#2- 4/21/2015 - 1:42 PM

RETROSPECTIVE ANALYSIS OF MEDICATION USE AND SYSTEMIC CONDITIONS IN 155 PATIENTS WITH BIOPSY PROVEN ORAL LICHEN PLANUS AND ORAL LICHENOID MUCOSITIS.

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INTRODUCTION: Many drugs have been reported as possible etiological factors for oral lichen planus (OLP) and oral lichenoid mucositis (OLM). This study was undertaken to further characterize the medication profile and medical history of patients with biopsy proven OLP or OLM in a tertiary referral clinic. MATERIALS AND METHODS: The UF College of Dentistry clinical record system was queried retrospectively from 2009-2014 for all patients with a biopsy proven diagnosis of OLP or OLM after IRB approval. Patients were excluded if they had concurrent dysplasia or carcinoma in the same biopsy site. Demographics, clinical parameters, systemic diseases, histological diagnosis, and direct immunofluorescence testing results were recorded for each patient. Medication categories such as antihypertensives, NSAIDS, etc. were recorded. These categories were based on their linkage with oral lichenoid disease in the literature. RESULTS: A total of 155 patients were included. The average age was 63.6 years. The majority were females (77%) and Caucasian (92%). Most cases were multifocal in nature and mixed (white/red) in appearance. The most common systemic conditions identified were hypertension (n=80, 51.6%), thyroid disease (n=52, 33.5%) followed by diabetes (n=26, 17.4%). The most common drugs comprising approximately one-third of the prescriptions were antihypertensives, followed by in descending order: NSAIDS, cholesterol lowering, psychiatric, and thyroid hormone replacements. Only 12.3% of the patients were not on any of the medication categories.CONCLUSIONS: Medication use is very common in patients with biopsy proven OPL/OLM. Although causation cannot be assessed in this study, the clinician should strongly investigate medication use as potential etiology in OLP/OLM patients.

#4- 4/21/2015 - 2:06 PM

CLEAR CELL CHANGES IN SALIVARY GLAND NEOPLASMS: A 20-YEAR RETROSPECTIVE STUDY

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Clear cells are observed histopathologically in both benign and malignant neoplasms but their presence in salivary gland tumors has not been quantitatively documented. With IRB approval, the archive of the University of Florida College of Dentistry oral pathology biopsy service was retrospectively searched from 1994-2014 for all benign and malignant salivary tumors. Epidemiological data, tumor location and duration, and type of tumor were recorded. A four reviewer panel examined the original slides. Reviewers stratified each case as 0 (no clear cells present), 1 (few to focal clear cells), 2 (moderate clear cells, less than 50%), and 3 (greater than 50% clear cells). A total of 535 cases were included; 48% of tumors displayed 0 clear cells (257/535), 31.4% (168/535) scored 1, 13.6% (73/535) scored 2, and 7% (37/535) scored 3. Of the 251 (47%) malignant neoplasms, 64% (160/251) demonstrated 0-1 clear cell change, while 36% (91/251) showed a score of 2-3. For the total 284 (53%) benign tumors, 93% (265/535) scored 0-1 and 7% (19/535) scored a 2-3 range. No statistical difference was noted for gender, age, or duration of time present in regards to presence or absence of clear cells. Statistically significant differences in clear cell presence were found between location groups (p= 0.001), between benign and malignant diagnosis (p=0.000), and between specific diagnostic groups (p=0.000). This study demonstrates the frequent presence of increased numbers of clear cells in oral salivary malignancies and highlights the importance of including malignant salivary gland tumors in the differential diagnoses when clear cell changes are present.

