HEAD & NECK PATHOLOGY

Solitary Myofibroma Arising from Adult Mandible

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Myofibroma is a rare benign neoplasm of myofibroblastic cells and can occur as a solitary or multicentric form. The latter was renamed “infantile myofibromatosis” by Chung and Enzinger because of its multiplicity and typical age distribution (first decade of life) with predilection for the head and neck. However, solitary myofibroma of adult mandible is extremely rare, and only 4 cases have been reported so far. The case of 31-year-old women with a symptomless solitary myofibroma arising from adult mandible is reported here. To the best of our knowledge, this is the first report of solitary myofibroma arising from adult mandible in Korea.

Key Words: Myofibroma; Mandible; Adult

Unusual Metastatic Pattern of Human Papillomavirus-Related Squamous Cell Carcinoma: Report of 2 Cases with Literature Review

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It is well known that conventional squamous cell carcinoma (SCC) usually has metastatic behavior to regional lymph nodes first then systemic spread. Recent studies reported that human papillomavirus (HPV) positivity SCC tends to have a favorable outcome. The distant spread pattern of HPV-related SCC may be under recognized. We reported 2 cases of HPV-related SCC with unusual pattern of distant metastasis. A 55-year-old white male who had a high grade SCC arising in the base of tongue. Pathology reported a SCC with bilateral neck lymph node metastasis. No distant metastasis was found at time of initial diagnosis. Fourteen months later, a 2 cm firm subcutaneous mass was found in right anterior thigh. A 47-year-old white male had long term anal high grade HPV related dysplasia, eventually developed invasive SCC, which was excised. Thirteen months later, he presented an enlarged neck mass, otherwise no other suspicious lesions noted. Biopsy in thigh and neck mass revealed poorly differentiated SCC, morphologically similar to prior SCC. Both metastatic SCC cases were confirmed by immunostains for diffusely positivity of p63 and HPV (p16). The immunoprofile of 2 metastatic tumors were compared with their primary tumors as well. Although HPV positivity in SCC is regarded as a favorable prognostic indicator. The impact of HPV infection on the tumor behavior is little known. One should be aware of unusual distant spread pattern of HPV-related SCC, as we described 2 unexpected metastasis.

Key Words: Human papillomavirus DNA tests; Distant metastasis; Carcinoma, squamous cell; Cyclin-dependent kinase inhibitor p16

PLEOMORPHIC ADENOMA WITH EXUBERANT SQUAMOUS METAPLASIA AND KERATIN CYSTS MIMICKING SQUAMOUS CELL CARCINOMA IN MINOR SALIVARY GLAND

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Salivary gland tumors, the second most common neoplasm of the mouth after squamous cell carcinoma, account for a significant proportion of tumors of the oral and perioral regions. An unusual case of adenoma presented as a solitary intraoral palatine mass in a 32-year-old woman is reported here. The tumor was interpreted as an unusual pleomorphic adenoma because of the presence of exuberant squamous metaplasia, clinically mimicking squamous cell carcinoma. Moreover, the presence of cystic structures filled with keratinized material was also salient feature. Pleomorphic adenomas may occasionally display focal squamous metaplastic changes; when extensive, it presents the potential for misinterpretation of the histology as indicative of well-differentiated squamous cell carcinoma.

Key Words: Adenoma, pleomorphic; Squamous metaplasia; Epidermal cyst; Carcinoma, squamous cell; Salivary glands

