REVIEW OF GUIDELINES FOR USE OF CONE BEAM COMPUTED TOMOGRAPHY IN PERIAPICAL PATHOLOGY BASED ON A CASE REPORT OF PERIAPICAL AGGRESSIVE CENTRAL GIANT CELL GRANULOMA

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Central giant cell granulomas of the jaws are typically known as being nonaggressive, nonneoplastic lesions initially termed giant cell reparative granulomas. These lesions most commonly present incidentally as a unilocular radiolucency in the mandible. However, some present with pain and perforation of the cortical bony plate. We present a case of a central giant cell granuloma referred for endodontic evaluation when the patient presented with pain, swelling, and a non-vital pulp. Radiographic evaluation showed a unilocular radiolucency associated with the root of a mandibular premolar causing spiking resorption. Further review of the patient’s radiographic history revealed the lesion was much smaller but visible at the initial visit 7 months prior to symptoms. Cone beam computed tomography (CBCT) evaluation revealed erosion of the buccal alveolar bone. Biopsy proved the lesion to be a central giant cell granuloma. As of January 2014, the patient has healed properly with no recurrence of the lesion. In our case, CBCT provided additional information leading to immediate biopsy rather than root canal therapy. Though in up to 70% of cases additional clinically relevant data is obtained, CBCT use is not routine in endodontic therapy. We review the current guidelines for CBCT use for evaluation of periapical pathology.

A REPORT OF A RARE CASE OF ORAL MELANOACANTHOMA IN WHITE MALE AND REVIEW OF LITERATURE. Hakeem A, Cohen DM, Bhattacharyya I, Fitzpatrick S, Islam MN. U. Florida, Gainesville. Oral melanoacanthoma, is a benign pigmented lesion characterized clinically by sudden appearance and rapid growth of a brown-black macule which may involve large areas of oral mucosa or may be multifocal. It can mimic malignant melanoma clinically due to its sudden rapid increase in size, varied coloration, asymmetry, and irregular borders. Oral mucosal melanoacanthoma when compared to the skin counterpart occurs in a younger population and is seen almost exclusively among black females with a predilection for the buccal mucosa. Histologically, melanoacanthoma is characterized by proliferation of the dendritic melanocytes in superficial layers of the epithelium. We present an unusual case of oral melanoacanthoma in a Hispanic white male and discuss the clinical and histologic spectrum of this condition. A 65-year-old male presented with multiple dark brown macules involving the labial mucosa. A lesion 5x2 mm on the right side of the lower lip was biopsied. Microscopic examination was consistent for melanoacanthoma. We review the literature on oral melanoacanthoma in context of Caucasian populations and stress the possibility of inclusion of this entity in the differential diagnosis of oral pigmented lesions even when presenting in a non-traditional clinical demographic.
SYPHILIS PRESENTING AS NON-SPECIFIC ORAL ULCERATIONS
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The reported number of cases of syphilis has been low for the past few decades, but the incidence of syphilis is on the rise. Syphilis is caused by the spirochete, Treponema pallidum. The infection may initially present as a slow healing oral ulcer, which due to its non-specific appearance often goes undiagnosed, thus delaying the diagnosis. We present two cases of non-specific oral ulcers with histological features suggestive of syphilis. These features led to confirmation of the infection by immunohistochemistry and serology. Case 1 was a 63-year-old healthy male with an irregular ulceration of the right buccal mucosa. The lesion was believed to be secondary to trauma and was treated with topical steroids with no improvement. Case 2 was a 32-year-old healthy male with ulcerations on the lower lip, which resembled aphthous ulcers. Biopsies of both patients demonstrated stratified squamous epithelium exhibiting spongiosis and exocytosis of neutrophils. The underlying connective tissue stroma demonstrated a prominent perivascular infiltrate of plasma cells. Because of the histologic picture, immunohistochemical stains for Treponema pallidum were ordered and yielded positive results. Serologic studies were confirmatory for syphilis in both cases. A histologic picture showing exocytosis of neutrophils and a marked perivascular infiltrate of plasma cells should warrant the pathologist to consider syphilis in the diagnosis of biopsies of non-specific oral ulcers. Appropriate immunohistochemical stains for Treponema pallidum are indicated to establish a diagnosis allowing treatment in a timely manner.

CHRONIC LYMPHOCYTIC LEUKEMIA/ SMALL LYMPHOCYTIC LYMPHOMA: A UNIQUE CLINICAL PRESENTATION.

Background: Chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/SLL) is a neoplasm derived from mature B lymphocytes characterized by small, round nuclei and scant cytoplasm admixed with prolymphocytes forming proliferation centers. Distinction between CLL and SLL depends on distribution and number of circulating leukemic cells. Diagnostic criteria for CLL include unexplained lymphocytosis for at least 3 months. Clinically, CLL usually occurs in elderly patients with no symptoms. Unbalanced cytogenetic anomalies are present in more than 80% of patients with CLL, including deletions of 13q14.3, 13q24, 17p13.1, 11q22.3 and trisomy 12. Methods: Case study of a 29 year old female who presented with a firm, non-tender nodule on the lower right buccal mucosa and a history of unexplained lymphocytosis. Microscopic examination revealed a buccal lymph node with effaced architecture and a diffuse proliferation of small lymphocytes and larger lymphoid cells constituting proliferation foci. Immunophenotypic analysis demonstrated CD5, CD20, CD23, CD43, Bcl2 and CD79a positivity. Analysis of peripheral blood showed a CD5 positive monoclonal B-cell proliferation. Fluorescence in situ hybridization analysis was performed, but target probe signal patterns did not reveal any assay specific abnormalities. Cytogenetics revealed an abnormal female karyotype: 45, X, -X{10} / 46, XX{10}. Although monosomy X in the bone marrow is a recurrent anomaly seen in lymphoid malignancies, its occurrence in CLL is rare. Conclusion: CLL/SLL presenting as a palpable buccal lymph node in a young adult with lymphocytosis is unique in our experience. Biopsy of the node defined the lymphocytosis and lymphadenopathy as CLL/SLL. Molecular assays for CLL/SLL can vary and change over time.
#5

MALIGNANCY ADJACENT TO DENTAL IMPLANTS: A CLINICAL DIAGNOSTIC TRAP

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Aim: Present clinico-pathological features of 7 new cases of malignancy adjacent to dental implants, and increase awareness to the diagnostic trap due to clinical similarity to perimplantitis (PI).

Methods: Retrospective analysis and literature review.

Results: The study group included 3 males and 4 females, age 44-89 years. 4 cases involved the mandible and 3 the maxilla. In 4 cases the diagnosis was primary squamous cell carcinoma, one case each primary high-grade large B-cell lymphoma, metastatic carcinoma of lung origin and basal cell carcinoma, extending from lower lip. Only in one case a risk factor (heavy smoking) had been identified. The clinical presentation mimicked PI (at least initially), with features such as swelling, erythema and bone loss. Diagnosis was delayed in half the cases, which had been treated conventionally as PI for up to 6 months.

Literature review: 41 cases have been retrieved from the English literature, mean age 68, equal gender distribution. 93% involved the mandible. All but 2 were SCC, the remaining sarcoma and metastasis from breast cancer. The majority of cases presented risk factors (previous oral SCC, lichen planus, erythroplakia, smoking). The clinical diagnosis had been PI in 26.8%, 53.6% presenting as a swelling or mass. The global incidence of peri-implant malignancy is very low, and no conclusive evidence exists to suggest implants may have a role in inducing malignancy.

Conclusions: There is a need to increase awareness that peri-implant cancer may closely mimic PI. Failure to respond to conventional treatment should immediately raise suspicion. Biopsy is essential for diagnosis, although not yet a routine procedure in treatment of PI.

#6

MALIGNANT RHABDOID TUMOR OF THE FLOOR OF THE MOUTH: CASE REPORT AND REVIEW OF THE LITERATURE

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Malignant rhabdoid tumor (MRT) was first described in 1978 by Beckwith and Plamer. Initial cases of MRT were reported as pediatric renal tumors and were thought to be a variant of Wilms tumor. Subsequent studies have reported malignant rhabdoid tumors in extra-renal sites. These sites include the mediastinum, retroperitoneum, and the parapharyngeal space. Rhabdoid tumors present with unique histologic and molecular characteristics. The tumors are composed of large polygonal cells with eccentrically placed nuclei. Necessary for the diagnosis are paranuclear eosinophilic condensations which compress the nuclei. Molecular studies have identified a deletion or mutation of the hSNF5/INI1 gene found on chromosome 22. This loss of INI1 gene expression can be demonstrated by immunohistochemical studies. Malignant rhabdoid tumors act in an aggressive fashion with most patients succumbing to their disease. The current case is that of a 51 year old female who presented with a swelling in the left floor of the mouth. Microscopically, the biopsy specimen showed a tumor composed of sheets of polygonal cells. The lesional cells contained hyperchromatic and eccentrically placed nuclei with paranuclear eosinophilic condensations. Immunohistochemical studies revealed positivity for vimentin and neurofilament. The tumor cells lacked expression of INI1. In accordance with the unique histologic appearance and immunohistochemical profile of the lesion, a diagnosis of malignant rhabdoid tumor was rendered. Consequently, the patient underwent resection of her tumor with subsequent neck dissection.
#7

NECROSIS OF THE MYLOHYOID RIDGE FOLLOWING ENDOTRACHEAL TUBE PLACEMENT

Prior to the description of bisphosphonate-related osteonecrosis, jaw necrosis with bone sequestrum was a relatively rare occurrence that was most often reported in the setting of previous radiation therapy or osteomyelitis. Mucosal ulceration associated with bone exposure is a cardinal feature of most forms of jaw necrosis. While this appears to be a key preceding event, the pathomechanisms that underlie the subsequent development of necrotic bone remain elusive. Roles for vascular compromise, periosteal disruption, alterations in bone metabolism and angiogenesis, and others have been proposed. We describe two cases of localized mandibular necrosis in patients who had recently undergone surgical procedures requiring anesthesia with endotracheal tube (ETT) placement. Both patients presented with acute pain involving the lingual mandible which reportedly began immediately after their surgeries. Their medical histories were negative for bisphosphonate use or radiation to the jaws. Intraoral examination of both patients revealed mucosal ulceration with exposed bone in the mylohyoid region. The first patient required assisted mobilization of the sequestrum which was confirmed to be non-vital bone exhibiting peripheral resorption histopathologically. Spontaneous exfoliation of the sequestrum occurred in the second patient. Mucosal trauma during ETT placement or laryngoscopy was suspected as the inciting event in both cases. Osteonecrosis following general anesthesia has rarely been documented in the literature, although it may be underreported due to lack of detection or spontaneous resolution without intervention in some cases. Clinicians should be cognizant of this potential complication from the perspectives of diagnosis, management, and prevention.