CRIBRIFORM ADENOCARCINOMA: A TUMOR OF MINOR SALIVARY GLAND ORGIN WITH DISTINCT IMMUNOHISTOCHEMICAL AND HISTOLOGIC FEATURES

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Cribriform adenocarcinoma of minor salivary gland (CATMSG) is a low grade malignant salivary gland tumor described by Skalova et al. This tumor occurs in the minor salivary glands of the oral cavity and has the potential to metastasize to cervical lymph nodes. The histomorphology of CATMSG is similar to that of papillary thyroid carcinoma in that both contain papillary structures and clear to vesicular nuclei with an open chromatin pattern. Other histological features seen are cribriform areas, tubular pattern and solid islands which show an artefactual splitting of the basal layer of cells. Cribriform, solid and tubular areas are commonly seen in other malignant salivary gland tumors such as adenoid cystic carcinoma (ACC) and lobular carcinoma (LC). The aim of this study was to assess whether tumors originally classified as Adenocarcinoma NOS (Adca,NOS), ACC and LC could be reclassified as CATMSG. Tumors diagnosed between 1992 and 2014 at Oral Pathology Laboratory, Inc (NYHQ) were selected. Each lesion was review by 3 pathologists to confirm the morphological features seen in CATMSG. After review, 11/79 Adca,NOS, 5/38 ACCs, and 5/23 LCs met the histological criteria of CATMSG. One case diagnosed as CATMSG in 2014 was used as a control and the following stains were completed: EMA, HBME-1, p16, and CAM 5.2. Eleven Adca,NOS, 2-ACC, and 5-LC underwent immunohistochemical (IHC) staining to support reclassification as CATMSG. Positive HMBE-1, p16 and CAM 5.2 staining along with negative staining for EMA were considered supportive of a diagnosis of CATMSG. 7- Adca,NOS, 0- ACC and 2 -LC fulfilled the IHC criteria. Based on strict histologic and ICH features, we were able to reclassify 9 tumors as CATMSG.

SPECTRUM OF ACINIC CELL CARCINOMA-LIKE MALIGNANCIES OF THE SALIVARY GLANDS

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Acinic cell carcinoma (ACC) is a rare salivary gland malignancy that represents up to 17% of salivary gland malignancies. Even though most cases exhibit a well-recognized histologic pattern, some cases may exhibit variable patterns & more than one pattern may be potentially present in a given tumor, making the diagnosis potentially challenging & adding to the difficulty in precise classification of ACC. A combination of basic histomorphological examination, selective immunohistochemical (IHC) & special stains, as well as molecular analysis may be collectively useful in differentiating ACC from other entities entertained in its differential diagnosis. A great deal of attention and effort have been recently devoted to differentiating ACC from a close mimicker; salivary mammary analogue secretory carcinoma (MASC) which lead to reclassifying some of the ACC into MASC following the establishment of characteristics balanced chromosomal translocation t (12; 15) (p13; q25) which results in fusion gene between the ETV6 gene on chromosome 12 & NTRK3 gene on chromosome 15in MASC. We further explored the role of IHC & molecular studies in differentiating ACC from MASC in 21 major salivary gland tumors that were originally diagnosed as ACC. IHC staining for all cases was performed for DOG-1 and Mammaglobin. All but 3 cases (14%) stained positive for DOG-1, in keeping with the original diagnosis of ACC, while the 3 cases stained positive for Mammaglobin; favoring a revised diagnosis of MASC. Nevertheless, the intensity of immunoreactivity varied between cases, and therefore correlation of the diagnosis with molecular studies was further carried out on all cases. The clinicopathologic features, differential diagnosis, management and follow-up data are also presented.