JAW AND SINOSAL TUMORS: FIVE YEARS RETROSPECTIVE STUDY AND REVIEW OF LITERATURE

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Background: To study the incidence, mode of presentation and histopathological features of jaw and sino-nasal lesions in the surgical pathological material. Methods: Jaw and sino-nasal tumors biopsied or surgically excised over a period of five years diagnosed at B. P. Koirala Institute of Health Sciences and Civil Hospital Karachi. The histopathological records of these cases were analyzed to see the prevalence, common site, age of presentation and correlation between clinical and histopathological diagnosis. Results: In five years there were 135 jaw and sino-nasal tumor cases diagnosed representing 0.18% of all the surgical specimens received. Epithelial tumors outnumbered the non-epithelial tumors. Malignant tumors were seen predominantly in males. Benign lesions included squamous papilloma and inverted papillomas and angiofibroma. Squamous cell carcinoma was the commonest among malignant tumors. The second most malignant tumor was adenoid cystic carcinoma. Other rare types of malignant tumors included the variants of squamous cell carcinoma, malignant melanoma of the nose, glioma and neurofibroma, and neurofibromatosis. The commonest site was nasal cavity, followed by paranasal sinuses and external nose, infraorbital and jaw region. The age ranged from 12 to 70 years with pre-
Heterotopic Intestinal Cyst of the Submandibular Area: Report of a Case
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Heterotopic gastrointestinal cysts are rarely found in the oral cavity. Most of these cysts are lined with gastric mucosa and involve the tongue. There have been no reported heterotopic intestinal cysts of the submandibular gland that are completely lined with colonic mucosa. An 8-year-old girl presented with an enlarging swelling in the left submandibular area, and a 4-cm unilocular cyst was fully excised. The cyst was completely lined with colonic mucosa that was surrounded by a smooth muscle layer, and the lining cells were positive for CDX-2, an intestinal marker, indicating a high degree of differentiation. The pathogenesis remains unclear, but it may be related to the misplacement of embryonic rests within the oral cavity during early fetal development. Although heterotopic intestinal cysts rarely occur in the submandibular gland, they should be considered in the differential diagnosis of facial swellings in the pediatric population.

Key Words: Submandibular gland; Cysts; Heterotopia; Intestines

Early Squamous Cell Carcinoma of the Oral Tongue: Significance of the Margin Type
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Background: To evaluate the impact of margin sampling approach on local recurrence in patients with pT1-2pN0 squamous cell carcinoma of the oral tongue. Methods: Based on margin sampling, cases were grouped into group 1 (margins sampled from the glossectomy specimen only), group 2 (with revision of positive/close glossectomy margins), and group 3 (margins primarily sampled from the tumor bed). Results: Local recurrence rates were 8% (5/60), 20% (8/40), and 27% (7/26) in groups 1, 2, and 3, respectively. At 30 months, 89% of group 1 and 68% of group 2 patients were free of locoregional recurrence (p = 0.014). At 37 months, 89% of group 1 and 64% group 3 patients were free of local recurrence (p = 0.024). The only difference between the groups was the average distance from carcinoma to the closest margin (4, 1, and 2 mm for groups 1, 2, and 3, respectively; p < 0.001). While tumor bed margin status and other parameters (pattern of invasion, human papillomavirus status) did not correlate with local recurrence, glossectomy margin status did: 64%, 79%, and 93% of patients with positive, close (<3 mm), and negative (>3 mm) glossectomy margins, respectively, were free of local recurrence (at 37 months; p = 0.034). Conclusions: Margin status on the actual glossectomy specimen rather than that of separate tumor bed margin was prognostically relevant. Patients with revised margins, or margin status addressed primarily by tumor bed sampling had worse local control, likely due to the narrower initial resection.

Key Words: Margin; Carcinoma, squamous cell; Oral tongue; Human papillomavirus DNA tests; Cyclin-dependent kinase inhibitor p16

Adenocarcinoma Not Otherwise Specified of the Base of the Tongue: Relationship to Human Papillomavirus and Novel Actionable Genetic Changes
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The majority of human papillomavirus (HPV)-positive carcinomas of the oropharynx is squamous cell carcinoma. Recently, HPV was identified in a number of other non-squamous oropharyngeal carcinomas. Herein we report a case of adenocarcinoma of non-salivary origin and not otherwise specified, of a 70-year-old male non-smoker with a 2.8 cm base of tongue mass (cT2) and ipsilateral lymphadenopathy (cN2b) on computed tomography scan. Immunohistochemically, the adenocarcinoma was p63 negative and showed strong nuclear and cytoplasmic reactivity with p16 while synaptophysin, thyroid transcription factor, CDX-2, androgen receptor and prostate specific antigen were all negative. HPV positivity was shown by in situ hybridization. Anaplastic lymphoma kinase fluorescence in situ hybridization was negative. IonTorrent semiconductor sequencing analysis for 739 cancer-associated mutations in 46 actionable cancer genes was performed and PIK3CA exon 9 (p.E545K) and MET (p.E168D) mutations were identified. This is only the fourth instance of HPV-positive adenocarcinoma, not otherwise specified, of the base of tongue and the only case with extensive genetic testing.

