Oral Melanoacanthoma: A series of 33 cases and Review of the Literature.

Monday, 24th May - 08:00: Oral Presentations - Oral (Student/Resident) - Abstract ID: 28

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Background: Oral Melanoacanthoma (OM) is an unusual, likely reactive heavily pigmented, benign epithelial proliferation. OM often grows rapidly mimicking melanoma and leading to anxiety for both the patient and the clinician. We present a large series of OM including demographics, description of clinical appearance and characteristics, histology, and literature review. To the best of our knowledge, this is the largest series of OM reported to date. **Materials & Methods**: Following IRB approval, OM cases from the University of Florida Oral Pathology Biopsy Service archives (1998-2020) were included. Demographics and clinical features were collected and slides were reviewed. **Results**: 33 cases were included with a mean age of 38 years, female: male ratio of 2.6:1. The most common location was buccal mucosa (n = 16, 48.48%), followed by palate (n = 11, 33.33%), tongue and labial mucosa (n = 2 each, 6.06%), maxillary and mandibular gingiva (n = 1 each, 3.03%). Most lesions are dark black/brown, and often described as macular in nature. Duration ranged from one week to twelve months, and all cases were asymptomatic. The clinical impression in the majority of cases were that of a benign melanotic lesion. Ethnicity was only documented in 6/33 cases, of which five cases were African American and one was Caucasian. Histomorphologically, majority of cases (n=27, 81.8%) were hyperplastic/acanthotic, while atrophic epithelium cases were (n=4, 12.1%) and less commonly, spongiotic epithelium cases were (n=2, 6.06%). **Conclusion**: The findings of this study are consistent with those in the literature concerning demographics and clinical presentation. Histologically, presence of dendritic melanocytes extending into the spinous cell layer along with acanthosis of the spinous cell layer is diagnostic for OM when combined with the clinical presentation. However, it is important to add cases of OM to the literature so clinicians can be more aware of this lesion.

Post-radiation Osteosarcomas of the Jaws and a Review of the Literature

Monday, 24th May - 08:12: Oral Presentations - Oral (Student/Resident) - Abstract ID: 30

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Patients with a primary malignancy have a 1.29 times increased risk for developing a second malignancy compared to people with no history of malignancy. Radiation is an effective treatment for malignancies but is also known to induce tumor formation. The most common radiation induced sarcomas (RIS) include fibrosarcoma, chondrosarcoma, malignant fibrous histiocytoma and osteosarcoma. Radiation induced sarcomas of the head and neck are rare and are associated with poor long-term prognosis. The most common sites in the head and neck are the paranasal sinuses and nasal cavity, neck and mandible. Cahan's criteria for diagnosis of radiation induced sarcomas include history of radiation, latency period of several years, occurrence of sarcoma in the field of irradiation, and histologic confirmation. An approximate dose of 30Gy is known to induce RIS. A latency period of 10-12 years is supported by the literature. Between the years of 1986 to 2020 the Oral Pathology Lab at New York Presbyterian Queens diagnosed 29 cases of osteosarcoma, 10 cases of chondrosarcoma, and 9 cases of MFH. Only 6 of the 48 sarcoma cases were radiation induced and all of them were osteosarcomas. The mean age of the 6 osteosarcomas was 52.83 years. All our cases were in males. Based on past medical history 5 of the cases received radiation for squamous cell carcinoma and 1 for Hodgkin Lymphoma. Of the 4 cases with documented radiation timelines, a mean latency period of 11.87 years was identified. The submitting surgeons suspected malignancy in 5 cases based on clinical appearance. The literature states RIS usually occurs in bone, however, 5 of our cases occurred in soft tissue within the radiation field. Histologically, cases showed malignant spindle cells producing osteoid matrix except case 1 in which the tumor cells embedded in eosinophilic hyalinized stroma demonstrated SATB2 nuclear expression, supporting osseous differentiation.

CHANGING TRENDS IN BENIGN HUMAN PAPILLOMA VIRUS (HPV) RELATED EPITHELIAL NEOPLASMS OF THE ORAL CAVITY: 1995-2015

Monday, 24th May - 08:24: Oral Presentations - Oral (Student/Resident) - Abstract ID: 32