MELANOMA OF THE ORAL CAVITY: AN ANALYSIS OF 43 NEW CASES WITH EMPHASIS ON CLINICAL AND HISTOPATHOLOGIC CHARACTERISTICS

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BACKGROUND: Melanoma is a rare malignancy of the oral cavity that carries a very poor prognosis. We present 43 new cases of both primary and metastatic melanoma to the oral cavity. MATERIALS/METHODS: An IRB approved retrospective search for melanoma of the oral cavity was performed within the Oral Pathology Biopsy Service archives of the UF College of Dentistry (from 1994-2014) and the UK College of Dentistry (from 1997-2014). The original slides were reviewed. The location, age, race, gender, clinical impression, duration of lesion at biopsy, histologic diagnosis, and histologic features were recorded. Cases from the facial skin and those with an ambiguous diagnosis were excluded. RESULTS: A total of 23 females and 20 males with an average age of 64.6 (range 27-95) was found. The majority (86.5%) of the patients were Caucasian when race was known. Eleven of the cases were known metastases, and in 3 cases, a metastasis could not be ruled out. Twenty-five cases were from the maxilla, 12 were from the mandible, 4 from the tongue, 1 from buccal mucosa, and 1 from unspecified gingiva. The clinicians impressions varied from benign fibrous growths to high grade malignancies; 14 providers included melanoma in their differential, while 12 had considered only benign diagnoses. The histopathology varied widely among the cases; however three cell types predominated (often in combination): epithelioid cells (48.8%), spindle cells (44.2%), and oval cells (37.2%). An organoid pattern was seen in 30.2%, and only 60.5% of the cases had melanin pigmentation. CONCLUSION: Oral melanoma remains one of the most diverse clinical and histopathologic diagnoses. Further knowledge of this neoplasm will promote earlier diagnosis and lead to better outcomes for patients.

CONSTRUCTION OF A FLUORESCENT REPORTER GENE FOR THE ANALYSIS OF OGDH2 PROTEIN STABILITY IN HYPOXIA

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Hypoxia is a frequent feature of the tumor microenvironment and produces a variety of cellular metabolic adaptations. It was recently demonstrated that the ability of cancer cells to proliferate in hypoxia depends on critical regulatory changes in mitochondrial glutamine metabolism. This work also revealed that activation of the transcription factor HIF1α induces the ubiquitin ligase SIAH2 to target a key splice variant of the E1 subunit of the α-ketoglutarate dehydrogenase complex (OGDH2). The SIAH2-mediated proteolysis of OGDH2 redirects glutamine metabolism toward a reductive pathway, which generates citrate and lipids to support cellular proliferation. While OGDH2 has emerged as a critical factor in hypoxic tumor growth, the signaling pathways that regulate its destruction are poorly understood. To study OGDH2 regulation, we constructed a fluorescent reporter gene, combining a ruby red fluorescent gene with either wild type OGDH2 or a hypoxia-stable mutant of OGDH2 created by substituting an alanine for the ubiquitinated lysine residue. We stably expressed these fusion proteins in human colorectal and renal cell carcinoma cell lines. Fluorescence microscopy and Western Blot analysis confirmed the expression of the fusion protein, its mitochondrial localization, and the cytoplasmic distribution of the unmodified ruby protein. This fluorescent reporter protein will be used to follow OGDH2 protein cellular localization and stability in hypoxia. We are also preparing an shRNA screen to identify genes required for OGDH2 destruction. Regulation of hypoxic glutamine metabolism through OGDH2 may provide additional molecular targets for novel anticancer strategies.

