THE ROLE OF EPIGENETIC AND EPISTATIC INTERACTIONS IN THE PATHOGENESIS OF ORAL SUBMUCOUS FIBROSIS.

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Objectives: Epigenetic factors have shown to play an important role in the development of fibrosis. Persistent injury to oral mucosa because of habitual quid chewing resulting in the upregulation of inflammatory cytokines, leading to myofibroblastic persistence underlies an epigenetic aberration in oral submucous fibrosis (OSF). There is however, a paucity of literature showing the role of epistasis in the pathogenesis of OSF.

Findings: Epistasis of IGF-1, TGF-1, COX and Lipoxygenase (LIOX) on PTEN are some of the relevant epistatic interaction relevant to the pathogenesis of OSF. Additionally, NF-κB is epistatic to PTEN, which is specifically arbitrated via p65 subunit of NF-κB.

Conclusions: Given the importance of epigenetic modification in the pathogenesis of OSF the potential role of DNMT and HDAC inhibitors as a therapeutic option holds promise in OSF. Inhibitory microRNAs against profibrotic genes and/or stimulatory microRNAs against antifibrotic genes could be another viable in-vivo therapeutic alternative for the treatment of OSF.

AMELOBLASTIC FIBRO-ODONTOMA: A DISTINCT ENTITY.

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Background: Ameloblastic fibro-odontoma (AFO) is a benign odontogenic tumor first described by Hooker in 1967. Its etiology and behavior have long been debated, as some investigators have proposed that AFO may represent a stage in development of an odontoma. For this reason, AFO was eliminated from the most recent Odontogenic and Maxillofacial Bone Tumor section of the World Health Organization (WHO) Head and Neck classification system. Occasional AFOs, however, have been found in patients older than the proposed age for odontoma completion (22 years) or present as large radiolucent lesions consisting mainly of the ameloblastic fibroma (AF) pattern with only foci of mineralized product formation. Herein, we present seven cases of AFO, all of which demonstrate particularly aggressive radiographic and/or histopathologic features and do not support the contention that all AFOs represent maturing odontomas.

Materials and Methods: An IRB-approved retrospective search of the oral pathology biopsy services at the Universities of Kentucky and Florida between January 1, 1975 and January 1, 2018 was completed. Cases with appropriate histopathological and radiographic documentation were selected.

Results: Seven patient cases were identified with ages 8, 8, 12, 16, 17, 27, and 29 years. Six cases were from the posterior mandible, and one was located in the posterior maxilla extending into the maxillary sinus close to the floor of the orbit. Only two of the cases have follow-up information, both of which demonstrate no evidence of tumor following conservative treatment.

Conclusion: Although the majority of cases diagnosed as AFO likely represent developing odontomas, we present seven cases in which the clinical, histopathologic, and/or radiographic features suggest that AFO should exist as a distinct entity and be treated similarly to an AF.

GENETIC POLYMORPHISM AND GENE EXPRESSION OF PI3K GENE IN AMELO-BLASTOMA.

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Objective: Ameloblastoma is a benign and local aggressive odontogenic tumor. Many genes and their respective signalling pathways are involved in the pathogenesis i.e. Patch, SHH, SMO, PI3K, AKT, mTOR etc. PI3K has an important role i.e. cellular quiescence, proliferation, cancer, and longevity in the pathogenesis of Ameloblastoma through PI3K/AKT/mTOR signalling pathway. The study was designed to evaluate the gene expression and gene polymorphism of PI3K gene.

The present study was a prospective preliminary study, which was carried out in 20 patients of confirmed ameloblastoma cases. 5 tooth germs were taken as control to compare. Biopsy was taken with patient's consent. Genomic DNA was extracted to assess the polymorphism of PI3K gene gene sequencing method in exon 9 and exon 20 in association with immunohistochemical analysis respectively.

Findings: Insertion of AA is noticed as the most common variation among 12 samples out of 20 identified at Exon 9 near to the splice site of PIk3CA (g.24751_24752insAA) (chr3:178890652_178890653insAA). However, no variation at Exon 20 was observed. Variant was neither found in ExAC nor 1000G. No differences were noted in the frequency and type of mutations analyzed by sex, age, or histologic features. The gene expression of PIK3CA was significantly higher in tumor epithelial cells. Such genetic polymorphisms are vital because they can be used as biomarkers that indicate for prognosis of tumor and its biological behavior.

Conclusion: These results suggest that common genetic variations in these pathways may modulate risk and clinical outcomes of ameloblastoma. Further replication and functional studies are needed to confirm these findings. It will be of benefit to the patient, if we target the mutation or aberrant protein products at the appropriate time by intervention of précised therapy.

PLASMA CELL GINGIVITIS DUE TO COS-METICS RELATED IODOPROPYNYL BUTYL-CARBAMATE (IPBC) ALLERGY IN A TEENAGE FEMALE PATIENT MASKING AS DESQUAMA-TIVE GINGIVITIS..

