osteoalveolar bone formation were all noted. Osteosclerosis of the alveolar process was found in all radiographs. In the mandible, this sclerosis was especially distinct and noted to be located only above the inferior alveolar canal. Rarely were all radiographic features visualized in a single case. Another important finding was the presence of periodontal disease in all 29 of the cases that involved the jaws. This could be attributed to the fact that BP accumulates preferentially in sites of high bone turnover or remodeling.

**Conclusions.** Recognition of the radiographic features plays a crucial role in the early detection of osteonecrosis and treatment planning of patients on oral BP. In early stages, oral radiographic findings may be the only indicator of BONJ and can precede the finding of exposed bone.


Bisphosphonates are synthetic analogues of naturally occurring pyrophosphate, capable of binding hydroxyapatite of bone and inhibiting osteoclast-mediated bone resorption. This property has led to their use in cancers well known to metastasize to bone, most notably breast and prostate cancer. We show here that zoledronic acid (ZA) directly induces apoptosis, in a survivin-dependent manner, to a significantly greater degree in tumorigenic than in nontumorigenic primary tumors. Nontumorigenic (MCF 10A, LNCaP, respectively) and tumorigenic (MCF 7, PC3, respectively) human breast and prostate cell lines were exposed to different concentrations of ZA (0-10 μM/L), using 1/4 M as the baseline. A dose-response effect on apoptosis and cell proliferation (microscopic observation with annexin V and MTS, respectively) was observed with increasing ZA concentrations to a greater extent in the tumorigenic versus nontumorigenic cells. Gene expression analysis demonstrated the differential expression of multiple genes involved in apoptosis, including tumor necrosis factor, BCL-2, caspase, IAP, TRAF, and death domain families. Western blot analysis confirmed that antiapoptotic proteins survivin, BCL-2, and BCL-XL were down-regulated and that proapoptotic proteins caspase-2, -3, and -9 were up-regulated in the MCF-7 and PC 3 cell lines but remained unchanged in the MCF-10A and LNCaP cell lines, explaining, at least in part, the significantly increased levels of apoptosis within the tumorigenic cells compared with the nontumorigenic cells. The combined results from this study demonstrate that low concentrations of ZA rapidly and directly affect the metastatic lesions through the induction of a gene-regulated apoptotic process. These findings support the potential of ZA to directly affect the tumor, as well as to prevent bony invasion.


The true incidence, etiology, and risk factors that contribute to bisphosphonate (BP)-related osteonecrosis of the jaw (BRONJ) pathogenesis are not known. We conducted a retrospective study to evaluate the frequency, risk factors, clinical presentation, and management of BRONJ in cancer patients treated with intravenous BPs at the University of Minnesota Masonic Cancer Center and Park Nicollet Institute. Eighteen of 576 eligible patients (3.1%) developed BRONJ, including 8 (4.2%) of 190 patients with breast cancer and 6 (7.2%) of 83 patients with multiple myeloma. Ten of the 18 BRONJ patients (59%) developed it after tooth extraction, and 7 (41%) developed it spontaneously. The mean infusions and duration of BP treatment were significantly higher in BRONJ patients compared with control subjects (P < .001). Multivariate Cox proportional hazards regression analysis revealed that diabetes (hazard ratio [HR] 3.40, 95% confidence interval [CI] 1.11-10.11; P = .028), hypothyroidism (HR 3.59, 95% CI 1.31-9.83; P = .013), smoking (HR 3.44, 95% CI 1.28-9.26; P = .015), and higher number of zoledronate infusions (HR 1.07, 95% CI = 1.03-1.11; P = .001) significantly increased the risk of developing BRONJ. Based on the American Academy of Oral and Maxillofacial Surgeons staging system, 1 patient was initially diagnosed with a stage I lesion. 10 with stage II, and 4 with stage III lesions. Initial management of BRONJ was nonsurgical, with debridement performed at subsequent visits if needed. BRONJ lesions healed completely in 2 patients (11%), healed partially in 5 (28%), remained stable in 5 (28%), and progressed in 6 (33%). Increased cumulative doses and long-term intravenous BP treatment is the most important risk factor for BRONJ development. Type of BP, diabetes, hypothyroidism, smoking, and prior dental extractions may play a role in BRONJ development.