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Introduction: HPV-related benign papillary epithelial neoplasms are common lesions affecting any region of the oral cavity. This study evaluated the trends in frequency, location, and demographics of these lesions over 20 years. **Materials and Methods:** Following IRB approval, the archives of UF Oral Pathology Biopsy Service between 1995-2015 were queried. Squamous papilloma, verruca vulgaris, and viral papilloma/condyloma were included. Extrao- ral locations, inconclusive diagnoses, or syndrome-related HPV lesions (Heck disease) were excluded. Age, gender, location, clinical presentation, and diagnoses were recorded. Data from one calendar year per 5-year span was assessed including the years 1995, 2000, 2005, 2010, and 2015. **Results:** A total of 1458 cases were identified over the total 5 calendar years assessed. Papilloma as a percentage of total biopsies per year was as follows: 1995 (2.6%), 2000 (3.3%), 2005 (3.6%), 2010 (4%) and 2015 (4.5%), representing a 73% (1.9x) percentage increase. Males (56%) were affected more commonly; however, in patients under 19 years, a female predominance was observed. The overall percentage of lesions in females increased by 30.6% over the time frame. Mean age was 54 years (range 1-93 years) and increased by 10 years over time. About 1.1% of patients had multifocal lesions and 0.2% had a recurrence. In descending order of frequency, tongue, soft palate, and mandibular gingiva were most involved. Maxillary gingiva and lower lip were the most common locations in patients under 19. Location varied over time with the biggest increase noted on the gingiva. Squamous papilloma was the most common histologic variant (93.6%). **Conclusion:** The incidence of benign HPV-related oral lesions increased substantially over the 2 decades studied. Other trends noted included increase in the following: average age of patients, female involvement, and gingival location. Our results likely indicate an overall increase in the prevalence of benign oral HPV lesions in our population.

Osteosarcoma of the Jaws: A report of 23 cases and a review of the literature

Monday, 24th May - 08:36: Oral Presentations - Oral (Student/Resident) - Abstract ID: 36

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Osteosarcoma of the jaws (OSJ) comprise 6% of total cases of osteosarcoma. With the goal of better characterizing these tumors, we reviewed the files at the Oral Pathology Lab, NYPQ from 1984-2021 and identified 23 cases of OSJ. Of the 23 cases, a male predilection (56.5%) was identified with peak ages occurring in the 3rd (22%) and 6th (26%) decades. Seventeen cases were intramedullary, 6 cases in the maxilla and 11 in the mandible. One maxillary and 2 mandibular lesions were described as gingival lesions attached to the bone, but medullary or periosteal origin could not be determined. Three lesions were reported as gingival soft tissue masses. Intramedullary OS demonstrated a mandibular (64.7%) predilection with most occurring posteriorly (81.8%).

Clinical impressions ranged from benign to malignant. Paresthesia (8.7%), pain (13.0%) and bony swelling (43.5%) were the most common presenting features. Four cases had been previously treated by either endodontic therapy, extraction or incision and drainage. Radiographs were not retrievable for all cases, but 3 cases were described as radiolucent, 1 as radiopaque and 1 with calcifications.

Histologic subtypes included osteoblastic (15), chondroblastic (7), and fibroblastic (1). The osteoblastic OS had a male predilection (60.0%), while the chondroblastic OS had a female (57%) predilection. The fibroblastic OS occurred in a male. The osteoblastic OS age range spanned the 3rd-8th decade with relatively equal distribution. The chondroblastic OS spanned the 2nd-6thdecade with a peak in the 6th decade. The fibroblastic OS occurred in the 1st decade. Only the osteoblastic OS had clinical presentations of pain and/or paresthesia.

OSJ accounts for approximately 1% of all head and neck malignancies but was not included in the differential diagnosis on first presentation of 22 of our 23 cases. Therefore, despite their rarity, we emphasize the importance for clinicians to consider OSJ in their differential diagnosis.

HISTOPATHOLOGIC FEATURES AS STRONG PREDICTOR OF SYNDROMIC ODONTOGENIC KERATOCYSTS

Monday, 24th May - 08:48: Oral Presentations - Oral (Student/Resident) - Abstract ID: 48

Dr. Saja Alramadhan (University of), Dr. Sarah Fitzpatrick (University of Florida), Dr. Indraneel Bhattacharyya (University of Florida), Dr. Donald Cohen (University of Florida), Dr. Mohammed N. Islam (University of Florida)

Introduction: Odontogenic keratocyst (OKC) represents approximately 11% of all odontogenic cysts and may be an early sign of Nevoid Basal Cell Carcinoma syndrome (NBCCS). We aim to identify histologic variations in syndromic OKC in patients under 30 years of age that correlate with the protein patched homolog-1 (PTCH-1) immunohistochemical (IHC) staining.

Materials and Methods: An IRB approved retrospective search of the UF Oral Pathology biopsy service database between 1994-2020 was performed for OKC diagnosed in patients under 30. Demographics, medical history, and histology of all cases were reviewed to confirm diagnosis. PTCH-1 IHC staining was performed on selected tissue samples demonstrating our proposed histologic features.