#8

NON-SEBACEOUS LYMPHADENOMATOUS CARCINOMA OF THE SUBLINGUAL GLAND
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Background: Lymphadenomatous carcinoma of the salivary glands is a very rare lesion almost exclusively diagnosed in the parotid glands. Only one case of the non-sebaceous type has been previously reported. Rationale: Distinguishing this tumor from lymphoepithelial carcinoma, sebaceous lymphadenocarcinoma and non-sebaceous lymphadenoma is important as this may have great prognostic implications. Observations: A 42-year-old Southeast Asian woman presented with a right sublingual mass. Examination revealed a 3 x 2 cm firm, oval shaped swelling which yielded no fluid on aspiration. The medical history was uneventful. She underwent a complete excision of the swelling. Microscopic examination of the specimen showed a clearly encapsulated tumor comprising irregular shaped islands of neoplastic epithelial cells distributed in a lymphoid tissue stroma with irregularly distributed germinal centers. The epithelial cells showed moderate cellular and nuclear pleomorphism, irregular hyperchromatism, few mitosis, foci of necrosis and areas of clear pleomorphic cells especially in peripheral areas. The nuclei of the epithelial cells were vesicular with prominent nucleoli. The epithelial cells were generally PAS-negative but the basement membrane delimiting the islands was prominently highlighted by PAS. Some frank ducts which survived the acinar replacement by lesionai tissue were seen at the periphery. In the lesional epithelial tissue, some duct-like formation attempts were also observed. A diagnosis of lymphadenomatous carcinoma was rendered after reviewing immunohistological stainings. Conclusions: The clinical and histopathological characteristics of this very rare lesion are hereby discussed alongside its distinguishing features from the differential diagnoses.
ODONTOAMELOBLASTOMA: REPORT OF A CASE WITH 17 YEAR FOLLOW-UP
The odontoameloblastoma is an exceedingly rare mixed epithelial and ectomesenchymal odontogenic neoplasm combining the histomorphologic features of ameloblastoma with those of odontoma. Most cases arise within the first three decades of life in the posterior jaws, equally divided between the maxilla and mandible. It presents as a unilocular or multilocular lucent lesion with a variable degree of internal radiopacity and commonly displaces teeth. It is an unencapsulated, locally aggressive neoplasm that infiltrates the adjacent host bone. It should be treated in the same manner as conventional ameloblastoma. Earlier literature refers to this lesion as “ameloblastic odontoma.” The number of acceptable cases is less than twenty, as many of the reports fail to present convincing evidence to substantiate the diagnosis and likely represent ameloblastic fibro-odontomas or developing or mature odontomas. We report a case that arose in the right posterior maxilla of a 17 year old female, filling the right maxillary sinus with a 4.2 x 3.9 x 3.8 cm mixed lucent-opaque lesion that expanded the medial and lateral sinus walls, impinged on the orbital floor, eroded the anterior sinus wall and expanded the posterior alveolar ridge and palate. The patient received a local excision and was free from recurrence after a post-operative follow-up period of 17 years. Histologically, the lesion exhibited areas of typical ameloblastoma, but with focal dental hard tissue formation, transitioning into areas of complex odontoma. The odontoameloblastoma should not be considered a “collision tumor” as the mesenchymal, hard tissue component, consisting of enamel and dentin, is intimately admixed with the ameloblastomatous epithelial component.

ORAL AND DENTAL CHANGES IN AN 11-YEAR OLD WITH DYSKERATOSIS CONGENITA INVOLVING MUTATION IN SHELTERIN PROTEIN GENE TINF2
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Dyskeratosis congenita is an inherited bone marrow failure syndrome characterized clinically by the triad of abnormal nails, reticular skin pigmentation, and oral leukoplakia. Originally thought to be solely an X-linked genetic disorder, studies have established that dyskeratosis congenita can have both autosomal dominant and recessive inheritance patterns. Six genes important to telomere functionality have been identified in half of the cases of dyskeratosis congenita. TINF2 encodes a component of the protein shelterin, which provides telomeres protection from DNA damage repair mechanisms. Defective telomere maintenance resulting in shortened telomere length is thought to manifest a broad spectrum of related diseases. In addition to the clinical triad mentioned above, abnormal dental changes such as shortened roots and enlarged pulp chambers have been identified. Lastly, patients with dyskeratosis congenita are at a high risk of developing leukemia, solid tumors, and pulmonary fibrosis. We present a case here of an 11-year old boy with dyskeratosis congenita and severe aplastic anemia. Genetic testing confirmed a mutation of the TINF2 gene. Clinically, he presented with the classic triad of abnormal nails, reticular skin pigmentation, and oral leukoplakias, which involved buccal mucosa, gingiva, and the tongue. Panoramic image revealed dental changes that were suggestive of shortened, blunted roots and enlarged pulp chambers.
#11

PIGMENTED ODONTOGENIC LESIONS: REPORT OF AN UNUSUAL CASE AND REVIEW OF THE LITERATURE

Melanin pigmentation in intraosseous odontogenic lesions is uncommon and its etiology is unknown. Approximately 50 cases have been reported in the English literature since 1961. The two most common pigmented intraosseous lesions are the calcifying cystic (40%) and keratocystic, odontogenic tumor (16%). Other pigmented intraosseous lesions have rarely been reported. The origin of the melanin in these tumors is uncertain. In the oral cavity, melanocytes are found in the oral mucosa, dental lamina, and tooth bud. Since the vast majority of pigmented intraosseous odontogenic lesions have been reported in African Americans and Asians, researchers suggest that racial pigmentation is an important contributing factor. We report a case of an unusual pigmented dentigerous cyst with lateral periodontal cyst-like features in a 49 year old black female. To the best of our knowledge, this is only the fourth pigmented dentigerous cyst ever reported. The etiopathogenesis, histologic, and clinical spectrum of this unusual condition are presented along with a review of the literature.

#12

REMISSION OF PERIPHERAL T CELL LYMPHOMA FOLLOWING A GRAVIOLA DIET
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An 89-year-old female patient presented with three smooth-surfaced nodules on the dorsum of the tongue, buccal mucosa and back. These nodules have been present for 5 months. The nodular mass on the dorsal surface of the tongue was approximately 4 cm in diameter, painful and it caused difficulties for speaking and eating. The mass on the buccal surface was approximately 2 cm in diameter and asymptomatic. Both nodules were similar in color to the surrounding mucosa. The patient medical history was significant for diabetes mellitus type 2, hypertension and hypothyroidism. Biopsy and immunohistological studies of the three nodules showed, among others markers, CD3-positive and CD5, CD4 and CD8-partly-positive. A diagnostic of peripheral T cell lymphoma was made. The patient refused chemotherapy due to her advanced age. Instead, she was advised by a relative to follow a graviola diet. After 14 months no mass were identified by physical examination and the patient referred that the nodules diminished their size after 6 weeks following the graviola diet, being able to eat and speak normally.
SURGICAL CILIATED CYST OF THE MAXILLA SECONDARY TO A PRIOR SINUS EXPOSURE - CASE REPORT AND LITERATURE REVIEW

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Surgical ciliated cyst of the maxilla is a relatively rare condition in the United States, but is reported more frequently in Japan as a delayed complication of surgery. It is an iatrogenic cyst which typically develops following trauma or surgery, most commonly a Caldwell-Luc procedure for the treatment of maxillary sinusitis. Due to surgical manipulation, fragments of the sinus lining become entrapped within the bone during the healing process and the lesion begins the formation of an epithelial lined cavity. We report a 53-year-old Hispanic male with a 1 week history of swelling and pain in the upper right quadrant. Intraoral examination revealed an edentulous area in the region of tooth # 3. Ten years earlier, the patient resided in Cuba, where he had undergone a surgical procedure which resulted in the complication of a sinus exposure. Clinical evaluation revealed no TMJ pain and no cervical lymphadenopathy. The lesion measured 6 mm in diameter and spanned from teeth #2 to #5. This erythematic mass, revealed to be soft to palpation, mildly ulcerated, and exhibited a bluish tint with no associated fistula. Although, a preliminary diagnosis of a cyst or an infection was made and Amoxicillin was prescribed; the patient was advised to undergo a biopsy. The pathology report described the formation of a cyst, internally lined with pseudostratified ciliated columnar epithelium, with chronic inflammatory cells scattered within the cyst wall. Given the histopathological appearance, the diagnosis of surgical ciliated cyst of the maxilla was made. Conservative surgical enucleation was the treatment of choice.

