and diastase resistant, but did not stain with Congo red. Immunohistochemical studies showed that the spindle-shaped cells were positive for vimentin but negative for α-smooth muscle actin and S-100 protein. Review of the literature showed that ~70 cases of the mild form of the disease have been reported. We add our report of a case of this rare condition with an 11-year follow-up and review of the oral manifestations.

**CLINICAL AND HISTOLOGIC EVALUATION OF CHRONIC GRAFT-VERSUS-HOST DISEASE OF ORAL MUCOSA. M. Magalhães, K. Fernandes, F. Coracin, A. Luiz, P. Santos, University of São Paulo, Brazil.**

Chronic graft-versus-host disease (GVHD) is a major cause of morbidity and mortality in patients undergoing allogeneic hematopoietic stem cell transplantation, and it frequently affects the oral cavity. The diagnosis should be established based on clinical and histopathologic features. Histologic characteristics are not pathognomonic, and one of the main barriers to establish a final diagnostic of GVHD has been the absence of standardized criteria for histologic examination. The objectives of this study were: to evaluate the correlation between GVHD histologic categorization using the National Institutes of Health (NIH) Consensus Development Project Pathology Working Group and that using Horn’s classification; to identify any impediments to use the NIH proposal; and to check possible association between histologic and clinical classifications. Oral mucosa biopsies of 60 patients who had a clinical and histopathologic diagnosis of oral GVHD were analyzed. The histopathologic findings were observed in a blind fashion using 2 criteria: those recommended by the NIH consensus and those by Horn. Clinical features were collected retrospectively from patients’ charts and were classified according to Akpek. The histopathologic consensus classification proved to be valid, easily applied, and correlated with the Horn classification. There was no correlation between histologic classification and clinical stage of disease. The absence of clinical and histopathologic correlation does not diminish the importance of histologic analysis of GVHD. Biopsy should always be performed to establish the differential diagnosis with infectious lesions, drug reactions, or even neoplasias. In such cases, the treatments would be totally different, because GVHD is treated with immunosuppressants.

**Poster Abstracts**

**A REVIEW OF AN ORAL AND MAXILLOFACIAL SURGERY RESIDENCY PROGRAM’S BIOPSY SERVICE. J. Doscher, K. Ablow, J. Kelly, Hospital of Saint Raphael, New Haven, Connecticut.**

Background. The specific aims of this study were to determine the spectrum of oral and maxillofacial pathology (OMFP) in patients of a hospital oral and maxillofacial surgery (OMFS) clinic and to determine how often the surgeon’s clinical diagnosis correlates with the histopathology. This study provides an overview of the types of cases seen as well as valuable information regarding potential diagnostic strengths and weakness of OMFS residents. Thus, this study will provide a foundation for lecture design and clinical mentoring for OMFP instructors who teach OMFS residents.

Methods. This retrospective study used natural language search of the hospital pathology database. The selection criteria included anatomic location of biopsy, diagnosis comment(s), clinical diagnosis, and final diagnosis. The search included all cases submitted from the OMFS clinic between July 1, 2007, to April 1, 2011.

Results. Diagnoses included 275 reactive lesions (74%), 54 developmental lesions (16%), and 42 neoplastic processes (11%). In 142 cases, the diagnosis was not given (38%). In 130 cases, a clinical description was provided without a diagnosis (35%), in 75 cases the histopathologic and clinical diagnoses correlated (20%), and in 24 cases, the clinical and histopathologic diagnoses did not correlate (6%).

Conclusions. Overall, only 20% of cases submitted for histologic diagnosis were diagnosed correctly based on clinical presentation, although in most cases (38%) a diagnosis was not given. Therefore, it is difficult to assess from this study whether additional training is needed to improve the diagnostic skills of oral surgery residents or whether barriers in communication need to be addressed between the two specialties.


Background. Clinical assessment of palpable lymph nodes and masses of the head and neck is challenging and often includes a broad differential diagnosis. The differential diagnosis includes primary and metastatic
neoplasms, inflammatory and reactive lesions, infectious diseases, and developmental processes. Fine-needle aspiration cytology provides a useful triage tool and often results in a definitive diagnosis.

**Objective.** The aim of this study was to demonstrate the use of fine-needle aspiration cytology in the triage of selected head and neck masses and its role in directing specific imaging or diagnostic tests to support the diagnosis.

**Methods.** Selected case studies included: a 6-year-old girl with Langerhans cell histiocytosis, a 62-year-old woman with small cell lymphocytic leukemia/lymphoma, a 63-year-old man with metastatic squamous cell carcinoma, and a 60-year-old woman with breast cancer and noncaseating granulomatous lymphadenopathy.

**Results.** Work-up of each of the cases included immunohistochemistry, imaging, flow cytometry, positron-emission tomography, magnetic resonance imaging (MRI), and special stains for microorganisms to finalize the diagnoses.

**Conclusions.** Fine-needle aspiration cytology is a useful modality for triage and for initiating the diagnostic work-up of head and neck masses of varied etiologies.

**SALIVARY ENDOTHELIN-1 AS A POTENTIAL BIOMARKER FOR ORAL SQUAMOUS CELL CARCINOMA (OSCC) IN ORAL LICHEN PLANUS AND IN PREVIOUS OSCC PATIENTS.** Y. S. L. Cheng, T. Rees, L. Jordan, H. S. Chen, D. T. Wong, Texas A&M Health Science Center–Baylor College of Dentistry, Dallas, Texas, University of Medicine and Dentistry, Newark, NJ, and University of California, Los Angeles.

Endothelin-1 (ET-1) is a potent vasoconstrictor involved not only in vascular biology but also in carcinogenesis. Results of a study in 2007 suggested salivary ET-1 as a potential biomarker for oral squamous cell carcinoma (OSCC), but a more recent study showed conflicting results. The purpose of this pilot study was to investigate the feasibility of using salivary ET-1 as a biomarker for OSCC in 2 groups: oral lichen planus (OLP) patients and patients who previously had OSCC. Saliva samples were collected from 5 groups of subjects: patients with OSCC (group A; n = 18), patients with OSCC previously and in remission (group B; n = 15), patients with active OLP lesions (group C; n = 21), patients with OLP and in remission (group D; n = 28), and normal controls (group E; n = 24). Salivary ET-1 levels were determined by enzyme-linked immunosorbent assay, and the results were analyzed by Mann-Whitney U test. The mean salivary ET-1 level in group A was significantly higher than in group C (P = .001), group D (P = .015), and group E (P = .004). There was no significant difference (P > .05) in the mean salivary ET-1 levels between groups A and B, groups B and C, groups B and D, groups B and E, groups C and D, groups C and E, and groups D and E. Our results suggested that salivary ET-1 would be a good biomarker for OSCC development in OLP patients regardless of the degree of OLP disease activity. However, it appeared to not be a good biomarker for detecting recurrence of OSCC in patients in remission.

**TEMPORAL ALTERATIONS IN MICRO-RNA EXPRESSION DURING EXPERIMENTAL ORAL TONGUE CARCINOGENESIS.** L. Mosquera, J. Wu, J. Schaefer, N. Vigneswaran, University of Puerto Rico School of Dental Medicine, San Juan, and University of Texas School of Dentistry, Houston.