Results: A total of 554 OKC in patients under 30 were identified. Out of these, 33 OKC from confirmed cases of NBCCS were evaluated as the control group to establish microscopic criteria unique for syndromic OKC. The most prominent features include a variably thickened cystic lining with rete ridges formation, papillary projections, multilayer vacuolization within the lining, scant parakeratin, minimal corrugation, and full thickness hyperchromasia. The study group included 521 patients with no known history of NBCCS. Thirty-four percent of the study group matched the histologic criteria for a syndromic OKC diagnosis. IHC staining intensity scores of 0,1,2,3, with 3 being the strongest transepithelial staining pattern was noted in 8 of 10 stained cases from the control group and in 4 of 36 from the study group.

Conclusion: In this study, we report unique histological features that help discriminate syndromic OKC from sporadic ones. These features correlated well with relatively significant transepithelial PTCH-1 staining and hence may be used as a predictor of NBCCS in routine microscopy. PTCH-1 IHC reactivity in sporadic versus syndromic OKC is not well studied. Future large multicentric studies may be helpful in early and reliable identification of syndromic OKC.

Dysplastic Lesions of the Gingiva: Prevalence and Risk Factors Including Human Papillomavirus (HPV) Infection

Monday, 24th May - 09:00: Oral Presentations - Oral (Student/Resident) - Abstract ID: 50

Dr. Austin Belknap (University of Florida), Dr. Indraneel Bhattacharyya (University of Florida), Dr. Donald Cohen (University of Florida), Dr. Mohammed N. Islam (University of Florida), Dr. Sarah Fitzpatrick (University of Florida)

Background: Verrucous gingival lesions are common within the spectrum of proliferative verrucous leukoplakia (PVL), and the gingiva is not an unusual location for oral carcinoma. However, non-PVL associated dysplastic gingival lesions appear to be less common and may not progress directly to malignancy. In addition, it appears HPV likely plays a limited etiologic role in any form of dysplasia of the gingiva. **Materials and Methods**: Following IRB approval, all "dysplasia" cases between 2009-2019 were identified from the archives of the University of Florida Oral Pathology Biopsy Service. Exclusion criteria included verrucous lesions, lesions from multiple sites compatible with PVL, and cases diagnosed as mild atypia/dysplasia. The remaining gingival dysplasia cases were evaluated for age, gender, contributory history, clinical appearance/impression, symptoms, duration, and p16INK4a immunohistochemistry (IHC) results. **Results**: A total of 72 biopsies were included in our database from 54 patients. The mean age was 70.3 years (range of 27 - 90), with a female: male ratio of 1.4:1. 69.4% (n=50) were located on the posterior gingiva and 62.5% (n=45) the mandibular gingiva. Reported contributing histories included smoking (n=9, 12.5%), previous oral dysplasia (n=9, 12.5%), or oral cavity malignancy (n=24, 33.3%). The two most common clinical impressions were leukoplakia (n=16, 16.7%) and carcinoma (n=18, 25%). Twenty-five of the 72 cases (34.7%) were symptomatic with pain, swelling and/or bleeding. The most recent biopsy from 32 of the patients was low-grade dysplasia, 34 had high-grade dysplasia, and 6 koilocytic dysplasia. Only 4 of 6 koilocytic dysplasia cases were positive for p16, with no low-grade or high-grade lesions demonstrating positivity. **Conclusion**: This study confirms that p16 expression is rarely present in dysplastic lesions of the gingiva, unless koilocytic dysplasia is also present.

IMMUNOHISTOCHEMICAL ANALYSIS OF INFLAMMATORY RESPONSE IN MINOR SALIVARY GLAND BIOPSY AMONG PEDIATRIC PATIENTS WITH SJOGREN SYNDROME

Monday, 24th May - 09:12: Oral Presentations - Oral (Student/Resident) - Abstract ID: 54

Dr. Maram Bawazir (University of Florida), Dr. Seunghee Cha (University of Florida), Dr. Akaluck Thatayatikom (University of Florida), Dr. Sarah Fitzpatrick (University of Florida), Dr. Mohammed N. Islam (University of Florida), Dr. Donald Cohen (University of Florida), Dr. Indraneel Bhattacharyya (University of Florida)