A CASE OF HERPES ASSOCIATED ERYTHEMA MULTIFORME


A 20 year old black female presented complaining of bleeding to her lips and "canker sores" inside her mouth as well as a rash to her hands and elbows. First intraoral lesion was noticed to the upper inner lip mucosa 12 days prior to clinic presentation and the rash one week later. The ulcerations started getting progressively worse with more lesions appearing followed by swelling of her lips. On clinical exam, there is generalized erythema throughout the oral cavity. The buccal mucosa is markedly erythematos with hyperkeratotic, white, plaque-like lesions present bilaterally. 1-2mm sized ulcerations are present to both the hard and soft palate on erythematous bases. Extra orally, variably sized tender & erythematous blisters are noted to the palmar surfaces of the hands. Violaceous plaques, macules, & blisters of various sizes to the extensor surfaces of the hands, forearms, and elbows. PMH: Similar episode 6 months prior otherwise non-contributory PSH: none SH: Denies any history of tobacco, alcohol, IV drugs, or illicit drugs. Medications: Clindamycin 300mg po every 6 hours x 7 days and Acyclovir 800mg po 5 times daily x 7 days Differential Diagnosis: Pemphigoid Vulgaris, Dermatitis Herpetiformis, Pemphigus, Gingivostomatitis We present a case of a young woman with herpes simplex associated erythema multiforme.
BRAFV600E POSITIVE LANGERHANS CELL HISTIOCYTOSIS: PRESENTATION OF A CASE

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Background: Langerhans cell histiocytosis (LCH) is characterized by infiltrates of CD1a positive cells, similar to antigen presenting cells of the epidermis. Disease may be solitary or multifocal involving various anatomic sites including skin, mucosa, bone, lymph nodes, soft tissue, and organs. LCH occurs over a wide age range, yet is most commonly identified in the pediatric population. Historically, debate has focused on LCH as a neoplastic or reactive phenomenon. Willman and colleagues, in 1994, provided evidence that LCH was a clonal proliferation using the X-linked human androgen-receptor gene molecular assay. Recent studies have identified the BRAFV600E mutation in 38-69% of LCH cases. This is supportive of a neoplastic process.

Objective: To report the clinical, radiographic, pathological and genetic findings in a case of LCH. Observation: A two-year-old male presented to the emergency department with left sided facial swelling of one-week duration. Magnetic resonance imaging and computed tomography studies demonstrated multiple soft tissue masses and osteolytic lesions including foci in the craniofacial region. A diagnosis of LCH was established based on histopathology and immunohistochemical phenotyping of a cervical lymph node. Tissue was further analyzed for the BRAFV600E mutation. Results: The BRAFV600E mutation was identified. The BRAFV600E mutation has been observed in several entities including Erdheim-Chester disease, ameloblastoma, melanocytic nevi, melanoma, and a variety of other cancers. Therapeutic implications for patients with BRAFV600E positive LCH are under investigation.

CASE REPORT: CHONDROMYXOID FIBROMA OF MANDIBLE


Background: Chondromyxoid fibromas are uncommon benign neoplasms of bone that represent less than one percent of all bone tumors. They are most often found in the bones of the lower extremities and very rarely in the jaws with only 25 reported cases. Histologically, these lesions are characterized by lobules of spindle-shaped or stellate cells within a chondroid and myxoid matrix.

Case description: A 39-year old male presented with an asymptomatic unilocular radiolucent lesion with irregular borders in the right mandibular canine/premolar area with buccal bone expansion and erosion. The lesion was identified as an incidental finding. Teeth tested vital. The lesion was excised in toto and the periphery curetted. Microscopic evaluation revealed a uniform cellular fibrous connective tissue stroma with admixed interspersed areas of hypocellular myxochondroid matrix. Cellular atypia and mitotic activity were not observed. The histologic findings were consistent with chondromyxoid fibroma. Conclusion: The current case of chondromyxoid fibroma exhibited the clinical, radiographic and histologic features characteristic of this process. However, given the chondroid and myxoid stroma the differential diagnosis would include cartilaginous neoplasia such as chondrosarcoma and myxoid neoplasms such as myxoma and chondromyxosarcoma. Etiology and pathogenesis is undetermined though rearrangements in chromosome 6 have been suggested. Reported treatments have consisted of enucleation with or without curettage and enbloc resection, which have all been successful with rare recurrence. Awareness of this rare, benign jawbone entity is relevant to the practicing OMFP given the significant differential diagnosis and focal histologic overlap with benign and malignant neoplastic processes.
LICHEN PLANUS PEMPHIGOIDES: REPORT OF FOUR NEW CASES WITH LITERATURE REVIEW
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BACKGROUND: Lichen planus pemphigoides (LPP) is a rare autoimmune blistering dermatosis of the pemphigoid family of diseases; it is characterized by development of vesiculobullous lesions on or adjacent to areas of lichen planus. LPP primarily affects the skin with 37% of cases also affecting oral mucosa; oral involvement alone is rare. Epitope spread, a theory that inflammation releases previously sequestered antigens leading to an autoimmune response, is hypothesized to contribute to the pathophysiology of this disease.

METHODS: We present 4 cases with clinical, histologic and immunofluorescence features characteristic of LPP, 3 cases with oral involvement only.

RESULTS: The 4 patients (2 males) were aged 49, 50, 51, and 61. All patients presented with a working diagnosis of lichen planus and reported pain and mouth sores. Only one patient had skin lesions. Intraorally, reticular, erythematous and ulcerative lichen planus predominantly involved the gingiva and buccal mucosa. Mucosal biopsies revealed lichenoid mucositis with occasional subepithelial clefting. Direct immunofluorescence studies showed linear deposition of IgG, IgA and C3 along the epithelium-connective tissue interface.

CONCLUSION: LPP occurs uncommonly in the mouth and often presents similarly to erythematous and ulcerative lichen planus. Three of four cases in this series presented with oral findings alone. Correct diagnosis requires correlation of clinical findings with histologic and immunofluorescence findings.

LOCALIZED JUVENILE SPONGIOTIC GINGIVAL HYPERPLASIA (LJSGH) FEATURING UNUSUAL P16INK4A LABELING AND NEGATIVE HPV STATUS BY POLYMERASE CHAIN REACTION (PCR).

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Background: LJSGH represents a distinct type of gingival hyperplastic lesion with specific clinicopathologic features. Evaluation of the morphological characteristics of LJSGH indicates the potential role of HPV infection as an underlying etiopathogenetic mechanism.

Materials and methods: All cases diagnosed as LJSGH during the period 2008-present were retrieved. Clinical and demographic data were collected. HPV status was assessed by p16INK4A immunohistochemistry and PCR using MY09/11 primers for the L1 conserved region of the HPV genome and human beta-globin as an internal control.

Results: Twenty-one LJSGHs were identified (M:F= 2:1, age range: 8-36 years, mean:13 years). All lesions were well-demarcated, exophytic, erythematous with granular or slightly papillary surface and a preponderance for the maxillary gingiva (19/21). The mean follow-up period was 18.7 months. Two cases recurred 20 and 21 months after excision.

Histopathologically, LJSGHs featured epithelial hyperplasia with intense neutrophilic exocytosis and spongiosis. All 21 cases demonstrated positive immunostaining for p16INK4A with the majority of the specimens intensely decorated for p16INK4A in >50% of the overlying epithelium. Focal or diffuse immunostaining pattern was observed in 47.6% and 52.4% of the lesions, respectively. Thirteen cases were negative for HPV DNA by PCR, 5 cases lacked beta-globin amplification and were classified as insufficient for analysis while 2 were suspicious for HPV but limited DNA quantity impeded further typing. Interestingly, the last case displayed positivity for HPV-31. Conclusions: HPV does not participate in the pathogenesis of LJSGH. The observed expression of p16INK4A in the absence of HPV-PCR confirmation can be attributed to intense inflammation.
MAML2 REARRANGEMENTS IN ODONTOGENIC CYSTS WITH MUCOUS METAPLASIA: AN INSIGHT IN THE PATHOGENESIS OF INTRAOSSEOUS MUCOEPIDERMOID CARCINOMA.

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Background: The pathogenesis of intraosseous mucoepidermoid carcinoma (IMEC) remains unknown. Coexistence with odontogenic cysts (OCs) has been reported in 32-48% of IMEC suggesting a possible etiopathogenetic mechanism. Metaplastic mucous cells seen in the epithelial lining of OCs may support such a theory. The MECT1-MAML2 fusion transcript is a well-established genetic signature of 66% of MECs. Aim: To investigate the presence of MAML2 rearrangements in OCs with mucous metaplasia. Materials and methods: Ten cases of OCs with prominent mucous cell component and 3 cases diagnosed as IMEC were evaluated for the presence of MAML2 rearrangement using a MAML2-11q21 break-apart FISH probe. The clinical cutoff defining positivity was at 10%. Results: All OCs and IMECs occurred in the mandible. The former exhibited an M:F ratio of 2.3:1 (mean age 48.6 years) while all IMECs occurred in women (mean age 55 years). All 3 IMECs exhibited MAML2 rearrangement by FISH in 26-61% of cells. Successful hybridization was observed in 9/10 cases of OCs with mucous metaplasia. Among them, 2/9 were remarkable for MAML2 rearrangement in 12 and 24% of the cystic lining epithelial cells, respectively, and 3/9 albeit not fulfilling our criteria for positivity, showed rearrangement in 7-8% of cells. The remaining 4/9 cases were entirely negative. Conclusions: We identified MAML2 rearrangements in 56% of OCs with mucus-secreting cells. This finding suggests that a subset of OCs with mucous metaplasia may represent early malignant transformation towards IMEC.