**Background.** Micro-RNAs (miRNAs) are small non-coding single-stranded RNAs which negatively regulate gene expression. Specific miRNA expression signatures have potential diagnostic and prognostic utility in cancers.

**Objective.** The aim of this study was to profile and correlate miRNA expression with histologic and molecular abnormalities in a mouse model of oral tongue carcinogenesis.

**Methods.** CBA mice were given 4NQO (100 μg/mL) in drinking water for 16 weeks. Tongues of control (n = 8) and experimental (n = 8) mice were removed at 8, 16, and 21 weeks after treatment. The Cancer RT2 miRNA polymerase chain reaction (PCR) array and Taqman miRNA assays were used to analyze miRNA expression of RNA isolated from frozen or formalin-fixed tissue. Formalin-fixed tissues were used for histologic/immunohistochemical studies.

**Results.** 4NQO-exposed mice revealed moderate to focally severe epithelial dysplasia after 8 weeks (early) and severe epithelial dysplasia in situ and invasive carcinoma after 16-21 weeks. Analysis of miRNA PCR array data identified 28 (21 up- and 7 down-regulated) and 13 (11 up- and 2 down) miRNAs to be significantly (>2-fold) altered compared with control samples during the early (8 weeks) and late (>16 weeks) stages of carcinogenesis, respectively. MiRNAs 196a, 142-5p, 32, and 21 were the top 5 miRNAs that were up-regulated (>8-fold) during the early stage. Micro-RNAs 196a, 21, and 31 were the only miRNAs that were up-regulated in both early and late stages of carcinogenesis. Our studies showed that aberrant AKT-mTOR activation is an early event in 4NQO-induced carcinogenesis. Activation of AKT-signaling by miRNA 196a is...
implicated in colon cancer. MiRNAs 21 and 31 are oncogenic in various human cancers.

**Conclusions.** Aberrant expression of miRNAs 196a, 21, and 31 is an early event and is causally related to 4NQO-induced carcinogenesis.

**PRIMARY GLYCOGEN-RICH CLEAR CELL SQUAMOUS CELL CARCINOMA OF THE MANDIBULAR GINGIVA. J. Frazier, H. Sacks, P. Freedman, New York Hospital Queens and Jamaica Hospital Medical Center.**

Clear cell squamous cell carcinoma (CCSCC) is a rare variant of squamous cell carcinoma. CCSCC was first reported by Kuo in 1980, who described 6 cases of squamous cell carcinoma of the skin of the head and neck which were composed of cells with clear cytoplasm that he attributed to the accumulation of intracellular fluid and not the presence of glycogen, lipid, or mucin. This case report describes a 59-year-old woman with an exophytic hemorrhagic lesion of 2 months’ duration on the posterior mandibular gingiva. The lesion was biopsied, and histologic examination revealed dysplastic stratified squamous epithelium showing transition to an infiltrating tumor composed of islands of epithelial cells with clear cytoplasm. The cytoplasm stained positive with periodic acid–Schiff (PAS) and was PAS negative after diastase digestion. Mucicarmine stains were negative for intracytoplasmic mucin. This is the first reported case describing glycogen-rich clear cell squamous cell carcinoma of the mandibular gingiva.

**MODULATION OF THE ONCOGENIC STAT3 SIGNALING BY MITOGEN-ACTIVATED PROTEIN KINASES IN ORAL SQUAMOUS CARCINOMA CELLS. N. Nikitakis, I. Gkouveris, G. Rassidakis, A. Sklavounou, University of Athens, Greece.**

The oncogenic role of the constitutive activation of the signal transducer and activator of transcription (Stat3) signaling pathway in oral squamous cell carcinoma (OSCC) cells has been well established. Negative regulation of Stat3 signaling has been proposed as a valid target of chemopreventive and antineoplastic strategies; however, the molecular pathways responsible for Stat3 modulation in OSCC have not been fully elucidated. The purpose of this investigation was to assess the modulating effects of mitogen-activated protein kinases (MAPKs) on Stat3 signaling in OSCC cells. The constitutive expression levels of phosphorylated (activated) and total Stat3, ERK, p38 MAPK, and JNK were assessed in OSCC cell lines (SCC25 and Cal33) by Western blot. Inhibition of specific MAPKs was performed using selective inhibitors of p38-MAPK (SB203580), JNK (SP600125), and ERK (U0126). The experiments were performed in the presence and absence of 15d-PGJ2, a known inhibitor of Stat3 tyrosine phosphorylation. Selective inhibition of ERK and p38-MAPK, but not JNK, resulted in up-regulation of tyrosine-phosphorylated Stat3. 15d-PGJ2 down-regulated the tyrosine but increased the serine phosphorylation levels of Stat3 and induced phosphorylation of all 3 tested MAPKs. Treatment of cells with the specific JNK inhibitor had no effect on 15d-PGJ2–mediated inhibition of tyrosine-phosphorylated Stat3. On the other hand, selective inhibition of p38 MAPK or ERK reversed 15d-PGJ2–mediated Stat3 repression. These data provide preliminary evidence in support of the role of ERK and p38-MAPK, but not JNK, as negative regulators of the oncogenic Stat3 signaling in OSCC as well as mediators of the Stat3-inhibitory effect of 15d-PGJ2.

**CHONDROBLASTIC OSTEOSARCOMA OF THE MANDIBLE: A CASE REPORT. N. Nikitakis, D. Xygkas-Eftymiou, I. Chronas, N. Papadogeorgakis, University of Athens, Greece.**

Osteosarcoma is a malignant tumor characterized by the direct production of osteoid by atypical mesenchymal cells. Excluding multiple myeloma, osteosarcoma is the most common primary bone malignancy. In the head and neck area, osteosarcomas are rare and represent ~7%-10% of all osteogenic sarcomas. Chondroblastic osteosarcoma is the prevailing subtype found in the jaws. In the case reported here, a 53-year-old male patient presented with a nonpainful swelling in the right side of his mandible. It was covered by normal-appearing mucosa, and all involved teeth were vital. Radiographically, the lesion appeared primarily as a radiopacity with diffusely admixed less opaque areas and ill-defined margins. Other significant imaging findings were localized root diversion and widening of the peri-odontal ligament. A biopsy was obtained. The histopathologic examination revealed a cellular mass composed of pleomorphic malignant mesenchymal cells with extensive areas of chondroid differentiation with lobular arrangement. In addition, areas of direct osteoid production by malignant cells were discerned. A histopathologic diagnosis of chondroblastic osteosarcoma was rendered. Computerized tomography and bone scintigraphy did not reveal metastatic disease. The tumor was removed by partial mandibulectomy, followed by reconstruction with a titanium plate. The patient received chemotherapy and radiotherapy postoperatively. At 6- and 12-month postoperative follow-ups, no signs of recurrence or metastatic spread were found, allowing for the replacement of the reconstruction plate with a hip bone graft. Despite its rarity, chondroblastic
osteosarcoma should be included in the differential diagnosis of space-occupying lesions of the jaws.

**SINONASAL NONINTESTINAL-TYPE ADENOCARCINOMA.** V. Woo, J. Mason, A. Chi, E. Herschaft, J. Moxley, University of Nevada, Las Vegas, and Medical University of South Carolina, Charleston.