Introduction: Sjogren syndrome (SS) is a chronic autoimmune rheumatic disease characterized by lymphocytic infiltration of exocrine glands and other organs. The spectrum of clinical manifestations suggests that SS clinical phenotype in children is more heterogeneous than that in adults. The objective of this study was to perform histopathological and immunohistochemical analysis on labial minor salivary gland (LMSG) biopsy in pediatric SS (PSS). **Methods:** An IRB approved retrospective chart review encompassing years from 2018-2020, of the University of Florida Oral Pathology Biopsy Service and the Center for Orphaned Autoimmune Disorders, was performed. The inclusion criteria encompassed patients with LMSG biopsy suggestive of SS (positive focus score ≥ 4), and age under 18. Demographics, clinical data, laboratory test results, and microscopic diagnoses/slides were reviewed. Immunohistochemical staining with antibodies specific for CD4, CD8, CD20, CD27, FOXP3, and IL-17 were performed. Staining intensity/positivity was calculated with Aperio ImageScope, positive pixel count software. **Results:** Ten cases were included. The mean age was 14.3 years old (range 9-18) with 1:1 female to male ratio. Five patients reported dry mouth, and six reported dry eyes. Of ten patients, 70% of the patients were positive for anti-SSA, and 50% were positive for anti-SSB. Positive ANA was seen in nine patients. All biopsies demonstrated positive focal lymphocytic sialadenitis ranging from 6 to 17 foci per 4 mm^2. A predominance of CD4+T cells over CD8+T cells and CD20+B cells were noted in all biopsies. FoxP3+ regulatory T cells showed minimal inflammatory cell positivity with mean of 0.2%. The memory CD27+ B cells were almost equally expressed as CD4 with mean of 16.2% and 14.1% respectively.IL-17 positivity was diffuse in the stromal/glandular staining, which prevented a proper assessment with the pixel algorithm. **Conclusions:** LMSG infiltrates in PSS consist predominately of helper-T cells and memory-B cells with few suppressive regulatory-T cells.

Stromal inflammatory subtypes of oral squamous cell carcinoma correlate with patient clinical characteristics, demographics and gene expression.

Monday, 24th May - 09:24: Oral Presentations - Oral (Student/Resident) - Abstract ID: 59

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Introduction: Oral squamous cell carcinoma (OSCC) is the most common oral malignancy displaying significant mortality and morbidity. The current OSCC grading systems exclusively describe the tumor differentiation, and share limited morphologic characterization of the stroma. Herein, we present a comprehensive microscopic analysis of the OSCC stromal inflammation and its relation with clinical features, demographics and gene expression of these patients.

Materials and Methods:87 completely excised OSCC tissues were prospectively collected. OSCC microenvironment was characterized according to the immune phenotype, the degree of desmoplasia and the extent and localization of inflammation. Statistical correlations between the tumor stroma and the patients' characteristics were carried out using GraphPad Prism. KEGG pathway analysis of representative PanCancer IO 360™data was also investigated using nSolver software.

Results: Inflamed tumors were more commonly encountered (49 cases) compared with non-inflamed OSCC (31 immune-excluded and 7 immune-deserted). Peritumoral fibrosis (36 tumors) correlated with male gender (p=0.0043), smoking (p=0.0455), alcohol consumption (p=0.0044), increased tumor size (p=0.0054) and stage (p=0.002) while a peritumoral inflammation (60 cases) was mainly seen in females (p=0.0105), non-drinkers (p=0.0329), and was associated with decreased size (p=0.0044). No association between stromal characteristics and tumor grade was seen. Pathway analysis showed differential gene expression between triplicates of inflamed and immune-excluded tumors in cancer pathways and chemokine or cytokine signaling.

Conclusions: Our work describes the relation of carcinogens (alcohol and tobacco) with distinct stromal phenotypes in oral cancer. Additionally, the correlation with tumor size and stage complements previous work indicating a worst biologic behavior in "cold" tumors. In addition, the underlying molecular pathways that can be implicated in different stromal phenotypes are highlighted. Collectively, these findings in addition to the indications that the microenvironment shares microscopic features independent of the tumor grade highlight the necessity of their incorporation into future grading systems of OSCC.

IDENTIFICATION OF SECRETORY CARCINOMA IN ARCHIVAL MATERIAL BY HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL METHODS WITH MOLECULAR PROFILING OF ETV6 AND RET ON ALTERNATIVELY DIAGNOSED SALIVARY GLAND TUMORS

Monday, 24th May - 09:36: Oral Presentations - Oral (Student/Resident) - Abstract ID: 60

Dr. Shankar Venkat (University of Florida College of Dentistry), Dr. Sarah Fitzpatrick (University of Florida College of Dentistry), Dr. Donald Cohen (University of Florida), Dr. Mohammed N. Islam (University of Florida), Dr. Indraneel Bhattacharyya (University of Florida)