ORAL PEMPHIGOID WITH EXTENSIVE OCULAR INVOLVEMENT: A CASE REPORT

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BACKGROUND Mucous membrane pemphigoid (MMP) is a chronic blistering autoimmune disease in which autoantibodies are directed against components of the basement membrane. It affects mostly the oral mucosa but ocular and genital mucosa may also be involved. MMP affects the elderly population with a female predilection. It often presents in the oral cavity as a desquamative gingivitis with rarely seen bullae. Treatment of MMP is often individualized and varies from topical to systemic immunosuppressive drugs. We will present a case of a female patient with MMP and extensive ocular involvement. CASE A 57-year-old female patient with asthma was referred to evaluate and treat a persistent desquamative gingivitis. The case was challenging as the patient only spoke Spanish and was severely mentally impaired. Extra-oral exam revealed erythema, ulceration, and symblepharon of bilateral ocular mucosa but no skin lesions. The patient claimed that her eye doctor said she had a bacterial infection and was given eye drops. Her in-tra-oral exam showed erythematous desquamative gingivitis with a positive Nikolsky sign. A biopsy was performed and sent for microscopic exam and direct immunofluorescence (DIF). The H&E biopsy showed non-specific ulcer while the DIF reported a definitive diagnosis of pemphigoid. She was treated with prednisone doses that have been gradually tapered and both oral and ocular symptoms have significantly improved. CONCLUSION This case demonstrates the importance of recognizing other more serious diseases related to the gingiva and oral mucosa. It also shows the important role of a dentist in performing an extra-oral exam and discussing abnormal findings with the appropriate medical specialist. Finally, the role of DIF in making the correct diagnosis is emphasized.
MULTICYSTIC DISEASE OF THE NECK

A 49 year old women presented with a Multicystic Neck Lesion of several years duration. Routine hematologic and biochemical examinations, including thyroid hormonal evaluation, were within normal limits. FNAC from the anterior neck mass showed hypo cellular aspirate with clumps of mononuclear cells with heterogeneous and primitive nuclei and vacuolated deep basophilic cytoplasm which is consistent with a malignant lesion. Cultures were negative for aerobic and anaerobic bacteria. The upper anterior neck and the supraclavicularly lateral neck cysts both showed the appearances of a papillary thyroid carcinoma with occasional psammoma bodies seen. The tumor is infiltrating the surrounding muscle. The cystic mass in the middle of the chain (level III & IV) is lined by more than one layer of columnar epithelium. The wall of the cyst is infiltrated by lymphoid tissue diffusely or in form of follicles with prominent germinal centers. Some of the germinal centers contain tangible bodies usually encountered in the reactive lymphoid follicles. The follicles are positive for the B cell marker CD20. The area between follicles is positive for the T cell marker CD3. The sections are negative for BCL2 which excludes a follicular lymphoma. Diagnosis: Papillary thyroid carcinoma, lymphoepithelial cyst, and metastatic lymph node with cystic degeneration. In summary: An unusual case of synchronous papillary thyroid carcinoma and lymphoepithelial cyst (LEC) is reported in a patient without any identified environmental risk or predisposing factors. The metastatic lymph node was found in a cystic form and located supraclavicularly inferior to the LEC.

NF-KB AND IL-6 IMMUNOHISTOCHEMICAL EXPRESSION IN ORAL PREMALIGNANT AND MALIGNANT LESIONS
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Objective: Recent evidence suggests a molecular crosstalk between IL-6 and NF-κB signaling pathways in oral squamous cell carcinoma (SCC). The purpose of this study was to evaluate the immunohistochemical expression of NF-κB and IL-6 in oral malignant and premalignant lesions. Findings: Forty five oral cases comprising 4 normal mucosal controls, 11 hyperplasias, 21 dysplasias of various degrees and 9 SCCs were investigated. Immunohistochemical staining with NF-κB (p65) was performed and the intensity and percentage of positive epithelial cells were graded in a semiquantitative manner, in a scale of 0-3 for each parameter; a combined total score was also calculated (0-6). NF-κB expression was noted in all cases in both cytoplasm and nucleus of epithelial cells. The average total scores were 4.25 for normal mucosa, 4.5 for hyperplasias, 5.33 for dysplasias and 5.22 for SCC, respectively. The total scores in dysplasias and SCCs were higher than those in hyperplasias (p=0.041). Immunohistochemical staining for IL-6 was also performed and each case was characterized as positive or negative. IL-6 had a mild cytoplasmic staining in a few subepithelial inflammatory cells and in the adjacent epithelial cells of the basal or parabasal layer. IL-6 expression in the epithelial cells was detected in 2/11 (18.18%) of hyperplasias and 4/18 (22.22%) of dysplasias, whereas no positive case was detected for normal mucosa and SCC. Statistical correlation between the presence of subepithelial inflammatory infiltrate and the IL-6 expression in epithelial cells was detected (p<0.05). There was no correlation between NF-κB and IL-6 expression. Conclusion: NF-κB and IL-6 signaling pathways may be activated in the early stages of oral carcinogenesis.
#23

**NONNEURAL GRANULAR CELL TUMOR OF THE ORAL CAVITY**

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Classic granular cell tumors (GCTs) show strong cytoplasmic and nuclear expression of S100 and are believed to be of neural or Schwannian origin. We report a case of intraoral GCT that was negative for S100 but strongly positive for expression of CD10. A 52-year-old woman with a history of hypertension, diabetes, and hypothyroidism presented with an ulcerated, sessile, 1 cm nodule of the left buccal mucosa. The clinical diagnosis was “traumatic fibroma”. Microscopic examination revealed ulcerated fibrovascular connective tissue that contained a cellular population of large, ovoid cells with round, euchromatic nuclei and granular cytoplasm. Pleomorphism was not observed and mitoses were rare. Acute and chronic inflammatory cells were noted throughout the lesion with focal germinal center-like aggregates in the deeper connective tissue. Occasional binucleated and multinucleated cells, including Touton giant cells, were observed. Immunohistochemical studies revealed the lesional cells to be negative for S100 protein, CD1a, Melan-A, HMB-45, synaptophysin, smooth muscle actin and cytokeratins. CD163 and Factor XIIIa expression was identified among interspersed dendritic cells consistent with histiocytes, however, the granular cells were negative. Lesional cells demonstrated uniformly strong expression of CD10. Besides congenital epulis of the newborn, intraoral examples of non-neural GCT have rarely been described. Non-neural GCT is a diagnosis of exclusion based largely upon immunohistochemical findings and we cannot completely exclude the possibility that this lesion might represent a variant of fibrous histiocytoma.

#24

**PEMPHIGUS VULGARIS PRESENTING AS GINGIVAL HYPERTROPHY IN A CHILD**

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Pemphigus vulgaris is a mucocutaneous autoimmune disease caused by autoantibodies against the desmosomal proteins desmoglein 3 and desmoglein 1. Oral pemphigus vulgaris has rarely been reported to occur in children and adolescents. A current literature review reported 50 cases, 7 of which presented with oral lesions exclusively. Oral lesions of pemphigus commonly present as vesicles or bullae that ulcerate easily and occur most frequently in the buccal, palatal and labial mucosa. Gingival lesions usually present as desquamative gingivitis. We report a case of a healthy 17-year old Hispanic female, taking no medications, who presented with an 8-year history of gingival hypertrophy and no other oral, skin or other mucosal lesions. Clinically she had severe gingival hypertrophy affecting both the facial and lingual surfaces and covering most of the clinical crowns. The surface epithelium appeared eroded in areas and the tissues bled easily. Surgical excision of all hypertrophied gingival tissue was done in the operating room. The final diagnosis on light microscopy was inflammatory hyperplasia and ancantholysis. Direct immunofluorescence showed intercellular deposition of IgG and C3 and indirect immunofluorescence showed IgG positive intercellular staining a 1:80 dilution. Testing for serum antibodies against desmoglein 1 and 3 however was negative. After further evaluation with dermatologist, a diagnosis of atypical pemphigus vulgaris was made. Only 2 other reported cases of pemphigus vulgaris have presented with oral nodules or masses but none exclusive to the gingiva. This is the first documented case of pemphigus vulgaris presenting as gingival hypertrophy in a child without any other mucosal or skin lesions.
#25

PRIMARY MUCOEPIDERMOID CARCINOMA ARISING FROM ECTOPIC SALIVARY TISSUE WITHIN AN INTRAPAROTID LYMPH NODE


Ectopic salivary tissue is commonly found in intraparotid and periparotid lymph nodes. Warthin's tumor is the most common tumor arising in ectopic salivary gland tissue, and is found more often in intraparotid lymph nodes. Although rare, neoplastic transformation of the ectopic salivary tissues is conceivable and other types of salivary gland neoplasms arising in intraparotid lymph nodes have been reported. Herein we report a rare case of mucoepidermoid carcinoma (MEC) arising from ectopic salivary tissue in an intraparotid lymph node. A 32 year-old Kuwaiti Caucasian presented with a mass in the right parotid gland. Fine needle aspiration cytology was performed pre-operatively and suggested Warthin’s tumor. The patient subsequently underwent a superficial parotidectomy. The specimen showed a well circumscribed, thinly encapsulated, solid, tan mass within the parotid parenchyma abutting the deep margin. Hematoxylin and Eosin stained sections of the lesion showed solid islands and cysts composed of epidermoid cells, mucus cells and intermixed smaller “intermediate” cells within an intraparotid lymph node. The tumor was seen infiltrating the parotid parenchyma at the deep margin. Metastasis from distant sites was ruled out clinically, and the diagnosis rendered was mucoepidermoid carcinoma, low-grade, arising from ectopic salivary tissue in an intraparotid lymph node. Such cases are extremely rare and the presence of malignancies within lymph nodes may pose a diagnostic pitfall, which can affect patient management.