**RARE PRESENTATION OF METASTASIZING MIXED TUMOR WITH INTRAORAL METASTASIS TO THE MAXILLA.** R. Gopalakrishnan, A. Pearson, D. Basi. U Minnesota, Minneapolis.

Metastasizing mixed tumors are very rare salivary gland neoplasms that are histologically benign but clinically malignant as they metastasize to distant sites. The parotid gland is by far the most common location of the primary tumor, and the most common sites of metastasis reported in the literature include bone, lung, and lymph nodes. We report an interesting case of metastasizing mixed tumor in a 36-year-old man who presented with a mass in the left maxillary buccal gingiva and alveolar mucosa in the area of teeth #13 and #14 21 years after removal of a pleomorphic adenoma from the left parotid gland. Imaging studies showed that the lesion also involved the alveolar bone. Histologic examination revealed a benign salivary gland neoplasm that was consistent with pleomorphic adenoma. Review of the medical history revealed that the patient had 2 recurrences of the primary tumor and 5 metastatic presentations before the current lesion. The patient’s current and past clinical and histologic presentations and work-ups are discussed, along with pertinent review of the literature. As far as known, this is one of few reports of metastasizing mixed tumor with an intraoral presentation of the metastasis.

**DIAGNOSTIC IMAGING FEATURES OF INTRAOSSEOUS MUCOEPIDERMID CARCINOMA.** K.C. Chan, M.J. Pharoah, L. Lee, I. Weinrib, B. Perez-Ordonez. U Toronto, Princess Margaret Hospital, Toronto, Ont.

Intraosseous mucoepidermoid carcinomas of the jaws are rare, comprising 2%-4% of all mucoepidermoid carcinomas. A review of the English-language literature revealed a paucity of publications detailing the radiographic features of intraosseous
mucopidermoid carcinoma, and no review of advanced imaging characteristics. The purpose of this study was to present the common diagnostic imaging characteristics of intraosseous mucopidermoid carcinoma seen in plain radiography and computed tomography (CT). Two observers reviewed and recorded the imaging characteristics seen in plain films and 3 complete CT studies of 4 cases of histologically confirmed intraosseous mucopidermoid carcinoma. In addition, in 1 case the histopathologic features displayed in a whole section through the resected specimen correlated with the radiographic features. The following 5 imaging features were found to be common to all cases: a well defined sclerotic periphery, the presence of amorphous sclerotic bone within the lesion, numerous loculations (majority <8 mm in diameter), lack of septae bordering some of the loculations, and expansion and perforation of the outer cortical plate with extension into surrounding soft tissues. Other characteristics included tooth displacement and root resorption. Some of these characteristics are shared with both desmoplastic ameloblastoma and glandular odontogenic cyst; similarities and differences are presented.


We report herein our experience with 39 basal cell adenocarcinomas (BCACs; 1993-2010) to further define the clinicopathologic features of this rare salivary gland malignancy. The mean age at presentation was 57.6 years, with no gender predilection. The most common sites were parotid gland (82.1%), submandibular gland (5.1%), and upper lip (5.1%); 22.8% of patients had a synchronous or asynchronous salivary gland tumor. One of these patients had Brooke-Spiegler syndrome. Four histologic subtypes were identified: membranous (41.0%), tubulotrabecular (23.1%), solid (20.5%), and cribriform (15.4%). All histologically tubulotrabecular tumors were low-to-intermediate nuclear grade; whereas 87.5% of solid and 43.8% of membranous variants were intermediate or high grade. Angiolymphatic invasion was seen in 20.5% of tumors. Perineural invasion was present in 33.3% of tumors. Of cases with associated normal salivary tissue, 25.8% exhibited precursor lesions, including intercalated duct hyperplasia, striated duct hyperplasia, and in 1 case eccrine duct hyperplasia. Patients presented with recurrent disease in 11.1% of cases (mean time to recurrence 65.8 months), all if which were cytologically intermediate or high grade. Two patients showed evidence of metastatic disease with sites including distal extremities (finger) and brain. Although BCACs are typically indolent, they can occasionally show high-grade histologic features and behave in an aggressive fashion. Membranous and solid tumors appear more aggressive than tubulotrabecular BCACs. Precursor lesions, such as intercalated and striated duct hyperplasia, are not infrequent.