Introduction: Secretory carcinomas (SC) of minor and major salivary gland (SG) are rare neoplasms that demon- strate microscopic overlap with acinic cell carcinomas (ACC), adenocarcinoma NOS (AdNOS), and mucoepidermoid carcinomas (MEC) respectively. Recently alternative translocations of ETV6-RET gene locus have been recognized in a small group of SC. This study aims to identify previously undiagnosed SC, from the archival cases of tumors signed out as other salivary malignancies and identify the novel ETV6 and RET genes by Fluorescence in situ hybridization (FISH). **Materials and Methods**: We performed a retrospective search of ACC, AdNOS and MEC within the annals of the UF, Oral Pathology Biopsy service from 2000-2020. Inclusion criterion using histopathological characteristics of SC were created. A total of 205 cases encompassing ACC, AdNOS and MEC were retrieved. All cases were screened with established histologic criteria and were stained (IHC) with S100 and mammaglobin. FISH was performed on one case with sufficient tissue for testing to evaluate the presence of ETV6-RET fusion. **Results**: Ten out of 205 cases met the histologic inclusion criteria. Five out of these ten cases were positive for S100 and mammaglobin confirming the diagnosis of SC. These cases were previously diagnosed as AdNOS (n=2), ACC (n=2) and MEC (n=1) respectively. Most of the SC in this series were seen around the 5^{th} decade (mean age = 55.4) and demonstrated a slight male predilection. (71.4%). Buccal mucosa was the most affected site (60%), followed by hard palate and soft palate (40%). A single break apart probe of both ETV6 translocation and chromosomal deletion of RET was estab- lished in the tested case. **Conclusion**: SC is a recently accepted salivary gland neoplasm. Our study strengthens the understanding of this entity by assessing the histopathological features of SC and identifying a new subset of ETV6 and RET genes.

The Impact of Race on C-MYC Expression and Resulting Prognostic Implications in Head and Neck Squamous Cell Carcinoma

Monday, 24th May - 09:48: Oral Presentations - Oral (Student/Resident) - Abstract ID: 69

Dr. Austin Shackelford (Columbia University School of Dental Medicine), Dr. Fatemeh Momen-Heravi (Columbia University School of Dental Medicine), Dr. Sunil Dubey (Columbia University School of Dental Medicine), Ms. Nadia Mezghani (Columbia University School of Dental Medicine), Dr. Alison Taylor (Columbia University Medical Center), Ms. Alexandria Yao (Columbia College), Dr. Angela Yoon (Columbia University School of Dental Medicine), Dr. Elizabeth Philipone (Columbia University School of Dental Medicine)

Background: Epidemiological data identifies race-based disparities in Black patients for head and neck squamous carcinoma (HNSCC) screening, detection, treatment, and survival. Although socioeconomic and environmental factors play a role in the existing racial disparities, HNSCC incidence and survival rates in the Black population cannot be attributed to these factors alone. Analyzing the molecular profiles of HNSCC tumors has the potential to help elucidate the mechanisms behind these disparities. The overexpression of the proto-oncogene C-MYC across racial demographics is of particular interest in this study given its association with poor outcomes in HNSCC.

Materials and Methods: To investigate the effect of race on survival of head and neck cancer, we examined HNSCC samples from 49 Black and 446 white patients in The Cancer Genome Atlas (TCGA). We used cox proportional hazard models and Kaplan Meier curves to identify the effect of race on HNSCC survival outcome. We then characterized the extent to which molecular alterations in Black patients impact their clinical outcomes.

Results: We found that Black patients lived significantly less disease-free months and had a poorer overall survival than white patients. Black patients showed a higher frequency of human papillomavirus (HPV)-negative than HPV-positive tumors compared to white patients. Black patients were found to suffer higher rates of metastasis and more aggressive lymph node involvement. Lastly, we found a significant enrichment of MYC signaling and amplifications in the tumors of Black patients compared to white patients.

Conclusions: This project uncovers novel data toward gaining an understanding of the racial disparities in HNSCC and advances the research aimed at eliminating these disparities. Unique tumor mutations and molecular signa- tures such as C-MYC could be used for more targeted, individualized screening, diagnostic, and treatment modalitiesto reduce outcome disparities in the Black population.

Oncocytic variant of mucoepidermoid carcinoma – A report of two cases and review of histopathology, immunohistochemistry, and molecular profiling

Monday, 24th May - 10:00: Oral Presentations - Oral (Student/Resident) - Abstract ID: 87

Dr. Madhu Shrestha (Texas), Dr. Haiying Zhang (Baylor University Medical Center, Baylor Scott & White Health), Dr. Daniel A Gehlbach (Methodist Dallas Medical Center), Dr. Victoria Woo (Texas)