Key Words: Human papillomavirus DNA tests; Cyclin-dependent kinase inhibitor p16; Adenocarcinoma; Base of tongue; Oropharynx

The Clinicopathologic Significance of the Epithelial Mesenchymal Transition in the Head and Neck Squamous Cell Carcinoma by Immunohistochemistry
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Background: In many studies, the epithelial-mesenchymal transition (EMT) related biomarkers were significantly correlated with prognostic factors. We assessed the correlation between the expression of the several biomarkers related with EMT and the clinicopathologic parameters in variable subsites of head and neck squamous cell carcinoma (HNSSC).

Methods: The paraffinized tissue samples from 146 patients who were treated by elective surgical resection for HNSSC were made in tissue microarray, and the expression of the E-cadherin, β-catenin, vimentin, and enhancer of zeste homolog 2 (EZH2) was evaluated by immunohistochemistry.

Results: The E-cadherin negative group showed more poorly differentiated cancer cells and low survival rate (p = 0.016 and p = 0.020) and the high expression of EZH2 was significantly correlated with the presence of nodal metastasis, extracapsular extension of metastatic tumor in lymph node, and involvement of resection margin in surgical resection (p = 0.024, p = 0.001, and p = 0.003, respectively). But, all these markers were not significantly associated with patient’s survival by the Kaplan-Meier survival curves and Cox regression analysis.

Conclusions: The expression of EZH2 is significantly related with prognostic factors of HNSSC such as lymph node metastasis, extracapsular extension and margin status.

Key Words: Carcinoma, squamous cell of head and neck; Epithelial-mesenchymal transition; Cadherins; Beta catenin, EZH2 protein

Correlation of Jun N-terminal Kinase Activation and CRTC1/MAML2 Translocation in Mucoepidermoid Carcinoma of Salivary Gland

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Background: Mucoepidermoid carcinoma (MEC) is the most common malignant tumor of the salivary gland. Approximately 50% of MEC is associated with t(11:19), resulting in fusion of transcriptional activator CRTC1-MAML2. We reported previously that activation of CRTC1/MAML2 translocation is 92%. The positive and negative predictive values for JNK activation to CRTC1/MAML2 translocation are 89% and 100%, respectively.

Results: We demonstrate for the first time the overall good correlation between activation of JNK and translocation of CRTC1/MAML2 in salivary gland MEC. IHC stains for activation JNK may provide an alternative approach for FISH detection of CRTC1/MAML2 translocation. Larger sample size and multi-institutional collaboration is needed to validate these findings.

Key Words: Carcinoma, mucoepidermoid; Salivary glands; CRTC/MAML2 translocation; JNK activation

Correlation of Jun N-terminal Kinase Activation and CRTC1/MAML2 Translocation in Mucoepidermoid Carcinoma of Salivary Gland

Kyu Ho Kim · Chang Hwan Choi · Lucia Kim · Suk Jin Choi · Jee Young Han · Joon Mee Kim · Young Chae Chu · In Suh Park · Joo Han Lim

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Background: Epithelial mesenchymal transition (EMT) has an important role in invasion and metastasis of tumor cells. EZH2 overexpression is also commonly associated with poor prognosis in a variety of tumor types. However, the exact role of EZH2 and its clinical significance in laryngeal cancer are not yet known. The purpose of this study is to evaluate the roles of EZH2 and other EMT associated proteins on progression and metastasis in locally advanced node-negative laryngeal cancer.

Methods: We analyzed the significance of these EMT associated protein expression in curatively resected (R0) laryngeal cancer patients as a prognostic marker. Total twenty-nine consecutive patients were included in our study. We used protein immunohistochemistry to evaluate EZH2, vimentin, E-cadherin expression on tissue microarray in duplicate. Also we retrospectively reviewed all medical records and tried to analyze the relationship between the expression of EMT markers and prognosis. The relationship between these protein expressions and survival was plotted on a Kaplan-Meier curve.