#14- 4/21/2015 - 4:06 PM

THE IMPACT OF R740S MUTATION OF TCIRG1 ON DENTAL DEVELOPMENT IN OSTEOPETROTIC MICE

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Osteopetrosis is a rare disease characterized by sclerotic bone due to impaired osteoclast function. Over 50% of the cases of the most severe, autosomal recessive form of the disease are associated with a defect in the TCIRG1 gene encoding the a3 subunit of vacuolar-type H+-ATPase (V-ATPase). These patients have bone resorption defects, delayed tooth eruption and variable enamel defects; however, little is known about amelogenesis in this condition. We studied an osteopetrotic mouse with a point mutation (R740S) in the V-ATPase a3 subunit, resulting in severe osteopetrosis, hypocalcemia, and dental abnormalities. To elucidate the role of V-ATPases in amelogenesis, we investigated the cellular distribution of a3, spatiotemporal expression of enamel matrix proteins, and measured thickness and mineral content of the enamel in the R740S mouse. Micro CT analysis demonstrated a statistically significant decrease in mineralization and thickness of the enamel in the homozygote relative to the heterozygote and wild type mice. SEM analysis showed that enamel mineralization was slightly delayed in the homozygote, although minimal crystallization was noted in all genotypes. To assess spatiotemporal protein expression of the enamel proteins, mouse mandibles were collected on days 1, 5 and 9 postnatal, fixed, decalcified, and analyzed using immunohistochemistry (IHC). IHC demonstrated that amelogenin and amelotin expression patterns were similar among all genotypes. Expression of the a3 subunit was not detected in the ameloblasts, suggesting that the hypomineralized and hypoplastic enamel found in the R740S mouse may be due to underlying systemic conditions affecting the enamel microenvironment.

#16- 4/21/2015 - 4:30 PM

CHARACTERIZATION OF SPINDLE CELL/PLEOMORPHIC LIPOMA OF THE ORAL CAVITY: CLINICOPATHOLOGIC AND IMMUNOHISTOCHEMICAL ANALYSES

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Objective. Spindle cell/pleomorphic lipoma (SCPL) is a distinct histopathologic variant of lipoma and has been reported to rarely involve the oral cavity. The aim of our study was to analyze the clinical and immunohistochemical features of SCPL of the oral cavity. Methods. All oral cavity lipomas from two pathology services were reviewed (2004 to 2014) in order to identify cases of SCPL. The clinical and histologic features were reviewed. The following immunohistochemical stains were performed: CD34, S100, BCL2, AR, ER, PR, SMA, desmin, and STAT6. Immunopositivity was graded as 1+ (1-5%), 2+ (6-50%), 3+ (51-100%). Results. 56 SCPLs were identified from a total of 540 lipomas of the oral cavity in two pathology services. There was a male predilection (1.9:1). The mean age was 63 years (28-91 years). The most common subsites were: buccal mucosa (17), lip (15), and tongue (12). The most common clinical impressions provided were: fibroma (23) and lipoma (16). The mean tumor size was 1.3 cm (0.4-6.0 cm). Morphologically, all cases were well-demarcated, and contained adipocytes with intermingled fibrocellular to myxoid stroma, wiry/ropey collagen, and numerous mast cells. Nine cases were adipocyte poor, 7 cases had myxoid predominant stroma, and 2 cases had pleomorphic cells. Results of immunohistochemical stains are as follows: CD34 23/23 [20(3+), 3(2+), 100%], S100 0/23, BCL2 11/22 [10(3+), 1(2+), 50%], AR 13/22 [10(3+), 3(2+), 59%], ER 10/22 [5(3+), 5(2+), 45%], PR 2/22[1(3+), 1(2+), 9%], (SMA, desmin, and STAT6) 0/22. At least one hormone receptor was positive in 18/22 (81.8%) cases. Conclusion. SCPL is a distinct variant of lipoma, often with a fibroma-like clinical appearance. The frequent hormone receptor expression may be useful in supporting the diagnosis.

#18- 4/21/2015 - 4:54 PM

ENDOPLASMIC RETICULUM STRESS MAY CONTRIBUTE TO THE PATHOGENESIS OF PEMPHIGUS VULGARIS: AN IMMUNOHISTOCHEMICAL AND IN VITRO STUDY