Oncocytic changes have been described in approximately 10% of salivary gland tumors. It has been associated with a variety of benign and malignant tumors such as Warthin tumor, cystadenoma, pleomorphic adenoma, polymorphous adenocarcinoma, adenoid cystic carcinoma, and mucoepidermoid carcinoma (MEC), among others. MEC is the most common salivary gland malignancy and exhibits various histological patterns. Oncocytic MEC (OMEC) is a rare variant characterized by a predominant oncocytic cell population. Herein we present two challenging cases of OMECs. The first case was of a 63-year-old male with a mixed cystic to solid lesion in the superficial parotid gland. The lesion had ill-defined margins and no internal calcifications. The initial radiographic impression was that of a pleomorphic adenoma. The second case was that of a 67-year-old male with a parotid gland mass. Histologic ex-amination of both cases showed extensive areas of oncocytic differentiation with scattered sebaceous and mucous cells. Immunohistochemical analysis showed the neoplastic population to be positive for AE1/AE3, p63, and muci- carmine in the first case and p40 and mucicarmine in the second case. A diagnosis of low-grade mucoepidermoid carcinoma, oncocytic variant, was rendered in both cases. The first case was further analyzed for *MAML2*/*CRTC1* rearrangement by FISH and found to be positive. Differentiating between salivary gland neoplasms with oncocytic changes can be challenging due to significant histologic overlap. Ancillary studies to include immunostains and molecular testing can be useful in establishing a definitive diagnosis.

Mutation in Sodium Channel Gene SCN9A Causing Congenital Insensitivity to Pain Disorder, initially presenting with Riga-Fede ulcerations of the tongue.

Monday, 24th May - 10:12: Oral Presentations - Oral (Regular) - Abstract ID: 15

Dr. Kathleen Schultz (Department of Dental Medicine, Divisions of Oral and Maxillofacial Pathology and Pediatric Dentistry, Zucker School of Medicine at Hofstra/Northwell Health), Dr. Laura Pisani (Department of Medical Genetics, Zucker School of Medicine at Hofstra/Northwell Health), Dr. Matthew Taylor (Department of Dental Medicine, Division of Pediatric Dentistry, Zucker School of Medicine at Hofstra/Northwell Health), Dr. William Kotkin (Department of Dental Medicine, Division of Pediatric Dentistry, Zucker School of Medicine at Hofstra/Northwell Health)

Introduction:
Oral factitial injury caused by repeated trauma of the tongue contacting erupting primary incisors (Riga-Fede disease) can be observed in infants in the context of a behavioral habit, abuse or an insensitivity to pain syndrome. The differential diagnosis for Riga-Fede-like presentations with concern for self mutilation behaviors should include autism, Lesch-Nyhan syndrome, familial dysautonomia, and congenital insensitivity to pain.
Materials and Methods: An 18 month old male presented for evaluation and was found to have self injurious behavior without a typical pain response. This was diagnosed as Riga-Fede disease associated with erupting #O and #P. At subsequent visits, he presented with diffuse ulcerations of the tongue and buccal mucosa, non-healing ulcers of the fingers and a thermal burn to the palm of his hand. A biopsy of his tongue was read as a nonspecific ulcer with eosinophilia. The patient was further evaluated for a hereditary pain insensitivity disorder.
Results: A hereditary sensory and autonomic neuropathy panel was found to be significant for a homozygous variant of uncertain significance in the *SCN9A* gene which is consistent with congenital insensitivity to pain.
Conclusions: *SCN9A* codes for the voltage gated sodium channel type IX alpha subunit (Nav1.7). Located in peripheral neurons, Nav1.7 establishes the threshold for action potential formation and modulates pain response. Inactivating mutations of *SCN9A* causes congenital insensitivity to pain, which is an autosomal recessive disorder, resulting in injuries to nociceptive stimuli such as pin pricks or temperature extremes. Other sensory stimuli such as touch, vibration and motor function elicit a normal response. Self injurious behaviors observed in infancy are hallmarks. *SCN9A* congenital insensitivity to pain should be considered in the differential diagnosis in children with Riga-Fede ulcerations of the tongue.

#45 WHOLE EXOME SEQUENCING DETERMINES PLAUSIBLE VARIANTS IN AN ORAL COMPOSITE HEMANGIOENDOTHELIOMA WITH APPARENT YAP1-MAML2 FUSION.

Monday, 24th May - 10:24: Oral Presentations - Oral (Regular) - Abstract ID: 31

Dr. Ioannis G. Koutlas (University of Minnesota), Dr. Christy Henzler (University of Minnesota), Prof. Rajaram Gopalakrishnan (University of Minnesota)

Introduction: Composite hemangioendothelioma (CHE) is considered a borderline malignant vascular tumor.
Materials and Methods: 21-year-old female presented with painless left mandibular vestibular 1 cm mass of less than a year duration. H&E evaluation necessitated immunohistochemical studies that included CD31, CD34, D2-40, ERG, CAMTA1, and type IV collagen (COLIV). FISH was performed to investigate the presence of *YAP1* and *MAML2* aberrations and WES was performed to possibly identify causative gene variants.