Results: EZH2 was expressed in 11 patients (37.9%). Recurrence rate was significantly higher in patients with positive EZH2 expression than that of patients with no expression (recurrence rate, 72.7% vs 33.3%; p = 0.039). Patients with a positive EZH2 expression showed a tendency of shorter their disease progression free survival (median progression free survival [PFS], 11.8 months) than did the patients without expression (median PFS, 23.9 months). However there was no statistical significance (p = 0.0892).

Conclusions: EZH2 overexpression showed a close correlation in recurrence rate and relapse free survival. Our findings suggest an important role of EZH2 in progression of laryngeal cancer.

Key Words: Epithelial-mesenchymal transition; EZH2; Immunohistochemistry; Laryngeal neoplasms

Bisphosphonate-Related Osteonecrosis of the Jaw: A Case Report
Adenomatoid Odontogenic Tumor in Mandible: A Case Report

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Adenomatoid odontogenic tumor is a relatively uncommon odontogenic tumor with slow and progressive growth. Most adenomatoid odontogenic tumor occurs in female and anterior maxilla. We experienced a case of adenomatoid odontogenic tumor with a few glandular structures arising in mandible. A 39-year-old woman presented a swelling on right mandibular border. Computed tomography revealed an osteolytic cystic lesion with attachment of root of impacted tooth in right mandibular border. Also noted was a central small pebble-like teolytic cystic lesion with attachment of root of impacted tooth in right mandible. Sequestrum was removed and parotid duct was seen to have a covering of soft tissue. Histopathology showed amorphous material reminiscent of enamel matrix. A few gland-like structures were noted with eosinophilic thick fibrous capsule. The lesion consisted of spindle-shaped epithelial cells with no osteocytes in the lacunae, bacterial colonies adjacent to necrotic bone, and pseudoepitheliomatous hyperplasia in the periphery of the necrotic bone. The squamous epithelial cells were negative for p53, and Ki-67 proliferative index was less than 1%.

Key Words: Bisphosphonate-associated osteonecrosis of the jaw; Osteomyelitis; Alendronate

Bisphosphonates are commonly prescribed for the treatment of osteoporosis and bone cancers. These drugs come in both intravenous and oral forms. Because these drugs have become more prevalent, there have been increased reports of bisphosphonate-related osteonecrosis of the jaws (BRONJ). We report a case of BRONJ in an 84-year-old woman. She had been taking Fosamax (alendronate) for 6 years for treatment of osteoporosis. The patient had a 6-month history of pain and suppuration on the left lower gingiva. Dental computed tomography showed 3.0×1.7 cm-sized osteolytic lesion at the left lower seventh tooth root. She underwent tooth extraction and sequestrectomy. Histopathology of the sequestrum showed acute inflammation, necrotic bones with no osteocytes in the lacunae, bacterial colonies adjacent to necrotic bone, and pseudoepitheliomatous hyperplasia in the periphery of the necrotic bone. The squamous epithelial cells were negative for p53, and Ki-67 proliferative index was less than 1%.

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Frequency and Type of Epidermal Growth Factor Receptor Mutation in Basaloid Squamous Cell Carcinoma of the Upper Aerodigestive Tract

Kyoung-Ja Cho · Sung-Min Chun · Se-Jin Jung · Jong-Lyel Roh · Seung-Ho Choi · Soon Yuhl Nam · Sang Yoon Kim · Sang Bae Kim

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Background: Recent reports on non-small cell lung cancer (NSCLC) that epidermal growth factor receptor (EGFR) mutation status predicts response to EGFR-tyrosine kinase inhibitor (TKI) treatment signifies the importance of molecular footprint of EGFR. The mass array system has emerged as a more sensitive and economical method of mutation typing than direct sequencing. Methods: Twenty-three cases of basaloid squamous cell carcinoma (BSCC) of the upper aerodigestive tract (8 hypopharynx, 7 esophagus, 3 oropharynx, 2 oral cavity, 1 larynx, 1 paranasal sinus, 1 external auditory canal) with diffuse EGFR positivity were subjected to mutation analysis. Briefly, genome DNA from formalin-fixed paraffin embedded blocks were run through ASAN Panel, which addresses 74 somatic mutations including 38 point and 36 indel mutations for EGFR, KRAS, BRAF, and PIK3CA genes. Amplified