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Objective: Pemphigus vulgaris is one of the most common types of autoimmune bullous mucocutaneous diseases, with a predilection for the oral mucosa. It is characterized by the presence of auto-antibodies against desmogleins (Dsg) -3 and -1, and recent evidence showed that the Endoplasmic Reticulum (ER) stress may be linked to the pathogenesis of the disease. The induction of ER stress in oral biopsy specimens and a human cell line was evaluated, testing whether anti-Dsg auto-antibodies are associated with Unfolded Protein Response (UPR) induction. Methods: The expression of the molecular chaperone GRP78/BiP was examined immunohistochemically, in 42 oral pemphigus vulgaris specimens. The possible induction of UPR was also tested by Western Blot, after exposing HaCaT (human keratinocyte cell line) to various amounts of anti-Dsg1 and anti-Dsg3 for 24 hours. Results: The immunohistochemical evaluation revealed localized expression of GRP78/BiP in the acantholytic epithelial cells in 73% of specimens ($p <0.05$, X2-test). In vitro, Western blot analysis showed that exposure to increasing amounts of anti-Dsg1, but not anti-Dsg3, incited the expression of chaperones GRP78/BiP, calnexin and the pro-apoptotic CHOP, thus indicating that anti-Dsg1 may induce ER stress. Conclusion: Our preliminary data showed that ER stress may be implicated in the complex pathogenesis of pemphigus vulgaris. Further research should be conducted to clarify the association between ER stress and the autoimmune process of the disease.

#20- 4/21/2015 - 5:18 PM

CLINICOPATHOLOGIC CHARACTERISTICS AND LONG TERM FOLLOW-UP OF SQUAMOUS CELL CARCINOMA OCCURING IN PATIENTS WITH PROLIFERTAIVE VERRUCOUS LEUKOPLAKIA: IMPACT ON PROGNOSIS AND COMPARISON WITH CONVENTIONAL SQUAMOUS CELL CARCINOMA

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OBJECTIVE Oral squamous cell carcinoma represents a heterogenous group of malignancies. The purpose of this study was to compare the clinicopathologic features of patients with squamous cell carcinoma associated with proliferative verrucous leukoplakia (p-scca) and those with conventional squamous cell carcinoma of the buccal mucosa, gingiva and palate (c-scca) and to explain their prognostic differences. METHODS We retrospectively reviewed 15 PVL patients with multiple cases of p-scca (n=48) who were treated and followed between 1990 and 2014. Histologic characteristics including the histologic risk score, clinical stage, margin status, and short/long term prognosis were compared to 49 patients with c-scca. Immunohistochemistry was performed using antibodies directed against p16, p53 and ki67. RESULTS The groups with p-scca and c-scca were comparable regarding age, gender, histologic grade ($p = 0.3119$), ki67 ($p=0.6431$) and p16 ($p=0.8633$) expression, surgical margin status and long-term survival ($p=0.12$). Significant differences included tumor thickness ($p = 0.0001$), histologic risk score ($p=0.0004$), p53 expression ($p=0.0043$), clinical stage ($p=0.0001$) and short term (4 year) survival ($p=0.03$). CONCLUSIONS Better prognostic factors and longer short term survival were associated with p-scca suggesting that p-scca may represent a less aggressive and distinct clinical entity which may influence the treatment choice for these patients. Further studies on a larger cohort of patients are recommended.

#22- 4/22/2015 - 7:12 AM

RAP1 INDUCES RAC1-MEDIATED CELL-MATRIX ADHESION IN ORAL CANCER.

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Loss of cell adhesion is required for invasion and progression of oral cancer (OC). Cadherins are proteins that hold epithelial cells together. The interaction between cadherins and integrins is vital to tumor progression. Rap1 is a ras-like protein, which we previously showed has an important role in growth of OC. Rac1 is an integrin-linked, ras-like protein that promotes cell migration. Objective: To investigate the extent to which loss of cell-cell adhesion in OC impacts Rap1 and cell-matrix adhesion via Rac1. Methods: To address this impact, cell adhesion was disrupted biochemically. The signaling cascade was investigated in vitro using siRNA and a chemical agonist in wild type and stably transfected human OC cell lines. Rap1 and Rac1 activation were evaluated by pull-down assays. Results: Loss of cell-cell adhesion correlated with inactivation of Rap1 and reduced cell-matrix adhesion. Using complementary stimulation and inactivation approaches, we showed that active GTP-bound Rap1 is required for cell-matrix adhesion. Moreover, this adhesion to the extracellular matrix is regulated by Rac1, which induces cytoskeletal changes. Conclusions: Taken together our findings support that Rap1 induces cell matrix adhesion via Rac1; given the role of Rac1 in cell migration, these findings may have implications for tumor progression. (This work was supported by NIDCR grants DE018512 and DE019513).