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Plasma cell gingivitis (PCG) is a rare lesion found on the attached and free gingiva, often extending to the mucogingival junction. Clinically, PCG can appear as sharply delineated erythematous lesions which can be accompanied by edema. We present a case of PCG in a 13 year old female patient which

clinically presented as generalized desquamative gingivitis involving the facial aspects of the attached and marginal gingiva that persisted despite substituting to a non flavored dentifrice and failure to elicit any suspected drug or food allergies. Dermatologic patch testing proved positive for Iodopropynyl Butylcarbamate (IPBC), a water based preservative or biocide used in personal care products. Microscopically, there was an intense inflammatory infiltrate in the lamina propria composed predominantly of mature plasma cells. Immunohistochemistry and in situ hybridization showed marked unrestricted cytoplasmic positivity for kappa and lambda light chains. IPBC is used in personal care products comprising lip balms, moisturizers, sunscreens, concealers and body washes due to its effectiveness at preventing fungal growth in topical products. The maximum level for safe use in leave on products is 0.1% but cosmetic products continue to use 10 times more than the safe levels. In the differential spectrum it is pertinent to discriminate erosive lichen planus, cicatricial pemphigoid, acute leukemia, HIV infection clinically; multiple myeloma and plasmacytoma histologically. Our case highlights the importance of patch testing for IPBC allergies in the oral mucosa. IPBC can lead to sensitization and contact dermatitis due to prolonged exposure; as its use in cosmetics continues to rise, and it is difficult to completely eliminate exposure to products containing IPBC especially in the context of teenaged girls and adult female patients.

RAMAN SPECTRAL STUDY OF SALIVA: A NEW TOOL FOR DETECTION OF MALIGNANT AND PREMALIGNANT ORAL LESIONS.

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The overall aim of this study is to develop methodologies for analysis of human saliva using Raman spectroscopy with a future applicability for oral cancer diagnosis. Artificial saliva was prepared in different concentrations, aiming to optimise the spectroscopic acquisition protocol. Furthermore, saliva samples were collected from 10 healthy volunteers by a non-stimulated collection method and from 10 healthy volunteers by a stimulated collection method and frozen for further analysis. Also, saliva samples from 20 patients with oral cancer and oral dysplasia were collected for initial characterization and analysis. Centrifugal filtration was performed to concentrate the saliva samples. The optimization of the different parameters required for Raman spectral acquisition using a HORIBA Jobin-Yvon HR-800 confocal Raman microspectrometer was carried out. Raman spectra were recorded using different wavelengths (532nm and 785nm), various objectives (x10, x50 and x60) and a diffraction grating of 600g/mm using both upright and inverted geometries and different substrates. Following pre-processing, spectra were subjected to principal component analysis (PCA) and principal component-linear discriminant analysis (PC-LDA). The 532nm source, inverted geometry, 10x objective and 96 well plate produced the best spectral quality and may be considered readily adaptable for clinical applications. Centrifugal filtration using a 3K device improved the spectra of the concentrate. PCA-LDA could discriminate between the healthy volunteer samples collected by stimulated or non-stimulated methods with resonable accuracy (83%). Furthermore, a specificity and a sensitivity as high as 91% and 94%, respectively, could be achieved when diferentiating healthy volunteer samples from patient samples. In this study, methodologies for the analysis of saliva by Raman spectroscopy have been developed to demonstrate the applicability of Raman microspectroscopy for providing molecular level insights from human saliva samples. The study also indicates the future potential for screening of saliva samples for oral pre-cancer and cancer.

NON-HABIT RELATED ORAL SQUAMOUS CELL CARCINOMA: POSSIBLE ETIOLOGIC FACTORS AND PROBABLE PREVENTION IN INDIAN SCENARIO.

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Introduction: India has the highest number of oral cancer cases in the world. Approximately 130,000 people succumb to oral cancer in India annually. Habits such as tobacco and alcohol consumption are well established etiologic factors in causing oral cancer. However, in recent years oral cancer cases are in the rise which do not have any known causative factors and studies have associated nutritional status, Human Papilloma Virus or poor oral hygiene as the probable cause.

Objectives: This paper aims at finding the possible etiologic factors in non-habit associated oral cancer through an extensive literature search keeping in view the incidence of reported cases in the Indian sub-continent. Studies reveal that 4-6% of oral cancer cases are not associated with any oral habits. It is important to be aware of the possibility of other factors contributing to the occurrence of oral cancer and aim at its prevention.

Findings: Significant number of studies and reported cases in India have shown that incidence of oral cancer in women without the exposure of any potential risk factors is alarmingly on the rise. The age range is lower as compared to habit associated cases where middle aged men are predominant. Other etiologic factors correlated with OSCC are viral infections like EBV, HPV, immunosuppression, familial factors, genetic predisposition, chronic mechanical irritation, dietary factors and hormonal factors.

Conclusions: OSCC is more prevalent amongst the lower socio-economic strata of the society in India where oral deleterious habits are common. The rising trend of oral cancer affecting people, especially women, without exposure to potentially harmful irritants should motivate researchers in identifying the possible etiologic factors. HPV virus association, genetic counselling, hormonal and dietary factors are to be considered to correlate cause and effect of such non-habit associated OSCC and adequate measures taken towards its prevention.

INVESTIGATION OF FOREIGN MATERIALS IN GINGIVAL BIOPSIES: A CLINICOPATHO-LOGIC, ENERGY-DISPERSIVE X-RAY MICROANALYSIS, AND IN VITRO STUDY.

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