Sinosal adenocarcinomas are rare malignancies that are broadly categorized into intestinal or nonintestinal types. Distinct differences in etiology, histopathology and clinical behavior represent the primary bases for distinguishing between these 2 variants. Sinonasal nonintestinal-type adenocarcinomas arise most frequently in the ethmoid and maxillary sinuses, often presenting with nasal obstruction and epistaxis. They can be further subclassified as low grade or high grade depending on clinical and microscopic characteristics. Of note, pain and facial deformity are unusual findings that typically herald advanced disease and high-grade histology. We report the case of a 69-year-old man who presented for evaluation of increasing right cheek pain and worsening nasal congestion. Extraoral examination revealed malar fullness and mild elevation of the eye on the affected side. On intraoral examination, a right maxillary mass was identified that completely obliterated the buccal vestibule. Radiographic examination of the area showed a destructive radiolucency in continuity with an opacified maxillary sinus. Histologically, the tumor was composed of crowded glands without evidence of atypia or intestinal morphology, consistent with sinonasal nonintestinal-type adenocarcinoma. Interestingly, the lesion was ultimately diagnosed as low grade despite its clinically high-grade presentation. The distinction between the low- and high-grade variants of sinonasal nonintestinal adenocarcinoma has important prognostic implications, because low-grade lesions behave indolently whereas high-grade lesions are associated with dismal survival rates. Management of cases with a disparity between clinical and histologic features can be challenging, and guidelines have yet to be established.

**MAXILLARY GINGIVAL METASTASES FROM A CHORIOCARCINOMA: A REPORT CASE.** I. Velasco, B. Martinez, L. Aguilar, C. Venables, C. Mebus, University of Los Andes, Bogota, Columbia, University Mayor, Santiago, Chile, and Del Salvador Hospital, Santiago, Chile.

Metastatic tumors to the oral cavity are extremely rare lesions, representing 1% of all malignancies in jawbones and soft tissues. The vast majority of these lesions are located in the jawbones; metastases to oral soft tissues are rarer, with gingiva and tongue the sites of major prevalence. The primary tumors that frequently produce metastasis to the oral tissues are the lung, breast, and kidney. Gingival metastases have an unremarkable clinical appearance; they can be difficult to distinguish from more common hyperplastic or reactive lesions, such as peripheral giant cell granuloma, pyogenic granuloma, and peripheral ossifying fibroma. We report an unusual case of a 33-year-old Hispanic man with a testicular choriocarcinoma of 1 year duration already presenting metastases in the brain, neck, and lungs. The patient consulted because of a tumoral mass of 2 weeks’ duration in the anterior maxillary gingiva in relation with teeth 1.1 and 1.2 and that resembled a benign gingival mass. The histopathology demonstrated metastasis from the patient’s choriocar-

Background. Dyskeratosis congenita (DC) is an inherited bone marrow failure syndrome (IBMF) with a mucocutaneous triad of nail dystrophy, reticular skin pigmentation, and mucosal leukoplakia. Patients with DC have short telomeres and are at high risk for aplastic anemia and neoplasia. Dyskeratosis congenita is second only to Fanconi anemia for cancer risk among the IBMF syndromes. The most common cancer in DC is oral squamous cell carcinoma (SCC). The genetic basis of DC is complex with varied inheritance patterns. This genetic heterogeneity underlies a wide spectrum of disease severity. Specific gene mutations involved in telomere maintenance have been identified in DC.

Objective. We present a SCC of the maxillary alveolar ridge of rapid onset in a 15-year-old boy with DC.

Case report. The DC patient had defined shortened telomeres. The patient had a renal transplant at 2 years of age for multicystic kidney disease. Subsequently, he developed posttransplantation lymphoproliferative disorder of the small bowel, which was treated with resection. Immunosuppressive therapy was discontinued, and he rejected the transplanted kidney in 2009. In 2010, surveillance examination revealed a fungating mass of the right posterior maxillary alveolus. Biopsy and he rejected the transplanted kidney in 2009. In

Conclusions. This case describes an early onset oral carcinoma in a DC patient with a complex medical history. The difficulties in recommending conventional treatment protocols in this patient group are highlighted.

THE EXPRESSION OF PEROXIREDOXIN-1 IN EPITHELIAL CELLS FROM THE BUCCAL MUCOSA BEFORE AND AFTER PANORAMIC RADIOGRAPH. N. de Araújo, M. Felipe-Silva, A. Demasi, J. Junqueira, V. de Araújo, E. Martinez, São Leopoldo Mandic Institute and Research Center, Campinas, Brazil.

Background. Ionizing radiation promotes many important cellular processes, such as DNA damage, apoptosis, and oxidative stress. Earlier studies have shown that expression of peroxiredoxin (Prx) 1 in mammalian and in cancer cells increases after ionizing radiation, demonstrating that Prx1 plays an important role in protecting cells from ionizing radiation–induced cell death. Little is known about the involvement of Prx1 in protecting human cells from radiation-induced death.

Objective. The aim of this study was to evaluate the effect of x-rays in epithelial cells from the buccal mucosa in 13 patients before and after panoramic radiograph.

Results. According to the results obtained by indirect immunofluorescence it was possible to visualize an increase in the intensity Prx1 expression after the panoramic radiographs, which was confirmed after the quantitative analysis obtained by gene expression of Prx1 by quantitative reverse-transcription polymerase chain reaction ($P < .05$).
Conclusions. It is possible to conclude that panoramic radiography is able to induce a higher expression of Prx1 in epithelial cells from the buccal mucosa, indicating the effect of the radiation at the cellular level.


Poorly differentiated oral squamous cell carcinomas should be differentiated from other epithelial malignancies of primary or metastatic origin. However, in certain cases, the degree of anaplasia of tumor cells can provoke significant diagnostic dilemmas. We report a rare case of undifferentiated tongue carcinoma of uncertain origin. A 56-year-old woman presented with a painful ulcerative lesion of the tongue of 2 months' duration. Renal cell carcinoma had been diagnosed and treated 10 years before without recurrences. Clinical examination revealed a 1.5 x 1.5 cm ulcer on the left posterior lateral tongue. Firm, nontender, enlarged left cervical lymph nodes were noticed. Microscopic examination of the tongue lesion revealed diffuse infiltration of the connective tissue by overtly malignant cells exhibiting intense cellular atypia and pleomorphism, abundant eosinophilic cytoplasm, large nuclei with prominent nucleoli, and numerous atypical mitoses. Immunohistochemically, the neoplastic cells were diffusely positive for vimentin, focally positive for CD10, EMA, and CD138 and negative for pancytokeratin, keratins 1, 5/6, 7, and 20, S-100, HMB-45, MART1, LCA, CD56, and chromogranin. Fine-needle aspiration of the enlarged cervical lymph node revealed similar cytologic and immunohistochemical features. After appropriate consultations, a final diagnosis of undifferentiated carcinoma was rendered indicating that the exact primary or metastatic origin of the tumor could not be accurately determined. Despite intensive radiotherapy and chemotherapy, the patient died of disseminated metastatic disease within 6 months. Undifferentiated malignant neoplasms may cause significant diagnostic problems which may not be possible to solve by microscopic and immunohistochemical analysis.