#24- 4/22/2015 - 7:36 AM

MINIMALLY INVASIVE DIAGNOSTIC ADJUNCTS FOR SURVEILLANCE OF ORAL POTENTIALLY MALIGNANT LESIONS IN FANCONI ANEMIA PATIENTS

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Fanconi anemia (FA) is a genetic disorder caused by mutations of DNA repair genes. The risk of oral cancer (OC) among FA patients is 800-times higher than in the general population, occurring at younger ages. Hematopoietic stem cell transplantation (HSCT) in FA patients further increases their risk for OC. FA patients cannot tolerate chemoradiation therapy; hence, early detection of OC is critical to improve their survival. Objective: To determine the efficacy of autofluorescence visualization (AFV) using VELscope and a programmable bio-nano-chip-based brush cytology test (pBNC-BT) for surveillance of OC in FA patients. Methods: Patients attending the Meeting for Adults with FA in March 2014 underwent a conventional oral examination, AFV and brush biopsy of lesions. Results: Twenty-eight FA patients (Age range: 18-61 yrs., M=32%, F=68%; smoking =7%; alcohol consumption =86%) participated in this study, of whom 13 patients have had HSCT. Regular visits to dentists/physicians for OS surveillance were reported by 86% of patients. Lesions are detected in 68% of these patients of which 84% of them revealed loss of fluorescence with AFV. The p-BNC-BT revealed significant differences in cytometric and biomarker measurements between cytobrush samples of a tongue lesion in one FA patient compared to site matched samples of healthy volunteers. Excisional biopsy of this FA patients lesion confirmed the presence of moderate dysplasia. Conclusion: Lesions mimicking OC and its precursors are more prevalent in FA patients than the general population. Use of pBNC-BT in combination with AFV increases the efficacy of conventional oral examination for long-term surveillance of OC in this high-risk patient population, while minimizing unwarranted scalpel biopsies.

#26- 4/22/2015 - 8:00 AM

PHOSPHATURIC MESENCHYMAL TUMOR-MIXED CONNECTIVE TISSUE VARIANT OF THE GINGIVA

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Objective: Oncogenic osteomalacia (OO) is a rare paraneoplastic syndrome that is linked to phosphaturic mesenchymal tumor (PMT). It occurs in adults and the most common location is the lower extremities, followed by head and neck. Clinical and laboratory presentation includes osteomalacia, multiple bone fractures and hypophosphatemia. Due to the rarity of the lesion we report a case of phosphaturic mesenchymal tumor-mixed connective tissue variant that has been present for 6 years in the gingiva. Clinical presentation: A 60 year old Chinese male was referred to the clinic with an asymptomatic slowly growing mass in lower lingual mandibular gingiva opposite to tooth #19. Medical evaluation failed to reveal a cause of the acquired osteomalacia, osteoporosis in the 1/3 radius, and lower levels of serum phosphate. Intervention and outcome: Incisional biopsy was performed and microscopic features included spindle cells, multinucleated giant cells, and calcifications embedded in a chondromyxoid matrix. In situ hybridization of FGF-23 showed a strong diffuse cytoplasmic expression. Surgical removal resulted in serum phosphate levels returning to normal within a few weeks. Conclusion: PMT is a neoplasm that is difficult to diagnose due to its rarity; therefore a comprehensive evaluation of medical, laboratory, radiographic and histological findings is crucial for a definitive diagnosis. OO should be considered in a healthy patient that suffers from hypophosphatemia, bone pain, and multiple fractures. Phosphate levels are mediated through tumor secretion of FGF-23 which is a useful diagnostic adjunct.