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AP12-PP-0018

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AP12-PP-0016

Oct 3/4, CD24, and Nanog Expression in Oral Cancer: Effects on Response to Chemo-radiation

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Bisphosphonates are commonly prescribed for the treatment of osteoporosis and bone cancers. These drugs come in both intravenous and oral forms. Because these drugs have become more prevalent, there have been increased reports of bisphosphonate-related osteonecrosis of the jaws (BRONJ). We report a case of BRONJ in an 84-year-old woman. She had been taking Fosamax (alendronate) for 6 years for treatment of osteoporosis. The patient had a 6-month history of pain and suppuration on the left lower gingiva. Dental computed tomography showed 3.0×1.7 cm-sized osteolytic lesion at the left lower seventh tooth root. She underwent tooth extraction and sequestrectomy. Histopathology of the sequestrum showed acute inflammation, necrotic bones with no osteocytes in the lacunae, bacterial colonies adjacent to necrotic bone, and pseudoepitheliomatous hyperplasia in the periphery of the necrotic bone. The squamous epithelial cells were negative for p53, and Ki-67 proliferative index was less than 1%.

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polymerase chain reaction products in 8 separated multiplex fashion were treated with shrimp alkaline phosphatase, and followed by single base extension reaction using iPLEX-Pro kit from Sequenom with extension primers that hydridize immediately adjacent to the mutations. After incubation with resin for removing salt adductive, products were transferred to SpectroCHIP II for analysis using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. **Results:** Eight cases (35%) of BSCC were found to have substitution mutations or deletions in *EGFR* exon 18-21, including both sensitive (L858R, del19) and resistant types (T790M) to EGFR-TKI. Two cases showed *KRAS* or *PIK3CA* point mutation. **Conclusions:** The results confirmed the mismatch between EGFR expression and mutation status in BSCC, and the presence of various mutations like NSCLC. Tailoring EGFR-TKI therapy for a subset of BSCC patients is in prospect.

**Key Words:** Receptor, epidermal growth factor; Basaloid squamous cell carcinoma; Mutation; Mass array

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**Background:** Amplification of fibroblast growth factor receptor 1 (*FGFR1*) has been reported in squamous cell carcinoma of lung and oral cavity and may be a molecular target for therapy. However, little is known about clinical and demographics correlation of *FGFR1* amplification in tonsillar squamous cell carcinoma (TSCC). Moreover, human papillomavirus (HPV)-related TSCC has recently been characterized as a distinct subset with favorable prognosis. Therefore, we investigated the *FGFR1* amplification and HPV status in TSCC and analyzed the correlation between *FGFR1* amplification and clinical and demographics.

**Methods:** Eighty-nine cases of TSCC were selected and tissue microarray from formalin fixed paraffin embedded tumor tissue was constructed. HPV *in situ* hybridization and *FGFR1* fluorescence *in situ* hybridization were performed.

**Results:** Fourteen cases (15.7%) of 89 TSCC had *FGFR1* amplification and HPV was detected in 59 of 89 cases (66.3%) by *in situ* hybridization. *FGFR1* amplification status was not association among HPV *in situ* hybridization (p = 0.765) and clinical parameters including age, sex, TNM stage, smoking and alcohol history. Outcome was not significantly different between *FGFR1* amplified and non-amplified patients. Although *FGFR1* amplified patients (n = 4) in HPV *in situ* negative group (n = 30) had a tendency poorer overall survival than non-**FGFR1** amplified (n = 26), no statistical significance was identified (p = 0.150, log-rank).

**Conclusions:** *FGFR1* amplification is one of the pathogenesis in TSCC and could support new target for treatment regardless of HPV status. The lack of any specific clinical-demographic features that correlated with *FGFR1* amplification suggests that all TSCC patients should be tested for this genomic change.

**Key Words:** Receptor, fibroblast growth factor, type 1; Gene amplification; Human papillomavirus DNA tests; Carcinoma, squamous cell

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**Fibroblast Growth Factor Receptor 1 Amplification in Tonsillar Squamous Cell Carcinoma**

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Departments of Pathology, Medical Oncology, Radiation Oncology, and Head and Neck Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

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