Results: Non-encapsulated infiltrating tumor featured dilated vascular channels lined by cells exhibiting occasionally hobnail/matchstick-like arrangement. Intravascular cell proliferations and hyaline globules were also present. Lobular cell aggregates of spindle and epithelioid cells and slit-like spaces exhibiting a retiform or angiosarcomatous morphology were noted. Signet-ring and adipocyte-like cells were identified. Mitotic activity was exceptionally rare. Vascular spaces and the stroma featured lymphocytes and plasma cells.
Neoplastic cells were positive for CD31, CD34, D2-40 and ERG, negative for CAMTA1 while COLIV highlighted the plasmalemma of most neoplastic cells, vessels and hyaline globules. FISH revealed inversion gaps supporting *YAP1-MAML2* fusion.
WES identified three missense mutations (a) *FLT1* [c.3046A>G; p.R1016G], (b) *PIK3CA* [c.3140A>T; p.H1047L], (c) *C11orf42* [c.910G>C; p.A304P], and one mitochondrial DNA frameshift insertion in *MT-ND4* [c.1107_1108insC; p.P370fs].
Conclusions:

1. Histopathology and FISH support the diagnosis of CHE
2. *FLT1* (*VGFR1 precursor)* and PIK3CA variants may be driver mutations.
3. Alternatively, *PIK3CA* may relate to tumor growth/enlargement
4. *C11orf42* variant may be also tumorigenic
5. *MT-ND4*(NADH:Ubiquinone Oxidoreductase Core Subunit 4) variant possibly leads to altered reactive oxygen species hindering apoptosis.

Learning by concordance – a new tool for developing clinical reasoning in oral pathology and dental education.

Monday, 24th May - 10:36: Oral Presentations - Oral (Regular) - Abstract ID: 65

Dr. Gisele Mainville (Faculty of Dentistry, Université de Montréal), Dr. Bernard Charlin (Faculty of Medicine, Centre de pédagogie appliquée aux sciences de la santé (CPASS), Université de Montréal)

Introduction: Clinical reasoning is a complex task which is generally acquired through years of experience. Learn- ing by concordance (LbC) is an educational reflective tool that fosters clinical decision-making in complex situations.It is widely used and validated in medical education, but is new to dentistry. This presentation aims to familiar- ize oral pathology educators with LbC, the construction of a LbC activity, and its possible applications in dental education.

Materials and Methods: LbC activities were created and implemented in the undergraduate oral pathology curricu- lum at Université de Montréal. The principles behind LbC are presented, as well as the steps required to create a LbC activity, and the possible applications in oral pathology training. Student feedback is also presented.

Results: In a LbC activity, the student is presented a variety of clinical scenarios requiring them to interpret incom- ing information and make decisions. It focusses on the many micro-decisions that a clinician makes throughout a clinical exam in order to provide a diagnosis or institute treatment. After answering a question, the student receives immediate feedback from a panel of chosen experts, allowing the student to assess if there is concordance. Through online applications and educational plaforms, LbC is now accessible to dental educators.

Conclusions: LbC is a simple, low-cost and efficient way to help students reinforce their clinical reasoning skills and auto-evaluate their understanding by comparing their reasoning to that of experts located worldwide. It can also provide valuable assessment of what students think and how they reason. In addition to clinical reasoning, it can be used to teach and assess professionalism. Its online applicability provides new teaching opportunities in undergraduate, graduate and continued dental education, especially in the new context provided by the COVID-19 pandemic.

Head and Neck Mucosal Melanomas are Characterized by Overexpression of the DNA Mutating Enzyme APOBEC3B

Monday, 24th May - 10:48: Oral Presentations - Oral (Regular) - Abstract ID: 71

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Introduction: Primary head and neck mucosal melanomas (HNMMs) are rare and exhibit aggressive biologic behavior, dismal prognosis, and elevated mutational loads. The molecular mechanisms responsible for high genomic instability observed in HNMMs remain elusive. The DNA cytosine deaminase APOBEC3B constitutes a major endogenous source of mutation in a plethora of human cancers. APOBEC3B-related mutations are identified through C-to-T/-G base substitutions in 5'-TCA/T trinucleotide motifs. Herein, we provide immunohistochemical and genomic data strongly supportive of the role of APOBEC3B in HNMMs.

Materials and Methods: APOBEC3B protein levels were assessed in oral (N=16) and sinonasal (N=15) melanomas by immunohistochemistry using a custom rabbit monoclonal antibody (5210-87-13). Benign oral melanocytic nevi (N=13) served as a control group. Nuclear APOBEC3B immunoreactivity was visualized and quantified with theAperio ScanScope XT platform. Statistical differences between groups were calculated using Kruskal-Wallis one-way nonparametric tests. Publicly available genomic data were further analyzed to assess the impact of APOBEC3Bexpression in mucosal melanomas.