#28- 4/22/2015 - 8:36 AM

INTEROBSERVER VARIATION AMONG PATHOLOGISTS IN EVALUATING PERINEURAL INVASION FOR ORAL SQUAMOUS CELL CARCINOMA

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OBJECTIVE: The aims of this pilot study are as follows: 1) to assess variations among pathologists in evaluating perineural invasion (PNI) in oral squamous cell carcinoma (OSCC) 2) to survey histologic PNI criteria used by pathologists and how they came to adopt those criteria. METHODS: An electronic survey was sent to 7 board-certified oral and/or surgical pathologists. The participants were shown 15 photomicrographs and asked to rate whether PNI was present, absent, or uncertain. The survey also included questions regarding demographics, whether PNI criteria were taught during residency, criteria used by participants to evaluate PNI, how the participants developed their criteria, and agreement with proposed PNI definitions in the literature. RESULTS: All 7 pathologists completed the survey. The participants included 3 males and 4 females, with average age=55 yrs and average practice experience=27 yrs. Agreement between participants in rating PNI status for the provided images was moderate (º=.42, 95% CI .32 to .53). Three respondents indicated that they were taught PNI criteria during residency training. The basis for criteria currently used by participants included residency training (n=3), published literature (n=1), own experience/views (n=3), and consensus from tumor board discussions (n=1). Agreement regarding 6 previously published PNI definitions was slight (º =.19, 95% CI .02 to .37). CONCLUSIONS: Interobserver agreement in assessing PNI status was unsubstantial. Our results suggest that more widely accepted, objective, and reproducible criteria are needed for evaluating PNI in OSCC. Future studies with more participants will help formulate an improved definition, with increased reproducibility, for clinical outcomes validation.

DELINEATION OF THE MOLECULAR CHARACTERISTICS OF SO-CALLED JUVENILE GINGIVAL KERATOACANTHOMAS (GKA) OR JUVENILE GINGIVAL PSEUDOEPITHELIOMATOUS HYPERPLASIA (GPEH) BY MICROARRAYS AND PROBABLE IMPLICATION OF HPV 11

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Background: Previously, we reported that GKA or GPEH that appear indistinguishable from reported cases of juvenile gingival squamous cell carcinoma (SCC), feature, by multiplex qRT-PCR, a gene expression pattern more similar to cutaneous SCC than PEH. Although this method supports the diagnosis of SCC, such lesions, based on their clinicopathologic features and behavior, resemble closely KA. KA differs significantly from SCC as shown by microarrays. Also, there is known association of KA with HPV. Aim: 1) To compare GKA with KA and SCC by microarrays and 2) to investigate the presence of HPV by PCR. Materials and methods: We have collected the clinicopathologic data of six GKA (4 males & 2 females, ages 5-17 years; 4 maxilla, 2 mandible). Five of them were suitable for microarray evaluation using the Affymetrix U133plus2.0 array. The HPV status of three cases was investigated by PCR. Results: GKA clustered more closely with KA and were separate from SCC thus suggesting that GKA and KA are distinct from SCC. The gene numbers identified to be differentially expressed were as follows: Gingival KA vs. KA: 531; GKA vs. SCC 5,431; KA vs. SCC 8,299 ($p<0.01$ with at least 2.5 fold change in gene expression). The latter two comparisons identified many more differentially expressed genes than the first comparison, suggesting that GKA and KA are distinct from SCC and that GKA is more similar to KA. HPV PCR disclosed apparent presence of HPV11 in 2 of the three cases studied. Conclusions: Since the term GKA may not be appropriate, a working designation suggested is inverted gingival acanthoma, a tumor with a molecular profile close to KA and probably related to HPV 11. This lesion should be considered in appropriate cases to avoid unnecessary radical treatment in such patients.