IMMUNOHISTOCHEMICAL EXPRESSION OF HSP47 IN BENIGN AND MALIGNANT SALIVARY GLAND TUMORS. V. Papanikolaou, P. Argyris, N. Nikitakis, A. Sklavounou, J. Sauk, University of Athens, Greece, and University of Louisville, Kentucky.

Salivary gland tumors (SGTs) constitute a heterogeneous group of neoplasms with multiple histologic subtypes and a broad spectrum of pathologic appearances, frequently presenting difficulties in their final diagnosis and treatment. In recent decades, the molecular and genetic factors underlying the development and progression of human neoplasia have been the focus of exhaustive research. However, our understanding of the molecular mechanisms governing oncogenesis in SGTs remains limited. The aim of this study was to investigate and compare the immunohistochemical expression of Hsp47, a molecule involved in modulating collagen production and implicated in various forms of cancer, including benign and malignant SGTs. Eighteen benign SGTs (13 pleomorphic adenomas and 5 Warthin tumors) and 61 malignant SGTs (16 adenoid cystic carcinomas, 12 mucoepidermoid carcinomas, 11 polymorphous low-grade adenocarcinomas, 9 adenocarcinomas not otherwise specified, 6 salivary duct carcinomas, 3 carcinomas ex mixed tumor, 2 lymphoepithelial carcinomas, 1 myoepithelial carcinoma, and 1 clear cell carcinoma) were stained immunohistochemically for Hsp47. Hsp47 was expressed in all benign and in 48 (78.7%) of 61 malignant tumors, predominantly showing a diffuse pattern of immunostaining (>50% positive cells). The intensity of Hsp47 immunostain varied from weak to strong. Both positivity and intensity scores were significantly higher in benign compared with malignant SGTs (P < .001). In conclusion, similarly to tumors of other anatomic sites, such as esophagus and stomach, higher levels of Hsp47 are correlated with benign rather than malignant SGTs, suggesting that Hsp47 may serve as a protective factor in the evolution of carcinogenesis in SGTs.

INCREASED PDGF-A, PDGF-B, VEGF, AND FGF-2 EXPRESSION IN RECURRENCE OF SALIVARY GLAND PLEOMORPHIC ADENOMA. A. Soares, A. Demasi, A. Aleman, N. de Araújo, V. de Araújo, São Leopoldo Mandic Institute and Research Center and School of Medicine, State University of Campinas, Brazil.

Background. Pleomorphic adenoma (PA) is the most common salivary gland tumor. Although classified as benign, it has a tendency to recur (RPA), as well as the ability to undergo malignant transformation (TRPA). It has been suggested that mutations in various families of growth factors and growth factor receptors are involved in the autonomous growth of tumor cells.

Objective. The aim of the present study was to investigate the participation of fibroblast growth factor (FGF) II, Flg, Bek, platelet-derived growth factor (PDGF) A, PDGF-B, PDGF-R±, and vascular endothelial growth factor (VEGF) in PA, RPA, and TRPA.

Methods. Eighteen cases of PA, 19 cases of RPA, and 2 cases of TRPA were analyzed for growth factor expression with the use of immunohistochemical techniques via tissue microarray.
Results. There was a significant difference in PDGF-A, PDGF-B, FGF-2, Flg, Bek, and VEGF expression among all of the groups. There was no significant difference in the expression of PDGF-R. Comparing nonrecurrent with recurrent tumors, PDGF-A, PDGF-B, FGF-2, Flg (filaggrin), Bek, and VEGF reactivity in RPA was stronger than that observed in PA. All proteins were highly expressed in TRPA.

Conclusions. This research suggests that PDGF-A, PDGF-B, FGF-2, Bek, Flg, and VEGF may be related to the recurrence of PA. In addition, this study shows that TRPA cells overexpress all growth factors, which has been reported in association with the malignant transformation.

ANALYSIS OF THE CHEMOKINE CXCL13 IN SJÖGREN SYNDROME PATIENTS. J. Kramer, T. Rothstein, Feinstein Institute for Medical Research, Manhasset, New York.

Background. Sjögren syndrome (SS) is a rare autoimmune dyscrasia, most commonly seen in middle-aged women. Primary SS (pSS), or sicca syndrome, affects salivary and lacrimal glands predominantly, whereas secondary SS (sSS) occurs in conjunction with other autoimmune connective tissue disorders. In addition to reduced exocrine gland function, serious systemic aspects of the disease are recognized. Care for SS patients is palliative, because no established therapies address disease etiology. B-Cell abnormalities are seen systemically and within salivary glands of SS patients. However, the contribution of B cells to SS is poorly understood. For B cells to function most efficiently, they must be recruited to specific sites where they interact with other cells and secrete mediators to orchestrate immune responses. CXCL13 is a B-cell chemokine that is elevated in many autoimmune diseases. Accordingly, we hypothesized that CXCL13 is up-regulated during SS progression.

Methods. We quantified CXCL13 in sera (n = 18) and saliva (n = 20) of SS patients and healthy control subjects (n = 10) by enzyme-linked immunosorbent assay. Significance was determined by 2-tailed Mann-Whitney test (95% confidence interval [CI]).

Results. Primary SS patients have increased levels of serum CXCL13, and both pSS (n = 16) and sSS (n = 4) patients have elevated CXCL13 in saliva. Moreover, pSS patients with xerostomia (n = 7; 44%) have elevated serum and salivary CXCL13 levels compared with pSS patients with normal salivary flow (n = 9; 56%).

Conclusions. These data indicate that CXCL13 in salivary tissue and/or serum may be pathogenically involved in SS disease and may serve as a marker of SS progression and severity.

CARCINOMA EX PLEOMORPHIC ADENOMA OF THE PAROTID GLAND. R. Carlos, M. Nuyens, B. Andrade, M. Romañach, O. Almeida, Centro Clínico de Cabeza y Cuello/Hospital Herrera Llerandi, Guatemala City, Guatemala, and Dental School of Piracicaba, Brazil.

Carcinoma ex pleomorphic adenoma (CX-PA) is a rare malignant salivary gland tumor that mainly affects the parotid of patients in the sixth to seventh decades of life. It is characterized by the development of an adenocarcinoma in association with a primary or recurrent benign pleomorphic adenoma. We present a case of CX-PA affecting an 81-year-old woman with a painless swelling in the left parotid gland for 1 year. Her medical history included 3 surgical treatment attempts of a pleomorphic adenoma. Computerized tomography showed a 3.5 × 3 cm nodular lesion with intermediate density in the superficial aspect of the left parotid gland. Histologic evaluation revealed areas of typical pleomorphic adenoma next to an intracapsular poorly differentiated adenocarcinoma. Tumor cells (malignant and nonmalignant) were positive for cytokeratins AE1/AE3 and 8. Pleomorphic adenoma and myoepithelial cells of the adenocarcinoma were positivity for smooth muscle actin, calponin, and p63, and epithelial malignant cells were positive for epithelial markers. Ki-67 index labeling was 5% for the adenocarcinoma and fewer than 1% for the pleomorphic adenoma cells. The patient was treated by surgical excision and adjuvant radiotherapy, and there is no sign of local recurrence or distant metastasis after 6 months of follow-up.