Results: Focal to diffuse, nuclear APOBEC3B immunopositivity was observed in all oral melanomas (H-score range=9-72, median=39) and 12 of 15 sinonasal melanomas (H-score range=1-110, median=24). The intensity of immunohistochemical positivity demonstrated a wide range of inter- and intra-tumor heterogeneity. APOBEC3B protein levels were significantly higher in oral and sinonasal melanomas than oral nevi ($p<0.0001$ and $p=0.0032$, respectively), which were overall negative for APOBEC3B (H-score range=1-12, median=6). APOBEC3B levels, however, did not differ significantly between oral and sinonasal tumors ($p>0.99$). Genomic analysis showed that overall mutation load, number of C-to-T transitions, and proportion of APOBEC3B-related mutation signatures 2 and 13 were higher in HNMMs than melanomas developing in other mucosal sites, and cutaneous melanomas.

Conclusions: The mutagenic enzyme APOBEC3B is overexpressed in HNMMs but not benign mucosal melanotic neoplasms. APOBEC3B may be a novel biomarker and therapeutic target for this clinically aggressive type of human malignancy.

Evaluation of oral cancer-induced chemosensitivity

Monday, 24th May - 11:00: Oral Presentations - Oral (Regular) - Abstract ID: 41

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Introduction. Oral cancer patients experience severe function related pain that impacts quality of life. Some patients report sensitivity to spicy food. Pain is attributed to neuronal sensitization by the release of chemical mediators from the cancer and cancer microenvironment that activate TRPV1 (transient receptor potential cation channel subfamily V member 1). To better understand the underlying mechanisms of oral cancer pain, this study was designed to evaluate cancer-induced chemosensitivity in oral cancer preclinical models.

Materials and Methods. A two-bottle preference test was used to measure aversion to the TRPV1 agonist, capsaicin, the spicy compound in chili peppers. Naïve wild type mice (C57BL/6) were housed two to five mice per cage. Liquid intake over 5-7 day periods was measured from two drinking bottles one with water and capsaicin (0.25 μM – 1 μM) and the other vehicle (0.1% ethanol). Positions of the bottles were exchanged daily to avoid habituation.

Results. Female C57BL/6 mice drank less water with capsaicin for all tested concentrations of capsaicin, demonstrating aversion. Male C57BL/6 mice demonstrated aversion to capsaicin concentrations greater than 0.25 μM. Aversion increased in successive trials, suggesting conditioning or sensitization. Male mice that did not show aversion to 0.25 μM capsaicin over three successive trials demonstrated aversion to 0.25 μM capsaicin after injection in the tongue with complete Freund's adjuvant (20 μl) to generate inflammatory pain.

Conclusions. Female mice showed greater sensitivity to capsaicin than male mice. Aversion to a non-aversive concentration of capsaicin was demonstrated in male mice with inflammatory pain. The lowest dose of capsaicin is expected identify the change in chemosensitivity and difference between sensitive vs. non sensitive cancers.

ACTIVE DECOMPRESSION AND DISTRACTION SUGOSTEOGENESIS AS A NOVEL TREATMENT FOR ODONTOGENIC KERATOCYST: A CASE REPORT

Monday, 24th May - 11:12: Oral Presentations - Oral (Student/Resident) - Abstract ID: 13

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The Odontogenic Keratocyst is a rare but benign developmental cyst of the oral cavity that arises from cell rests of dental lamina; it is aggressive and typically appears during the second and third decades of life.[1] It is usually detected incidentally or by asymptomatic swelling; 50% of them are commonly located in the posterior body and lower ramus of the mandible.[1] Objective: present the effectiveness of a novel treatment for cyst decompression and distraction sugosteogenesis. Clinical presentation: A 59-year-old female was referred to clinic due to painless swelling in her posterior left side of the oral cavity with one year of evolution. The mass measured 2cmx2cm. After biopsy, a diagnosis of Odontogenic Keratocyst was determined. Radiographical evaluation showed a mass that started at the middle of the ramus and extended to the roots of the second molar, cortical bone from inferior border of the mandible was compromised. Intervention and Outcome: Active decompression of the cyst was elected as the treatment path. The application of negative pressure to osseous cells produces a stretching that creates mechanical cues that trigger signaling pathways, promote fluid flow, and enhance angiogenesis.[2]Two bone windowswere performed on the buccal aspect of the cyst, and a tube was placed into each one of them. One tube was connected to a saline bag, and the other tube was connected to a Hemovac device. For one month, the patient manually irrigated with saline the inside of the cyst through one of the tubes, and manually used the Hemovac pumpto aspirate the water out of the cavity. This procedure was performed three times daily. Results: After three months, radiographic evaluation showed remarkable cyst decompression. Conclusions: After three months of device use, we believe it has the potential to remarkably reduce the size of cystic lesions through distraction sugosteogenesis.