#26

PSEUDOXANTHOMA ELASTICUM: A RARE ENTITY PRESENTING IN THE MOUTH

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Pseudoxanthoma elasticum (PXE) is an inherited disorder of abnormal calcification of elastic fibers mainly in the skin, retina and cardiovascular system. Other systemic involvement can occur. It is caused by a mutation in ABCC6 gene that encodes Multidrug resistance associated protein 6 (MRP6). In the literature, the oral mucosa was rarely involved and if involved, it is in combination with systemic manifestations. They can present as yellow macule/s in the palate or labial mucosa. Other reported oral symptoms include Sjogren-like features, dental impactions and amelogenesis imperfecta. Herein we report a case that presented solely with oral lesions. A 77-year old male presented to the dentist with asymptomatic bilateral yellow lesions on the soft palate that was found incidentally on dental exam. His medical history includes hyperlipidemia, benign prostate hyperplasia, cataract and occasional HSV skin infection. He reported brown crusty spots on his skin due to aging. His brother and sister have similar brown spots on the skin. He is on pravastatin, valacyclovir and vitamin D supplements. He has no known allergies. He has a twin brother who had gastrointestinal cancer and was treated for it. His mother died from heart problems and his father died from brain cancer. Biopsy of the palatal lesions showed a localized collection of fragmented clumped basophilic fibers within the connective tissue. These fibers stained positive with elastic stain and Von Kossa stain. The histopathologic diagnosis was consistent with PXE. Presentation of PXE in the mouth is uncommon and if it occurs, it should initiate systemic investigation for other symptoms and close follow up of the patient.
RENAL OSTEODYSTROPHY OF THE MANDIBLE: A CASE REPORT

INTRODUCTION Renal osteodystrophy refers to bone diseases that result from the abnormal metabolism of calcium, phosphate and bone secondary to kidney disease and secondary hyperparathyroidism. In this report, we present a patient with generalized mandibular enlargement of unknown origin that was eventually diagnosed with underlying kidney disease. CASE SUMMARY A 23-year-old black male presented with a chief complaint of pain related to his lower third molars. He reported a medical history significant only for hypertension and was taking Norvasc and clonidine. He exhibited painless generalized mandibular enlargement. A panoramic radiograph was taken and revealed a diffuse “ground-glass” trabecular bone pattern. The clinician ordered a CT scan and bloodwork to rule out any systemic diseases. The patient returned 2 months later with pain related to the right lower third molar. He reported that he had recently started dialysis and was now diagnosed with focal segmental glomerulosclerosis and secondary hyperparathyroidism. The lower right third molar was extracted and tissue was curetted from the socket and submitted for histology. The biopsy specimen showed cellular fibrous connective tissue admixed with irregularly shaped viable bone trabeculae with a small focus of multinucleated giant cells. A diagnosis of benign fibro-osseous lesion consistent with renal osteodystrophy was rendered.

CONCLUSION This case shows how an unknown systemic disease can present with an oral manifestation that can lead to its diagnosis. This patient’s generalized mandibular enlargement with diffuse “ground-glass” radiographic changes was an oral manifestation of underlying metabolic kidney disease. Early diagnosis made by dentists will minimize the morbidity associated with this condition.

CHONDROSARCOMA OF THE TEMPOROMANDIBULAR JOINT - ONE INSTITUTIONS EXPERIENCE: A CASE REPORT AND REVIEW OF THE LITERATURE

Chondrosarcoma to the head and neck region is an uncommon event, representing 1% to 12% of all chondrosarcoma cases. When present, a vast majority of chondrosarcomas manifest in the bony skeleton (59.7%). The laryngotraheal cartilage (23.4%); soft tissue of the head and neck (11.2%); and separate anatomic locations such as the oral cavity, pharynx, tongue, and orbit (5.8%) make up the remaining distribution. With regard to oral cavity tumors, patients may present with complaints of swelling, pain, tooth mobility or occlusal discrepancy. If the temporomandibular joint (TMJ) is affected, additional symptoms may include trismus or hearing loss. Although rare, the surgeon and specialist must be aware of this phenomenon and be prepared to understand the potential therapeutic challenges associated with management. This paper describes a case of chondrosarcoma to the TMJ in a 53 yr old female veteran who presented with left facial swelling. Computed tomography demonstrated an expansile and destructive lesion of the left TMJ and condylar head. An open biopsy revealed a grade III/III chondrosarcoma of the left TMJ. She was treated primarily with composite resection of the right mandibular condyle and temporal bone along with superficial parotidectomy with facial nerve preservation and delayed reconstruction to improve tumor surveillance. Adjuvant intensity-modulated radiation therapy (IMRT) of 6000 cGy was administered following her resection. She is remains disease free at 18 months postoperatively. Chondrosarcoma to the TMJ presents a complex problem to the surgeon and clinician. A combined, multi-disciplinary approach may be necessary to effectively treat and monitory the disease as well as
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SMARTPHONE TELEMEDICINE: IMPROVING DIAGNOSIS CONSULTATION AND TREATMENT PLANNING


Smartphone telemedicine can be an efficient and effective way for remote Oral Pathology consultation. There are no reports to date, on the impact of smartphone telemedicine on the interaction of Oral Pathologists with multidisciplinary clinicians. A primary care physician has about 10 minutes to provide a clinical examination and formulate a treatment plan. In the past, under the presence of a suspicious oral lesion, the patient would be initially medicated with antifungal, antibiotics and antivirals; a few weeks later, when lesion did not resolve, the patient would be referred to a specialist for further evaluation. Today, a primary care physician can take a photograph of an oral lesion with a smartphone and send it to the oral pathologist with a description of signs and symptoms and medical history; the oral pathologist makes an assessment of the information and guides the clinician accordingly. Use of smartphone telemedicine in developing an accurate preliminary diagnosis is a great tool that can save a patient’s life. To illustrate this process we present cases, such as that of a 34 year old patient with lesion of the buccal mucosa which was photographed by the primary care physician, assessed by the oral pathologist and within a couple of weeks patient underwent resection of a T2N1M0 squamous cell carcinoma by the oral and maxillofacial surgeon. Without the use of smartphone telemedicine, the diagnosis and treatment would have been greatly delayed. To function effectively, it is crucial for smartphone telemedicine to include the participation of a multidisciplinary network. It is also very important for the oral pathologist to interact directly with primary care physicians.

#30

THE PREVALENCE OF ORAL LESIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is a group of idiopathic conditions characterized by chronic inflammation of the gastrointestinal tract, with Crohn’s disease and ulcerative colitis being two common forms of this process. Extra-intestinal expression of IBD is seen in over 50% of patients and can include cutaneous, oral mucosal, ocular, musculoskeletal and biliary manifestations. Oral lesions associated with IBD have very distinct clinical features, although some non-specific processes such as aphthous ulceration and candidiasis have also been linked to this condition. While characteristic oral manifestations of IBD are well-documented, limited data is available regarding the prevalence of such lesions. The objective of this study is to determine the prevalence and nature of oral mucosal changes associated with IBD in the United States.

Methodology: One hundred consecutive patients presenting to the Wexner Medical Center gastroenterology clinic with a prior diagnosis of either Crohn’s disease or ulcerative colitis were recruited. Subjects underwent a series of comprehensive oral examinations over a twelve months period during which all oral mucosal abnormalities were documented. Clinical findings were compared to a healthy age and sex matched control population from the College of Dentistry screening clinic. Results: Seven patients in the IBD group and one patient in the control group presented with non-specific oral lesions. Only one IBD patient reported a history of linear ulcerations in the mandibular vestibule, characteristic for oral manifestations of IBD. Conclusion: Based on these findings, the prevalence of oral lesions in IBD patients can be estimated to be less
than 1%.  