ONOCYTIC SALIVARY GLAND TUMORS: REPORT OF TWO CASES. R. Carlos, M. Peñalonzo, M. Nuyens, V. Toral-Rizo, M. Romañach, O. Almeida, Centro Clínico de Cabeza y Cuello/Hospital Herrera Llerandi, Guatemala City, Guatemala, and Dental School of Piracicaba, Brazil.

An oncocyte is characterized by abundant eosinophilic granular cytoplasm and central rounded nuclei. In the head and neck, various reactive and neoplastic lesions present are formed by oncocytes. Oncocytic sialolipoma is a rare benign salivary gland tumor characterized by neoplastic mature adipose tissue surrounding nonneoplastic salivary gland elements exhibiting oncocytic differentiation. Oncocytoma is a well circumscribed salivary gland tumor composed solely by oncocytes, accounting for 1% of all salivary gland tumors. We present cases of each of these uncommon oncocytic salivary gland lesions. The patient was an 81-year-old woman with an asymptomatic right parotid mass microscopically diagnosed as oncocytic sialolipoma. Interestingly, the same patient also presented a paraganglioma involving the right carotid bifurcation.
The second case was a 78-year-old woman with an asymptomatic mass in the right submandibular gland. The tumor was removed, and the microscopic diagnosis was oncocytoma. Oncocytic cells of both lesions were positive for epithelial membrane antigen, cytokeratins AE1/AE3, 7, 18, and 19, and negative for p63, calponin, smooth muscle actin, vimentin, S-100, and carcinoembryonic antigen. Oncocytic sialolipoma cells were positive for cytokeratins 5 and 14, and oncocytoma cells were negative.

COMPARISON OF MINOR SALIVARY GLAND MUCOUS RETENTION CYSTS AND SIALOLITHS.

E. Peters, J. Coutu, R. Sihra, S. Wong, University of Alberta, Edmonton, Canada.

Minor salivary gland–associated mucous retention cysts (MRCs) and minor salivary gland sialoliths (MSGSs) share histologic similarities, which include epithelium lined cystic spaces and variable inflammatory changes. The relationship between these entities was investigated by comparing the age, gender, site, and histologic presentation of all such cases presenting sequentially over a 20-year period. A total of 84 MRCs and 24 MSGSs were identified, representing, respectively, 15% and 3% of all cases of minor salivary gland pathosis. Significant gender predilections were not noted. MRCs had a generalized distribution as follows: 28% floor of mouth (FOM), 26% buccal mucosa/mucobuccal fold (BM/BF), 14% palate, 17% lower lip, 12% upper lip (UL), and 4% retromolar pad. In comparison, MSGSs had a restricted distribution as follows: 58% UL, 29% BM/MF, 4% palate, and 8% unstated sites. There were overlapping histologic features as follows: cuboidal/columnar lining only: 80% MRCs and 5% MSGSs; cuboidal/columnar lining with squamous metaplasia: 15% MRCs and 29% MSGSs; squamous lining only: 5% MRCs and 40% MSGSs. Twenty-five percent of MSGSs had no lining epithelium. Histologic similarities were influenced by site, with squamous metaplasia evident in only 5% of FOM MRCs. There was inflammation in 41% and 83%, respectively, of MRCs and MSGSs. There was a difference (P < .05) in the mean presentation age for MRCs (49.4, SD 18.2) compared with MSGS (60.5, SD 12.7). However, the site-matched mean age for UL and BM/BF MRCs (58.1, SD 13.4) was similar to MSRGs. In contrast, FOM MRCs, a site in which MSGSs were not found, showed a significant (P < .05) age difference (37.7, SD 16.1). The results suggest that in UL and BM/MF sites, MRC and MSGS cases share epidemiologic and histologic similarities.

FIBROBLAST GROWTH FACTOR SIGNALING IN MOUSE ODONTOGENIC EPITHELIAL STEM CELLS. J. Chang, J. Wright, H. Kessler, R. d’Souza, F. Wang, Baylor College of Dentistry, Dallas, and Institute of Biosciences and Technology, Texas A&M Health Science Center, Houston.

Constant supplies of odontogenic epithelial cells from stem cell niches in the cervical loop (CL) enable mouse incisors to grow continuously throughout life. Fibroblast growth factor 10 (FGF-10) and FGF receptor (FGFR) 2 have been shown to be essential for maintenance of incisors’ CL during prenatal development. Whether FGF signaling is required for postnatal odontogenic epithelial stem cells (OESCs) remains unknown. The purpose of this study was to elucidate the role of FGF signaling in OESCs. We established an in vitro sphere culture to isolate the stem cells derived from postnatal mouse incisor CL. Stem cell properties were evaluated by the sphere forming (self-renewal) ability, label retention (slow cycling), and the differentiation potential. Knockout FGFR was compared with wild-type flox mice. The requirement for intact ERK and AKT pathways were evaluated by specific ERK and AKT inhibitors. The dissociated cells from CL were able to self-renew and expand to form spheres for ≥18 generations in the sphere culture. The sphere’s cells were less differentiated but epithelial in origin, as evident by lineage tracing and CK14 immunoreactivity. These sphere cells could be further stimulated to become amelogenin-expressing and mineral material–producing cells. Sphere-forming OESCs could also be cultured from the postnatal unerupted mouse molar. Knockout FGFR and both ERK and AKT inhibition impaired the sphere-forming ability. This study provides a substantial advance in the isolation of the mouse postnatal OESCs. We also suggest that the FGF through ERK and AKT signaling is required to regulate proper growth of postnatal OESCs. The existence of stem cells in the mouse molar suggested that there might be OESCs present in humans which might be the origin of odontogenic neoplasms.

P53 MUTATION ANALYSIS OF ODONTOGENIC CYSTS WITH AND WITHOUT DYSPLASIA. D. Cox, University of California, San Francisco.

Background. Overexpression of p53 protein is well described in odontogenic cysts (OCS), including those with epithelial dysplasia. However most p53 antibodies stain both wild-type and mutated p53 protein and may not reflect genotype. Direct sequencing of the p53 gene has not identified mutations in OCS.

Objective. The purpose of this study was to determine the molecular basis of p53 expression in several types of OCS with and without dysplasia.
Methods. The study material comprised 13 OCs: odontogenic keratocyst (n = 5); orthokeratinized OC (n = 5); dentigerous cyst (n = 2); lateral periodontal cyst (n = 1); and unspecified OC (n = 1). Five of these had features of mild or moderate epithelial dysplasia. One intraosseous squamous cell carcinoma (SCC) that was believed to have arisen from an antecedent dysplastic orthokeratinized odontogenic cyst was also included. Immunohistochemistry was performed using the DO7 monoclonal antibody which recognizes wild-type and mutated p53. DNA was extracted from microdissected tissue for all samples, and exons 4-8 of the p53 gene were direct sequenced.

Results. In 4 of 5 OCs with dysplasia, there was strong nuclear staining of basal and suprabasal cells. In all cases without dysplasia, nuclear expression in basal cells was either negative or weak and was absent in suprabasal cell nuclei. A mutation in exon 6 of the p53 gene (E224D) was identified in both the dysplastic orthokeratinized odontogenic cyst and the subsequent intraosseous SCC.