THE INCREASED MUC1 EXPRESSION IN RECURRENT AND MALIGINATION OF SALIVARY GLAND PLEOMORPHIC ADENOMA. A.B. Soares, V.C. de Araujo, A. Altemani. São Leopoldo Mandic Institute and Research Center, State U Campinas, Brazil.

Background. Pleomorphic adenoma (PA) is the most common salivary gland tumor. Although classified as benign, it presents a tendency to recur (RPA) and a risk of malignant transformation. It has been suggested that MUC-1 plays a role in the progression of many tumors, and in the salivary gland it was indicated as a marker to predict RPA. The aim of this study was to evaluate the MUC-1 expression in different phases of the adenoma-to-carcinoma sequence.

Study design. Twenty-one cases of PA, 18 cases of RPA, 3 cases of RPA with focal transformation, and 11 cases of carcinoma ex pleomorphic adenoma were analyzed for MUC1 expression by immunohistochemical technique using the antibodies MUC1/DF3.

Results. There was a significant difference in MUC1 expression in all of the groups. Comparing nonrecurrent with recurrent tumors, MUC1 reactivity in RPA was stronger than in PA. In all of the different groups of carcinoma, MUC-1 expression was significantly higher in carcinoma than in RPA and PA.

Conclusion. This study shows that carcinoma cells overexpress MUC1 and that this molecule is associated with the malignant transformation of this tumor. In addition, this research confirmed that MUC1 is related to the recurrence of PA.


Background. Salivary gland tumors comprise a group of tumors with a complex and unclear process of tumorigenesis. Previously we have shown a significant overexpression of Akt and Mdm2 in these tumors. Akt coordinates many proteins within the cell. PTEN and NFkB may play important roles in the understanding of the activation of Akt pathway. PTEN negatively regulates the Akt/PI3K pathway, which is important for cell growth, proliferation, and survival. NFkB activation is responsible for direct transcription of over 180 known NFkβ target genes involved with survival and proliferation.

Objective. The aim of this study was to analyze the expression of PTEN and NFkβ proteins in salivary gland tumors. Thirty-eight cases of adenoid cystic carcinoma (ACC), 45 of pleomorphic adenoma (PA), and 13 of carcinoma ex pleomorphic adenoma (EXPA) were submitted to immunohistochemistry. Normal salivary gland (NGS) was used as control.

Results. Strong cytoplasmic and negative nuclear staining of NFkβ in almost all tumors was seen. Eight samples of PA and 1 EXPa showed low rates of nuclear staining. NGS showed variable cytoplasmic expression rates. PTEN stained the cytoplasm of all tumors and NGSs. Also, high rates of nuclear PTEN in all ACC and low rates in 3 EXPa were seen. NGS showed negative nuclear expression. Nuclear PTEN may be associated with other proteins blocking or inactivating tumor suppressors and its own function; therefore, in ACC PTEN may indicate an unexpected activity toward the classic PTEN pathway, and PTEN protein may also be associated with other proteins inactivating tumor suppressors.

Conclusion. This study strongly suggests that PTEN may be involved in tumor progression of ACC. On the other hand, cytoplasmic expression of NFkβ is probably not significant due to the similarity with NGS.