THE DIAGNOSTIC ROLE OF KERATIN 6, 7, 8, 14, 16, 18, 19 IN MELANOMA AND UNDIFFERENTIATED TUMORS OF THE ORAL AND MAXILLOFACIAL REGION

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Objective. To investigate the role of keratins as an aid to exclude melanoma from its mimics in the head and neck region. Materials and Methods. Immunohistochemical expression of K6, K7, K8, K14, K16, K18, K19 was studied in 29 oral and maxillofacial melanomas (4 oral mucosal, 17 cutaneous, 11 metastatic), 6 neuroendocrine carcinomas (NEC), 7 neuroblastomas (NB), 6 sinonasal undifferentiated carcinomas (SNUC), 15 undifferentiated nasopharyngeal carcinomas (UNPC), 19 anaplastic large cell lymphomas (ALCL), 16 poorly differentiated squamous cell carcinoma (PDSCC), and one case of Ewing’s sarcoma (ES). Stained sections were reviewed using light microscope for pattern and intensity of expressions. Results were statistically analyzed using Fisher’s exact test. Results: All of the studied keratins were expressed in varying extents in melanoma except K6. K6 was positively expressed in NEC, NB, UNPC, and PDSCC. K7 was positively expressed in melanoma, NEC, SNUC, UNPC, PDSCC but negative in NB, ALCL and ES. K8 was positive in all study groups except ALCL and ES. K14 was positive in melanoma, SNUC, UNPC, PDSCC, ES and negative in NEC, NB, and ALCL. K16 was positive in melanoma, UNPC, PDSCC. K18 and K19 were positive in all groups except ALCL and ES. Keratin expression was observed more in metastatic melanoma compared to primary melanoma with statistically significant difference for K8 and K18. K14 and K16 expressions were significantly higher in PDSCC compared to the other groups. ALCL was negative for all studied keratins. Conclusion: Positive keratin expression in an undifferentiated neoplasm should not exclude the diagnosis of melanoma. Metastatic melanoma is more capable of expressing keratins compared with primary melanoma.

TOLL-LIKE RECEPTOR-MEDIATED REGULATION OF ADENOSINE RECEPTORS IN ORAL SQUAMOUS CARCINOMA CELLS

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Background: The microenvironment of oral squamous cell carcinoma (OSCC) is colonized by microorganisms and is inflamed, which includes monocyte infiltrates. Little is known about the regulation of inflammation in the OSCC microenvironment. In monocytes, microbial products induce toll-like receptor (TLR)-mediated activation of NF-kB, which regulates the expression of adenosine receptors (AR) that bind adenosine, the product of dephosphorylation of ATP. This is important, because extracellular ATP, enzymes that dephosphorylate ATP, and adenosine, are present in large amounts at sights of inflammation and in cancers. Three of four known AR (A2a, A2b, A3), are important regulators of inflammation. Previously we showed that OSCC cells express functional TLR. Approach/Results: The impact of TLR2/1 and TLR4 activation on AR expression in OSCC cell lines using culture experiments, followed by PCR and Western blotting, and by immunohistochemistry in oral specimens. TLR2/1 and TLR4 stimuli induced AR upregulation in positive control monocytoid THP1 cells. OSCC cell responses were orders of magnitude smaller than THP1 responses. In contrast to THP1 cells, OSCC cell TLR2/1, but not TLR4 activation, stimulated AR A2a and A3 expression, with differential effects on A2a and A3, but no A2b modulation. In oral mucosal specimens, A2a labeling was stronger on basal and parabasal normal and malignant squamous cells than on differentiated cells. Conclusion: Together, these data are consistent with our previous observations that TLR are functional in OSCC cells, and that TLR2/1 activation is more effective than TLR4 activation. Further characterization of OSCC cell AR
expression and function is in progress. Supported in part by the GRU Pilot Study Research Program grant.
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FINDING AND VISUALIZING INFORMATION ABOUT POTENTIAL PROGNOSTIC BIOMARKERS OF ORAL SQUAMOUS CELL CARCINOMA: A PATHOLOGY INFORMATICS STUDY

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Background: The impressive growth in the biomarker literature poses a serious barrier to finding information. E.g., it is increasingly difficult to find relevant studies on potential prognostic biomarkers of oral squamous cell carcinoma (OSCC) as simple keyword searches retrieve too many irrelevant studies. Pathology informatics can address this problem by using natural language processing (NLP) and information extraction and retrieval methods to build tools. Evaluating NLP tools typically involves testing against a 'gold standard' corpus. In many informatics problems, a gold standard does not exist and its creation is a necessary first step. This study describes the creation of a gold standard corpus about studies on potential prognostic biomarkers in OSCC, as well as a novel tool for viewing content. Methods: Two annotators screened titles and abstracts of prognostic studies of OSCC retrieved from MEDLINE. We developed a guideline to aid identification of a subset of prognostic biomarker studies, which we labeled as relevant. Calibration trials preceded annotation of the corpus. We measured inter-annotator-agreement (IAA) using Cohen's kappa. Results: We retrieved 1818 citations. Three calibration trials involved screening 51 citations (2.8%); after IAA stabilized, we screened the remaining corpus (n=1767; 97%; 8 = 0.76). The gold standard corpus has 497 (27%) relevant citations. Our group also developed the EDDA Lens to view various aspects of the corpus, including open access images. Conclusion: We developed a gold standard corpus with studies about potential prognostic biomarkers of OSCC and a prototype for viewing content. This was an important first step towards development of informatics resources to meet the information needs of pathologists and researchers.

#34

IS LICHEN PLANUS A PRECANCEROUS LESION?

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One of the most controversial aspects of oral lichen planus (OLP) is its malignant potential. The aim of this study was: to look critically at OLP particularly those associated with dysplastic changes. To localize the immunoglobulins (IgG, IgM, IgA) and finally to localize Carcinoembryonic antigen (CEA) in OLP with or without epithelial dysplasia to predict the potentiality of its malignant transformation. Materials and Methods: 42 cases of OLP were collected from oral pathology and maxillofacial departments. Faculty of Dentistry. University of Alexandria. Sections were stained with H & E for diagnosis, incubated in monoclonal CEA antibody (Cat.#MS-613, Thermo Fisher Scientific Fermont, CA94538, USA) as well as normal swine serum, anti-human IgG, IgM and IgA antibodies using PAP technique (According to the manufactures’ instructions). Results: histopathologically, 2 cases showed frank invasion, and 3 displayed early invasion. The rest of cases had different degrees of dysplasia. Immunoglobulins IgG, IgM and IgA as well as CEA antibodies were detected in all cases of OLP with epithelial dysplasia with varying degrees of intensity and distribution. Conclusion: The presence of the immunoglobulins IgG, IgM, IgA and CEA antibodies and their distribution pattern in the dysplastic epithelium of OLP may aid in understanding the biological behavior of certain cells that undergo differentiation to premalignant or neoplastic cells. This will help in accurate diagnosis and, in turn, a definite line of treatment will be easily achieved.
MOLECULAR SIGNATURE FOR PREDICTING RISK OF CANCER DEVELOPMENT IN ORAL LESIONS WITH DYSPLASIA

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Identification of oral lesions with dysplasia at high risk of malignant transformation remains a major clinical challenge. It is of utmost importance for identifying patients in whom early intervention will lead to more effective disease management. Currently, there are no biomarkers that can be used in clinics to predict these high risk lesions. There is an urgent clinical need for biomarkers that allow identification of high-risk oral lesions. We identified and verified five potential markers - S100A7, prothymosin α, 14-3-3γ, 14-3-3δ and heterogeneous nuclear ribonucleoprotein K (hnRNPK) using proteomics to distinguish oral lesions with dysplasia and oral cancers from normal oral tissues. We evaluated their potential for identification of oral dysplasia at high-risk of cancer development. Using immunohistochemistry, expressions of S100A7, prothymosin α, 14-3-3γ, 14-3-3δ, hnRNPK and p16 (a surrogate marker for HPV) were analyzed in 110 patients with oral dysplasia and known clinical outcome over ten years of follow up. Cancer-free survival was determined using Kaplan-Meier survival analysis and significant factors were identified by Cox regression multivariate models. Cytoplasmic S100A7 overexpression emerged as the most significant candidate marker associated with cancer development in dysplastic lesions (p = 0.041, Hazard’s ratio =2.36). The performance of S100A7 was further improved using a panel of proteins that constitute a molecular signature for predicting risk of cancer development in oral lesions with dysplasia with high sensitivity and specificity. Our molecular signature is likely to find utility in clinical practice for predicting patients having oral lesions with dysplasia who are at high risk of cancer development.

METASTATIC CARCINOMAS TO MANDIBLE AND MAXILLA. REPORT OF SEVEN CASES

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Metastatic tumors to the oro-facial region are rare and may occur in soft tissues or bone. In the mandible and maxilla, metastases appear more often than primary malignancies. In 25% of cases the metastasis is the first sign of malignant disease. Lung, breast, kidney, colon, prostate and thyroid carcinomas are reported as the most common metastatic diseases to the area, specially, breast in women and lung in men. The clinical presentation of metastatic lesion to mandible or maxilla can be variable leading to misdiagnosis of a benign process. In general, an early metastasis to the maxillofacial complex is asymptomatic. Therefore, a biopsy is mandatory in patients with a known history of carcinoma and a non-diagnosed mandible/maxilla radiolucent or mixed lesion. We report seven cases from NOVA Oral pathology department with the purpose to provide awareness about metastatic tumors to the jaws.
**#37**

PEAU D'ORANGE MUCOSA: A CLINICAL PEARL FOR IDENTIFICATION OF POLYMORPHOUS LOW-GRADE ADENOCARCINOMA?
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BACKGROUND: The clinical presentation of polymorphous low-grade adenocarcinoma (PLGA) is relatively non-specific. We have observed cases in which the overlying mucosa has exhibited a finely stippled, slightly papillary, or "peau d'orange" appearance. Microscopic examination of such cases exhibits slightly pebbly to markedly papillary hyperplasia of the surface epithelium, with tumor often infiltrating just beneath the epithelium. OBJECTIVES/STUDY DESIGN: In order to assess how frequently this type of papillary epithelial hyperplasia may be found in association with various minor salivary neoplasm types, we conducted a retrospective clinicopathologic review of archived cases of PLGA, adenoid cystic carcinomas (ACC), mucoepidermoid carcinomas (MEC), and pleomorphic adenomas (PA) of the oral cavity and oropharynx. RESULTS: Among cases in which surface epithelium was present for evaluation, the frequency of marked papillary epithelial hyperplasia, slightly pebbly surface epithelium, and no surface epithelial change for each tumor type was as follows: PLGA (n=23) 35%, 26%, 39%; ACC (n=18) 0%, 44%, 56%; MEC (n=17) 0%, 41%, 59%; PA (n=28) 0%, 46%, 54%. Among these cases, the most common site of involvement was the palate (PLGA 83%, ACC 59%, MEC 65%, PA 86%). The sensitivity and specificity of marked papillary epithelial hyperplasia for PLGA were 35% and 100%, respectively. CONCLUSIONS: Marked papillary epithelial hyperplasia was present in only a small proportion of PLGA. However, our findings suggest that when present within the context of a palatal salivary neoplasm, papillary epithelial hyperplasia may be highly specific for PLGA. Accordingly, peau d'orange mucosa may represent a useful clinical clue for identification of PLGA.