Conclusions. OCS with features of dysplasia show increased expression of p53 protein that does not reflect p53 mutational status. One dysplastic odontogenic cyst shared the same p53 mutation with a subsequent intraosseous SCC, indicating that p53 mutation may be associated with malignant transformation in this case.

DETECTION OF EPSTEIN-BARR VIRUS IN ODONTOGENIC TUMORS. H. Rivera, O. Mamaeva, A. Gallard, M. MacDougall, Central University of Venezuela, Caracas, and University of Alabama, Birmingham.

Background. Epstein-Barr virus (EBV) is the member of the human herpesvirus group. It has been considered to be an oncogenic virus, being associated with the etiology of Burkitt lymphoma, lymphoproliferative disorders of B-cell origin, and B-cell lymphomas in immunosuppressed individuals, nasopharyngeal carcinoma, in thymic lymphoepithelial carcinoma, and squamous cell carcinoma. A few studies on oral tumors have demonstrated the presence of EBV.

Objective. The purpose of the present study was to reveal the presence of EBV in odontogenic tumors.

Methods. Ten cases with the definite diagnosis of keratocystic odontogenic tumor (KCOT), 2 cases of calcifying epithelial odontogenic tumor (CEOT), and 10 cases of solid ameloblastomas were selected from the files of the Oral Pathology Laboratory, School of Dentistry, Central University of Venezuela. DNA was extracted from formalin-fixed paraffin-embedded tissues with the use of QIAamp DNA Tissue Kit. (Qiagen, Valencia, CA). Polymerase chain reaction was performed using specific primers for EBV—EBNA 2A, EBNA 2B, BAMC, BAMW, IR3, BMRF-1, BMLF-1, and BNRF-1 region—and GAPDH as a housekeeping gene. Adequate positive and negative control samples were included.

Results. One case diagnosed as solid ameloblastoma was positive for the BACM region of EBV, and 3 cases corresponding to the diagnosis of KCOT were positive for the BMLF-1 region.

Conclusions. Our results indicate that EBV can be detected in odontogenic epithelial-origin tumors. This study is the first report on the presence of EBV in 3 different epithelial-origin odontogenic tumors. Further molecular analysis including more cases and close follow-up of the positive cases should be conducted.

THE ODONTOGENIC KERATOCYST: AN ARGUMENT FOR THE CAUTIOUS INTERPRETATION OF RADIOGRAPHIC AND HISTOLOGIC FINDINGS. N. Odingo, D. Colosi, D. Trochesset, State University of New York School of Dental Medicine, Stony Brook.

The odontogenic keratocyst (OKC) is classified as a benign developmental odontogenic cyst. Accurate diagnosis of OKC is critical owing to its potential for clinically aggressive behavior. We report a case of a 71-year-old man with an incidental radiographic finding of a large radiolucent maxillary lesion. The lesion was suspicious for an aggressive benign lesion, such as OKC, or a low-grade malignancy. Cone-beam computerized tomography (CBCT) was performed to delineate the borders of the lesion. A review of CBCT images reinforced the differential diagnosis. The patient was referred to the oral surgery department for treatment. An incisional biopsy returned a diagnosis of cyst of the maxilla. Two months later, the patient underwent conservative enucleation of the lesion. This treatment plan was based on the presumption that the “cyst” originated from an endodontically treated tooth. The surgical specimen was diagnosed as OKC. Owing to the high recurrence rate of OKCs, the patient was given the option of peripheral ostectomy with extraction of teeth at the surgical site, or indefinite periodic follow-up with radiographic imaging; he opted for the latter. In view of our original high index of suspicion for OKC, it is suggested that the biopsy results should have been interpreted with caution. A review of the literature supports the conclusion that OKCs should be included in the differential diagnosis for periradicular lesions that are refractory to endodontic therapy. In our case, this conclusion was also supported by CBCT interpretation. CBCT could also have been used for optimal selection of an appropriate biopsy site. It is recommended that surgical treat-

Traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) is a lesion of the oral mucosa with unknown pathogenesis that may clinically resemble a squamous cell carcinoma. A biopsy characteristically reveals a dense cell infiltrate composed of eosinophils, lymphocytes, and large mononuclear cells whose origins have been a matter of debate. These large mononuclear cells may be alarming for a malignant process, and immunohistochemical staining usually reveals that in up to 70% of cases, these cells are CD30+ T cells, needing differentiation from CD30+ T-cell lymphoproliferative disorder of the oral mucosa. This has been regarded as the oral counterpart of cutaneous CD30+ lymphoproliferative disorders such as lymphomatoid papulosis or anaplastic large cell lymphoma. We present the case of a 71-year-old woman with recurrent CD30+ T-cell lymphoproliferative disorder of the oral mucosa which resolved without treatment. The recurrent lesion presented as an ulcer on the buccal mucosa near the commissure. The initial and recurring lesions revealed similar histologic features including eosinophils, lymphocytes, and large mononuclear cells with strong immunoreactivity for CD30, CD3, CD4, CD8, and LCA, but they failed to reveal ALK1 and ALK2. Immunohistochemical staining revealed a dense cell infiltrate composed of eosinophils, lymphocytes, and large mononuclear cells whose origins have been a matter of debate.

EBV-POSITIVE MUCOSAL ULCERATION IN A PATIENT WITH PREVIOUSLY UNDIAGNOSED MULTIPLE MYELOMA. B. Martin, W. Zhao, F. Racke, Y. Efebera, J. Kalmar, C. Allen, Ohio State University, Columbus.

Epstein-Barr virus (EBV)–induced disorders are a varied group of diseases with biologic behavior ranging from self-limiting reactive processes to aggressive malignant lesions. Due to the similarities in clinical presentation, morphologic features, and immunohistochemical phenotypic, these lesions are often a diagnostic challenge. Recently, EBV-associated mucocutaneous ulcers exhibiting distinctive clinical and histopathologic features have been described in immunosuppressed patients. A 66-year-old woman presented with a recurrent ulcer of the left posterior palatal and maxillary facial gingiva. Biopsy revealed ulcerated mucosa and underlying granulation tissue that supported a polymorphous inflammatory cell infiltrate, including eosinophils and numerous large atypical mononuclear cells with pleomorphic nuclei. Immunohistochemical studies using antibodies directed against CD20, CD30, and PAX5 showed positivity in the large atypical cells. These cells were positive for EBV-encoded RNA with in situ hybridization. Antibodies directed against Ki-67 showed a proliferation index of 60%-80% among these cells. A preliminary diagnosis of EBV-driven B-cell lymphoproliferative disorder was rendered with a comment that further medical evaluation was indicated. Hematologic evaluation revealed previously undiagnosed multiple myeloma. A final diagnosis of EBV-positive mucosal ulceration secondary to immune suppression was made. The ulcer healed 3 weeks after the biopsy. The patient later underwent autologous hematopoietic stem cell transplantation, and at the time of writing was in complete remission.

SPINDLE CELL LYMPHOMA: REPORT OF A RARE CASE ARISING IN THE ORAL CAVITY AND REVIEW OF THE LITERATURE. A. Chi, J. Lazarchick, R. Coles, B. Neville, Medical University of South Carolina School of Dentistry, Charleston and Private Practice, Mauldin, South Carolina.

Prominent spindle cell or sarcomatoid morphology is an infrequent finding in lymphomas. Anaplastic large cell lymphoma is the most common type of lymphoma to exhibit sarcomatoid features; however, spindle cell variants of B-cell lymphomas have been described rarely as well. We report an unusual case of a spindle cell variant of diffuse large B-cell lymphoma arising in a 40-year-old woman. The patient presented with a painful multinodular gingival swelling in the left lower quadrant. The mass was associated with paresthesia and submandibular lymphadenopathy. Radiographic examination showed an ill-defined moth-eaten radiolucency in the left posterior mandible. Widening of the periodontal ligament spaces was noted among the adjacent teeth. An incisional biopsy showed a proliferation of pleomorphic, spindle-shaped, and ovoid cells arranged in intersecting fascicles. Immunohistochemical stains showed the tumor cells to be strongly positive for CD45 and CD20 and negative for CD3, S-100, AE1/AE3, and myeloperoxidase. A review of the literature revealed only 26 previously reported cases of B-cell lymphomas...
with prominent spindle cell features. Most investigators have considered these lesions to represent unusual variants of diffuse large B-cell lymphoma or follicular lymphoma. The most commonly affected sites are the skin (especially of the head and back) and soft tissue, with only 3 previously reported cases involving the oral cavity. It is important for pathologists to avoid mistaking spindle cell lymphoma for other malignant spindle cell neoplasms, such as sarcoma, spindle cell carcinoma, and melanoma. Recognition of focal round atypical lymphoid cells and inclusion of lymphoid markers in the immunohistochemical profile should aid in proper diagnosis.

THE CLINICAL SPECTRUM OF ORAL T-CELL LYMPHOMAS. J. Whitt, J. Rokos, B. Barker, C. Dunlap, University of Missouri, Kansas City.

Lymphomas of T-cell origin are among the least common of the non-Hodgkin lymphomas to involve the head and neck. T-cell lymphomas are a diverse group of lesions which exhibit a broad spectrum of clinical behavior ranging from clinically indolent lesions that may exhibit spontaneous regression to highly aggressive lesions associated with significant morbidity and mortality. We present a series of 4 cases of T-cell lymphomas that involved the oral cavity. An incisional biopsy of the oral mucosal lesion established the initial diagnosis of lymphoma in each of these patients. At the indolent end of the spectrum, a 47-year-old woman presented with a 2.5 cm indurated painless ulceration involving the buccal mucosa. The oral lesion regressed within 3 weeks of an incisional biopsy. The histologic findings supported a diagnosis of cutaneous T-cell lymphoma (lymphomatoid papulosis). At the aggressive end of the spectrum, 25- and 29-year-old women presented with painful, rapidly enlarging, ulcerative lesions of the hard palate. The histologic findings supported diagnoses of NK/T-cell lymphoma, and melanoma. Recognition of focal round atypical lymphoid cells and inclusion of lymphoid markers in the immunohistochemical profile should aid in proper diagnosis.


Background. Hamartoma is defined as a benign tumor-like nodule composed of a disorganized overgrowth of mature cells and tissues normally present in the affected part, with 1 element predominating. In leiomyomatous hamartoma (LH), the presence of smooth muscle tissue dominates over other tissues. It is a rare oral lesion, often present at birth and involving the midline portion of the maxilla (incisive papilla), palate, and tongue. The age of patients diagnosed with LH range from 3 months to 8 years. LH exists in other regions, such as the skin, and is less prevalent in lungs or kidneys or as a component of liver hamartoma. LH consists of a proliferation of nonencapsulated smooth muscle cells characterized by eosinophilic fusiform cells, with blunt end nuclei, in transversal or longitudinal fascicles. Immunohistochemical stains for smooth muscle markers are positive.

Case report. A 4-year-old girl presented with a 1-cm lobulated smooth nodular mass at the midline maxillary alveolus, clinically suspicious for mucosal neuroma, possibly associated with multiple endocrine neoplasia. Microscopic examination of the excisional biopsy revealed the histopathologic features of LH. The management of LH is surgical excision; recurrences are not observed.

Conclusions. Hamartomatous processes are not easily distinguished from neoplasia. The differential diagnosis of a nodular lesion of the anterior palate or middle of the tongue in an infant or child should include LH.


Melanoma is defined as a malignant neoplasm of melanocytic origin. The most common site is the skin, although it can be seen in any region with melanocytes. Noncutaneous melanomas, especially oral melanomas are extremely rare and represent <1% of all melanomas. Oral melanomas tend to be more aggressive than their cutaneous counterparts. The most common intraoral location is the palate, followed by maxillary gingiva. Primary melanoma of gingiva constitutes ~27% of all intraoral melanomas, although most of these are located on the maxillary gingiva. Primary intraoral melanoma of mandibular gingiva is extremely rare, with <50 documented cases in the English-language literature.
We report a case of melanoma on the mandibular gingiva of a 72-year-old caucasian woman. The lesion was located on the lingual gingiva of the edentulous area of tooth #18. Clinically, it presented as a raised, pigmented, and ulcerated lesion measuring ~1 × 1 cm. The lesion had been present for 1 month. An incisional biopsy was performed. The microscopic examination displayed numerous neoplastic melanocytes with varying degrees of nuclear pleomorphism and hyperchromatism. Immunohistochemical studies showed S-100 protein, HMB-45, and Melan-A reactivity of the lesional cells, favoring a diagnosis of melanoma. The patient was treated surgically. We discuss the clinicopathologic features, differential diagnosis, and prognosis of intraoral melanomas. We also present a review of literature to show the prevalence of intraoral melanoma on the mandibular gingiva.

CHRONIC LINGUAL PAPULOSIS—NEW INDEPENDENT ENTITY OR MATURE FORM OF TRANSIENT LINGUAL PAPILLITIS? S. Adibi, J. Bouquot, University of Texas, Houston.

Background. Several acute, usually pediatric, variants of edematous, usually symptomatic, fungiform papillitis have been reported since the 1990s, most notably transient lingual papillitis; but no chronic forms have been mentioned. Is there a chronic fibrotic counterpart, akin to the fibroma-like masses of older palatal examples of inflammatory papillary hyperplasias (IPH)? One affecting other papillae? Affecting older persons?

Objective. The aim of this study was to clinicopathologically characterize a new lesion with clustered chronic fibrous papules (nonsyndromic) of the tongue.

Methods. Cases were collected from clinics in 2 dental schools.

Results. Four female and 3 male patients were identified with multiple, moderately firm, slightly pedunculated, normally colored or slightly erythematous masses clustered at the tip of the tongue (n = 4), covering the dorsal surface (n = 2), or on the lateral border (n = 1); 1 showed several erythematous edematous papules (similar to IPH) admixed with fibrous papules. Patient ages ranged from 37 to 62 (average 51) years. All lesions were asymptomatic except for the lateral border lesion, which presented with a burning sensation and mild tenderness (which disappeared with antifungal medication). All lesions had been present for years; 5 were associated with mouth breathing or a tongue thrust habit. Four papules were biopsied: All were composed of dense avascular fibrous tissue with no or very few inflammatory cells; 1 had focal dilated capillaries and edema. The lesion appeared to represent altered filiform papillae rather than fungiform papillae.

Conclusions. We suggest the name chronic lingual papulosis as a fibrous hyperplastic response of filiform papillae to mild trauma/irritation or chronic desiccation; it is probably not a chronic counterpart to transient lingual papillitis.