**#38**

THE EXPRESSION OF CELL ADHESION MOLECULE (CD44) IN MUCOEPIDERMOID CARCINOMA AND ITS PROGNOSTIC VALUE
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Abstract: The most common malignant salivary gland tumors that affect both adult and children is mucoepidermoid carcinoma (MEC). It usually affects both minor and major salivary glands but parotid gland is considering the most common site in which this tumor arises. Histologically, MECs are composed of epidermoid, mucous, and intermediate cells and graded to low, intermediate, and high according to one of the following grading systems: modified Healey system, the AFIP grading system, and Brandwien system. This grade scheme for MEC is important to determine the tumor progression and patient management. A total of 15 cases of MECs will be evaluated immunohistochemically for CD44 expression. CD44, a trans-membrane glycoprotein, is an adhesion molecule of cell surface that play a role in the connections between cell-cell and cell-matrix. Many malignant tumors express high levels of CD44 like breast and prostate cancer, thus, CD44 may be used as an indicator of aggressive behavior of some human malignancy. However, the role of CD44 in MEC remains unclear. The purpose of the present study is to evaluate the immunohistochemical staining of CD44 in different grades of mucoepidermoid carcinoma (MEC). This result will further correlated with clinic-pathological data to determine if this staining can predict the tumor biological behavior.
CLEAR CELL VARIANT OF ORAL SQUAMOUS CELL CARCINOMA

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The clear cell variant of squamous cell carcinoma (CCSCC) was recently first described in the oral cavity by Frazier et al. (2012), as an infiltrating gingival tumor predominantly composed of epithelial cells with clear cytoplasm containing glycogen. We present a single case of CCSCC in a 60-year-old female patient. The lesion was noted 4 months before the first consult and clinical examination revealed a 4 x 3 cm asymptomatic ulcerated swelling in the posterior buccal mucosa extending to the soft palate. Microscopically, tumor islands with cellular pleomorphism and mitotic figures exhibited central epithelial cells with clear appearance. The glycogen intracytoplasmic content was confirmed after periodic acid Schiff staining. By immunohistochemistry, the tumor cells were positive for CK AE1/AE3 and p63, and negative for vimentin and CD10. The final diagnosis was of clear cell variant of oral squamous cell carcinoma. The patient was submitted to surgical removal and adjuvant radiotherapy. Local recurrence was observed 6 months after the surgery with no signs of regional metastasis. Currently, there is no sign of recurrence 12 months after the second surgery. This is the second reported case of CCSCC of the oral cavity. The study of large series of CCSCC cases are necessary to clarify whether clear cells are important for the prognosis or only represent an additional microscopic detail.

B-CELL LYMPHOMA, UNCLASSIFIABLE, WITH FEATURES INTERMEDIATE BETWEEN DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) AND BURKITT LYMPHOMA (BL): A REPORT OF 5 CASES IN THE ORAL CAVITY

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Background: The 4th edition of the World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissues introduced the category of B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and BL (DLBCL/BL). DLBCL/BL includes a subset of double/triple-hit B-cell lymphomas (with rearrangements of both MYC/8q24 and BCL2/18q21 and/or BCL6/3q27). DLBCL/BL has high-grade morphologic features which includes the presence of many mitoses, abundant apoptosis with a starry-sky pattern due to many tingible body macrophages, and a monotonous infiltrate of smaller, more intermediate-size cells, of similar size to macrophage nuclei. The CD10 positive B-cell phenotype frequently seen in DLBCL/BL is similar to that of BL, but unlike BL the neoplastic cells are usually Bcl-2 positive and display a slightly lower Ki-67 proliferative fraction (>90%) compared to BL (100%, or close to 100%). Methods: All available cases of large B-cell lymphoma from the oral cavity accessioned from 2003 to 2012 were retrieved and classified on the basis of the 2008 WHO criteria. All available IHC and FISH studies were reviewed. Results: 5 cases of DLBCL/BL were identified. The mean age at presentation was 76 years with a 4:1 female to male predilection. The sites involved were base of tongue 2, tongue 1, palate 1, and maxilla 1. Immunohistochemically, the lymphomas were positive for CD20 (5/5, 100%), CD5 (1/5), CD10 (4/5, 80%), Bcl-6 (3/4, 75%), MUM1 (1/3), Bcl-2 (4/5, 80%), Cyclin-D1(0/5), EBER, (0/5), and Ki 67(mean 96%, range 90-100). Of the cases 5 of DLBCL/BL, 1 was a double-hit lymphoma (MYC/BCL6). Conclusions: DLBCL/BL occurs in the oral cavity and is important to recognize because of the reported aggressive clinical course and poor response to therapy.
DEVELOPMENT OF AN ACTIONABLE TEST FOR RISK STRATIFICATION OF ORAL PREMALIGNANT LESIONS

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Early detection of at-risk oral lesions followed by effective intervention is the key to control oral cancer. Both retrospective and prospective cohorts from our group have shown that loss of heterozygosity (LOH) at 9p21 is a risk marker for cancer progression. However, the technique used is radio-isotope-based electrophoresis (RE) with costly, labor-intensive and time barriers. The purpose of the study is to develop a comparable lab-friendly actionable test using fluorescence-based capillary electrophoresis (FCE). Methods: A total of 52 FFPE samples of low-grade lesions (LGL; 29) and high-grade lesions (HGL; severe dysplasia/CIS 23) from the surgical samples were analyzed for LOH at 9p21 using RE and FCE. Paired connective tissue was used as control. RE used 4ng template DNA, radio-isotope-labeled primers, large polyacrylamide gel, negative films, and visual interpretation; FCE used 2.5ng template DNA, 5-carboxyfluorescein (FAM)-labeled primers, 16-capillary electrophoresis (ABI 3130xl Genetic Analyzer), and GeneMapper® Software V4.1 (LifeTechnologies, CA). On FCE, automated calculation of 60% difference was scored as LOH. Results: The time required for LOH analysis was considerably lower with FCE (60 minutes) compared to RE (>8 hours). A total of 208 PCRs were run on each technique. When using software interpretation on FCE results, there was a 97% consistency between the two techniques. Both approaches detected significant LOH in HGLs (87%) compared to that in LGLs (59%) (P=0.03). Conclusions: With the advantage of low cost, fast turnover, less amount of template DNA, and objectivity, the FCE on 9p21 has provided a potential actionable test for the risk assessment of oral lesions. (TFRI 2009-24; SOF141, co-sponsored by Genome BC and LED Medical Inc.)

EFFECTS OF SALVADORA PERSICA EXTRACT ON DOK ORAL EPITHELIAL DYSPLASIA AND PE/CA-PJ15 ORAL CANCER CELL LINES

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Objectives: To investigate the effects of S. persica on human oral squamous cell carcinoma (PE/CA-PJ15), oral epithelial dysplasia (DOK), and normal periodontal ligament fibroblast (PDL) cell lines, and to determine its potential chemopreventive or inhibitory effects on oral cancer. Materials and Methods: Aqueous extracts of S. persica of various concentrations ranging between zero (negative control) and 15.75 mg/ml were applied to cultured PE/CA-PJ15, DOK, and PDL cell lines. Six independent runs were performed for each concentration. Effect on cell proliferation and survival was tested by the MTT assay. Average optical density readings from the MTT assay for various concentrations were compared to the average reading for the negative control group using the student t-test. The differences were considered significant at a value of p < 0.05. Results: Cytotoxic effects were significant (p < 0.05) at concentrations of 11.25, 13.50 and 15.75 mg/ml for PE/CA-PJ15 and DOK cell lines and of 13.50 mg/ml for PDL cell line. Conclusions: Cytotoxic effects of aqueous extracts of S. persica on both oral cancer and epithelial dysplasia cell lines were significant at a concentration lower than the concentration which is significantly cytotoxic for the normal periodontal ligament fibroblast cell line. The results suggest therapeutic anticancer and cancer preventive potentials of S. persica.
ANALYSIS OF BIGLYCAN IN SALIVARY TISSUE: IMPLICATIONS FOR SJOGREN'S SYNDROME

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Toll-like receptors (TLRs) are upregulated in salivary tissue from Sjögren's syndrome (SS) patients, although the functional effects of receptor ligation are poorly understood. Moreover, the ligand(s) that activate TLRs in the context of SS remain unknown. TLRs are enhanced early in SS disease in mouse models, and this may represent a critical event in pathogenesis. Danger associated molecular patterns (DAMPs), including extracellular matrix (ECM) proteins, bind specific TLRs and are implicated in numerous autoimmune diseases, but have not been evaluated in SS to date. Objective: To determine whether biglycan activates Tlr4 in salivary cells, and whether Biglycan is upregulated in submandibular salivary gland (SMG) tissue in early SS. Methods: We used the rat parotid cell line Par-C10 to determine whether biglycan enhances expression of Tlr4 and Tlr signaling intermediates by quantitative PCR (qPCR). We then isolated SMG tissue from an SS mouse model (NOD/ShiLtJ) prior to disease development. We used NOD/ShiLtJ female animals (n=10) at four weeks of age. Age and sex matched BALB/c animals were used as controls (n=10). Expression of Biglycan in SMG tissue was evaluated by qPCR. Results: Preliminary data suggest biglycan upregulates Tlr4 and MyD88 expression in Par-C10 cells. Biglycan is elevated in SMG tissue of NOD/ShiLtJ mice several weeks prior to lymphocytic infiltration. Conclusion: Biglycan stimulated Par-C10 cells express enhanced Tlr4 and MyD88. Biglycan expression is enhanced in SMG tissue from NOD/ShiLtJ mice several weeks prior to lymphocytic infiltration, suggesting aberrant expression of DAMPs may activate Tlr4 signaling, and this may represent an early event in SS pathogenesis that is amenable to therapeutic targeting.