IS PERI-IMPLANTITIS MORE THAN SIMPLE INFLAMMATION? PATHOLOGIC FINDINGS OF 100 BIOPSIES AROUND AILING AND FAILING IMPLANTS. I. Kaplan, A. Hirshberg, G. Eliyahu, D. Schwartz-Arad, Tel-Aviv University, Tel Aviv, Israel, and Schwartz-Arad Day-Care Surgical Center, Ramat-Hasharon, Israel.

A retrospective cohort study was conducted on 100 biopsies of peri-implant tissue submitted for pathologic diagnosis from ailing and/or failing implants. The study population included 29 men and 45 women, age range 21-78 (mean 55.2) years. The mean period between implantation and biopsy was 10.1 (range 0.25-16.6) years. Histologic analysis confirmed the diagnosis of peri-implantitis: Fibroepithelial hyperplasia and inflammation were found in 95% of the biopsies; Actinomyces-related inflammation (30%), pyogenic granuloma (24%), and giant cell granuloma (10%) were also found. These results indicated that the clinical presentation of peri-implantitis in ailing and/or failing implants exhibits microscopic evidence of potentially aggressive reactive lesions rather than simple inflammation in 64% of cases. These lesions are recognized as potentially aggressive when they occur around teeth; however, their contribution to the failure of implants has not been investigated before. This study presents the largest series of peri-implant biopsies with pathologic examination. These results suggest that it may be important to biopsy peri-implantitis at earlier stages. Further investigation is required to better understand the role of reactive lesions as well as Actinomyces in peri-implantitis.

THE PREVALENCE OF PSEUDOXANTHOMA ELASTICUM–LIKE CONNECTIVE TISSUE CHANGES IN AN ORAL BIOPSY SERVICE. C. Harrington, C. Allen, F. Beck, J. Kalmar, Ohio State University, Columbus.

Pseudoxanthoma elasticum (PXE) is an autosomal recessive disorder with potentially significant effects on elastic tissues of the eyes, skin, and cardiovascular system. It is caused by mutation of the ABCC6 gene. The true prevalence of PXE is unknown but estimated to range from 0.001% to 0.004%. The frequency of the mutation is also unknown but estimated to be 0.625% to 1.25%. Phenotypic expression of the mutated gene is highly variable, and clinical manifestations in heterozy-
gotes have been documented. Diagnosis of PXE can be suggested by the detection of fragmented calcified elastic fibers in lesional skin. Infrequently, similar connective tissue changes have been noted coincidentally in dermal and oral mucosal biopsies obtained for other conditions, resulting in patient work-up and confirmation of PXE in previously undiagnosed individuals. An acquired form of these connective tissue changes, however, has also been reported to occur in otherwise normal persons. The purpose of this pilot study was to determine the frequency of PXE-like changes in oral mucosal biopsy samples. We examined 500 cases submitted to our oral biopsy service with the use of hematoxylin-eosin, Verhoeff-von Gieson, and von Kossa stains to identify coarse, fragmented, calcified elastic fibers. Cases were divided into 4 age intervals, each with 125 sequential patients. Characteristic connective tissue changes occurred more frequently than the reported prevalence of PXE. Overall results showed a prevalence of 9.8%, with upper and lower confidence bounds (95% CI) of 12.8% and 7.3%, respectively. There were no positive findings in the first 2 decades, and the prevalence increased with age. These results support the need for additional studies to determine the clinical significance of PXE-like connective tissue changes.

**PAPILLARY TIP MELANOSIS (BROWN BUMPS): UNUSUAL VARIANT OF PHYSIOLOGIC AND DRUG-INDUCED MELANOSIS.** S. Adibi, P. Suarez, J. Bouquot, University of Texas, Houston.

**Background.** Since 1967, at least 9 cases of pigmentation of the fungiform papillae have been reported, 1 congenital, all in Africans and Asians. Suggested names have included pigmented fungiform papillae and black bump. One report suggested that ≥25% of adult Africans showed this sign, but this has not been substantiated, and the lesion has, to the best of our knowledge, never been reported in a dental journal.

**Objective.** The aim of this report was to clinicopathologically characterize an entity which we suggest be called papillary tip melanosis (PTM).

**Methods.** Cases were collected from the authors’ patient panels.

**Results.** Eight female and 3 male patients were identified with multiple brown fungiform (sometimes filiform also) papillae of the lingual dorsum; 2 showed a diffuse background melanotic macule. Pigmentation was concentrated at the tips of the papillae. Affected papillae were generally clustered on dorsal (n = 7) or lateral (n = 2) regions of the tongue, sometimes randomly scattered over the entire dorsum (n = 2). Ages ranged from 12 to 57 (average 44) years; all affected individuals were of African (n = 7), Asian (n = 3), or Hispanic (n = 1) racial descent. All lesions were asymptomatic, and no papillae were larger than normal. All cases were present for “years,” and at least 3 were present since childhood; 1 case developed during chronic use of ketoconazole. No biopsies were performed, but earlier authors have reported a concentration of melanosis in the tip epithelium of the papillae, with an abundance of pigment incontinence.

**Conclusions.** We suggest PTM as an unusual variant of physiologic pigmentation, probably developing during childhood and typically lasting for years (possibly a lifetime?). It needs no treatment or biopsy. Occasionally, melanosis-inducing drugs may produce the same effect.

**EXTRASKELETAL MESENCHYMAL CHONDROSARCOMA OF ORAL CAVITY: A CASE REPORT AND LITERATURE REVIEW.** A. Grandhi, R. Wiston, R. Reich, P. Freedman, New York Hospital Queens and Yorktown Heights.

Mesenchymal chondrosarcoma is a rare histologic subtype of chondrosarcoma first described by Lichtenstein and Bernstein in 1959. This malignant cartilaginous tumor has a predilection for the facial skeleton with 22%-27% of all cases involving the jaw bones. It can also occur as a primary extraskeletal tumor, with one-third of cases seen in the soft tissues of the head and neck, especially the orbit and the cranial and spinal dura mater. Dowling, in 1964, reported the first case of extraskeletal mesenchymal chondrosarcoma, which is usually a rapidly growing tumor with a high incidence of metastasis. To the best of our knowledge, we report the first case of an intraoral extraskeletal mesenchymal chondrosarcoma in the English-language literature. This case is that of a 67-year-old woman who presented to an oral surgeon with a round buccal gingival mass in the relationship with the left mandibular second premolar. Histopathologic examination of the biopsy demonstrated an infiltrative tumor composed of ovoid to spindle-shaped cells set in a chondromyxoid stroma. Scattered mitotic figures were also seen. In areas, the lesional stroma exhibited a pericytoma-like vascular pattern. Also noted were foci of cartilage with tumor cells appearing to be set within lacunae and focally arranged in a lace-like pattern. Immunohistochemistry showed that the tumor cells were focally positive for S100 and negative for P63, calponin, CAM 5.2, and AE1/AE3. The patient was treated by surgical excision 2 months later. There was no evidence of recurrence 5 months after surgery. Due to the rarity of this tumor, care must be exercised during examination of histologic features and immunohistochemical profile for prompt diagnosis and improved outcome.