LATE POSTOPERATIVE HEMORRHAGE IN A PATIENT

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COX has 2 isoforms: COX-1 and COX-2.5,6 COX-1 is expressed constitutively in most tissues, and COX-2 is induced primarily by inflammatory mediators.7,8 Although both isoforms are present in platelets, COX-1 is the major isoform that contributes to coagulation, because it is critically important in the formation of thromboxane A2 (TXA2) by way of the arachidonic acid (AA) pathway.9 AA is a potent inducer of platelet aggregation.1,3,4 When AA is exposed to an activating agent, such as ADP, it undergoes a series of enzymatic reactions that culminates in the production of TXA2.10 TXA2 is the predominant product of the COX-1 pathway and is a major metabolite of AA in platelets. TXA2 is necessary for normal platelet function. Therefore, the inhibition of, or a deficiency in, COX-1 will compromise the AA pathway, thereby reducing platelet secretion and altering normal platelet aggregatory function.1,3 COX-1 deficiencies are usually caused by drug interactions with the enzyme itself. In addition, studies have identified genetic mutations that can result in COX-1 deficiency.2 We present the hospital course, management, and diagnosis of a patient with an undiagnosed COX-1 deficiency who had had third molars removed.
DENTAL EPITHELIAL STEM CELLS IN AMELOBLASTOMAS
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Recent research and our previous work have shown the existence of dental epithelial stem cells (DESC) in the continuous growing mouse incisor cervical loops. Some markers have been identified for marking these DESC, including Sox2, Lgr5, and CD49f (intergrin alpha6). In some organs, stem cells are uniquely poised to serve as tumor cells of origin. Whether DESC are present in ameloblastoma and serve as tumor cells of origin remains unclear. Purpose: to determine if DESC exist in ameloblastomas using DESC markers, Sox2, Lgr5 and CD49f. Method: We used Sox2, Lgr5 in situ hybridization and Sox2, CD49f immunohistochemistry to examine 10 ameloblastomas and compared those results with the expression in mouse incisor cervical loops. Results: Our results showed that the majority of the epithelial nests of ameloblastomas are immunoreactive for Sox2, consistent with previous report. However, the oral mucosal epithelial cells are also immunoreactive for Sox2. CD49f is also immunoreactive in some ameloblastoma nests, but less extensive than Sox2. Both Sox2 and Lgr5 RNA signals can be identified in ameloblastoma nests. Similar to the expression in mouse incisor cervical loops, Sox2 signals distribute more extensive than Lgr5. However, although Lgr5 is mainly expressed in the stellate reticulum in mouse incisor cervical loops, Lgr5 is expressed mainly in peripheral cells rather than stellate reticulum-like cells in ameloblastomas. Conclusion: Our results showed all three DESC markers, Sox2, Lgr5, CD49f, are expressed in the tumor cells in ameloblastoma, although their distributions are not exactly the same. This result suggested that there might be DESC present in ameloblastoma, making DESC a candidate for the origin of odontogenic neoplasms.

EFFECTS OF SECRETED OSTEOPONTIN FROM HUMAN OSTEOBLASTIC CELLS ON ADHESION AND MIGRATION OF AN ORAL SQUAMOUS CELL CARCINOMA CELL LINE
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Squamous cell carcinoma is the most prevalent malignant neoplasm of the oral cavity, which may invade and destroy bone tissue due to increased osteoclast activity. The matricelular protein osteopontin (OPN) has been associated with more aggressive tumors, since OPN can promote cell adhesion, proliferation and invasion. In bone, OPN is the most abundant non-collagenous protein, especially concentrated at bone interfaces, and play important roles in osteoblast adhesion and function. The present study aimed to investigate the effects of OPN secreted by human osteoblastic cells (SAOS-2) on cell adhesion and migration of a human squamous cell carcinoma cell line (SCC9). SCC9 cells were plated on Transwell® and cocultured with SAOS-2 at the time of OPN peak expression (day 10 of SAOS-2 culture). SCC9 cells exposed to SAOS-2 with over 90% inhibition of OPN expression by RNAi, and SCC9 cells grown alone were used as controls. After 4 and 24 h, SCC9 cells were enzymatically detached from Transwell®, and counted using a hemocytometer for quantitative evaluation of cell adhesion. SCC9 cell migration was determined after 24 h. Briefly, the remaining cells on the upper surface of Transwell® were completely removed and the cells on the opposite surface were stained with toluidine blue and counted using a x20 objective. SCC9 cell adhesion was similar among the groups at 4 h (Kruskal-Wallis, p > 0.05). However, SCC9 cells cocultured with SAOS-2 showed a significantly higher cell adhesion compared with both controls at 24 h (Kruskal-Wallis, p < 0.05). SCC9 cell migration was not affected by either the presence of SAOS-2 or OPN (Kruskal-Wallis, p > 0.05). In conclusion, osteoblast-derived OPN may promote SCC9 cell adhesion, but not its migration, in vitro.
INTRAOSSEOUS XANTHOMATOUS LESIONS OF THE MANDIBLE. REPORT OF THE CLINICOPATHOLOGIC CHARACTERISTICS OF 7 CASES AND LITERATURE REVIEW.
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Background: Intraosseous xanthomatous lesions (IXLs) constitute a heterogeneous family of rare, non-neoplastic pathoses generally classified as xanthomas (IXs) and xanthogranulomas (XGs). IXs manifest as solitary, primary lesions or in association with other cutaneous and/or endocrine-metabolic diseases. Histopathologically, IXs are characterized by the presence of abundant lipid-containing macrophages. XGs, also known as “benign fibrous histiocytoma of the bone”, feature numerous lipid-laden, non-Langerhans histiocytes and a prominent fibroblastic component. Reports of IXs of the jaws are scarce with only 4 well-documented examples in the literature. Herein, we report our clinicopathologic experience with IXLs of the jaws and review the pertinent literature.

Materials and Methods: All histologic cases of IXLs in the period 2000-2014 were retrieved and information regarding the epidemiologic, radiographic and microscopic characteristics of the lesions were collected. Results: Seven IXLs were identified; 5 cases were diagnosed as IXs, 1 as XG and another as IXL with atypical cell component. All 7 cases affected the mandible (M:F=4:3, age range: 15-46 years, mean: 25.7 years). Radiographic features varied with the majority of IXLs presenting as ill-defined radiolucencies. Interestingly, 1 IXL was associated with traumatic bone cyst. Conclusions: IXLs of the jaws are rare. A strong predilection for the mandible is observed, in accordance with other reported examples. Differential diagnosis between IX and XG is challenging due to subtle histopathologic differences. Exclusion of an underlying lipid or metabolic disorder is required.

INTEREST AND KNOWLEDGE OF FLORIDA DENTISTS AND UNIVERSITY OF FLORIDA COLLEGE OF DENTISTRY STUDENTS ABOUT ORAL SOFT TISSUE BIOPSY AND BIOPSY TECHNIQUES

Purpose: In an effort to improve prognosis for oral cancer patients, early detection is paramount. To this end, the ability and knowledge of performing oral soft tissue biopsies is critical. Although dental schools place an emphasis on oral cancer screenings, the interest levels, knowledge, and ability of dental students and dentists to perform biopsies remains largely unknown. This study aims to determine the confidence and knowledge of performing biopsies in these groups. Materials and Methods: Following IRB approval, two Qualtrics® based surveys were conducted via email distribution. One targeted 3rd and 4th year UF dental students and dental residents and the other was directed to UF College of Dentistry alumni and Florida dentists. The surveys included a combination of closed- and open-ended questions directed toward skill and confidence levels of oral lesion detection and biopsy techniques. Results: A total of 184 responses were received; 84 from students/residents and 100 from alumni dentists. From the student survey, 90% felt general dentists should be able to perform biopsies, but only 7% of dental students felt confident performing a biopsy. About 90% were interested in taking an elective course about biopsies. Among the dentists surveyed, 83% indicated that general dentists should perform biopsies, 46% felt confident performing an oral biopsy and 71% were interested in continuing education courses addressing identification of lesions and biopsy techniques. Conclusion: Current dental curriculum should address the knowledge gaps and include information regarding why, when and how of oral biopsies. In addition, continuing education courses should be designed to address this issue and are needed to improve outcomes to enhance patient care.