

Herein, we report an atypical clinicopathological presentation of amelanotic melanoma first diagnosed in the oral cavity of a 68-year-old man. The tumor was immunopositive for HMB45 and S-100, and weakly positive to Melan A. PET (positron emission tomography) and CT (computed tomography) scans demonstrated widespread organ and bone metastases, obviating surgical intervention. Standard immunotherapy was instituted with ipilimumab and nivolumab. At 3-weeks, near resolution of the oral lesion was evident and repeat imaging showed resolution of the left lung lesions and marked reductions in size of other affected sites. The patient subsequently experienced and recovered from multiple immune-related adverse events, including autoimmune carditis, which was managed with steroid administration. Following subsequent immunoregimens and 4 months since the initial diagnosis, the patient succumbed to sudden apparent cardiac arrest. Historically, surgery, chemotherapy, and radiotherapy to manage mucosal melanoma have yielded poor long-term outcomes, necessitating alternative efforts to improve patient care. Immunotherapy is an emerging modality for management of late-stage melanoma and has shown promising results to extend overall survival.

**DOES THE GERMLINE DEFICIENCY IN TOLL-LIKE RECEPTOR (TLR)2 AFFECT THE 4-NITROQUINOLONE N-OXIDE (4-NQO)-INDUCED CARCINOGENESIS IN THE UPPER AERODIGESTIVE TRACT? DR. ZOYA KURAGO<sup>A</sup>, DR. CHITHRA PALANI<sup>A</sup>, DR. SANTHAKUMAR MANICASSAMY<sup>A</sup>, DR. LALITHA RAMANATHAPURAM<sup>B</sup>. <sup>A</sup> AUGUSTA UNIVERSITY, <sup>B</sup> MEMORIAL SLOAN KETTERING CANCER CENTER**

TLR2 is implicated in the development and/or progression of several cancer types. We showed recently that activated TLR2 in human TLR2-high oral squamous carcinoma cells (OSCC) directly promote their growth and survival via the extracellular regulated kinases (ERK)1/2 signaling, among other functions (Palani et al, *Oncotarget* 2018;9:6814-29). However, most of the mechanisms of TLR2 function in squamous carcinogenesis remain unknown.

**Objectives & Approach:** To develop protocols and cell lines for targeted studies of squamous carcinogenesis in upper aerodigestive tract (UADT), we used an established (Protocol #1) and a modified (Protocol #2) 4-NQO carcinogenesis models in wild-type, TLR2<sup>-/-</sup> and TLR4<sup>-/-</sup> mice. Protocol #1 included carcinogen alone x 10 weeks, followed by 10% ethanol for 26 wks total. Protocol #2 included carcinogen and 5% ethanol x 19 weeks total. The study was approved by AU IACUC.

**Results:** Both protocols produced epithelial dysplasia and SCC in the oral and esophageal mucosae. In Protocol #1, fewer SCC developed in the absence of TLR2 than in the WT hosts (p=0.03). In contrast, Protocol #2 produced somewhat fewer SCC in WT hosts than in either TLR2<sup>-/-</sup> or TLR4<sup>-/-</sup> hosts (difference not significant). Moreover, there was marked intraepithelial exocytosis of leukocytes throughout the UADT in Protocol #2, irrespective of TLR expression. This contrasted with minimal exocytosis induced by Protocol #1. The characterization of the mucosal inflammation is ongoing. In addition, two OSCC cell lines were established for use in orthotopic models.

**Conclusions:** 1) The two protocols induced UADT SCC, but differed in the levels of mucosal inflammation. 2) TLR2 may have contributed to carcinogenesis in Protocol #1, but not in

Protocol #2. 3) The specific roles of TLR in mucosal squamous carcinogenesis may depend upon additional factors, such as inflammation.

**EPSTEIN-BARR- VIRUS (EBV)-NEGATIVE PLASMABLASTIC LYMPHOMA: A CASE REPORT. DR. ANDRÉ MYLLER BARBOSA SILVA<sup>A</sup>, PROF. OSLEI PAES DE ALMEIDA<sup>B</sup>, PROF. FLÁVIA SIROTTHAU CORREA PONTES<sup>C</sup>, PROF. HÉLDER ANTÔNIO REBELO PONTES<sup>C</sup>, PROF. FELIPE PAIVA FONSECA<sup>A</sup>. <sup>A</sup> SCHOOL OF DENTISTRY, FEDERAL UNIVERSITY OF MINAS GERAIS, <sup>B</sup> PIRACICABA DENTAL SCHOOL, UNIVERSITY OF CAMPINAS, <sup>C</sup> JOAO DE BARROS BARRETO UNIVERSITY HOSPITAL, FEDERAL UNIVERSITY OF PARÁ, BELÉM**

Plasmablastic lymphoma is an aggressive neoplasm with poor response to therapeutic management. It is commonly associated with HIV infection and it is strongly associated with Epstein-Barr virus (EBV) in most of the cases, although negative cases to EBV can be occasionally identified. The aim of this report is to describe an original case of a 52-year old male patient referred to our department due to maxillary swelling causing facial asymmetry of the right side. His medical history was positive for HIV infection. The extraoral examination revealed hemifacial edema on the right side, involving the middle and lower thirds of the face, while intraoral exam showed an ulcerated swelling extending through the hard and soft palate on the right side, involving the buccal vestibule. CT scan revealed the presence of a hypodense image destroying the maxilla, involving the maxillary sinus, floor of the orbit and the nasal cavity. Incisional biopsy was done revealing a sheet-like proliferation of atypical large cells with plasmablastic appearance. Individually, these cells had eosinophilic cytoplasm with high nuclear-to-cytoplasmic ratio. Centrally and eccentrically cellular nuclei, with vesicular chromatin and evident nucleoli, with a starry-sky appearance were found. Immunohistochemistry was positive for CD138, EMA and MUM1, negative for CD20 and LCA, demonstrating monoclonality to lambda light chain. EBER was negative and final diagnosis was rendered as EBV-negative plasmablastic lymphoma. Unfortunately, the patient died two months after diagnosis.

**ORAL IATROGENIC KAPOSÍ'S SARCOMA: CASE REPORT. DR. ANDRÉ MYLLER BARBOSA SILVA<sup>A</sup>, PROF. JULIO CESAR TANOS DE LACERDA<sup>B</sup>, MS. JOSÉ AUGUSTO DIAS ARAÚJO<sup>C</sup>, MS. ALINE FERNANDA CRUZ<sup>D</sup>, PROF. RICARDO ALVES MESQUITA<sup>A</sup>, PROF. PATRÍCIA CARLOS CALDEIRA<sup>A</sup>, PROF. RENATA GONÇALVES RESENDE<sup>E</sup>. <sup>A</sup> SCHOOL OF DENTISTRY, FEDERAL UNIVERSITY OF MINAS GERAIS, <sup>B</sup> SCHOOL OF DENTISTRY OF THE FACULDADE NEWTON PAIVA/ HOSPITAL METROPOLITANO ODILON BEHRENS (HMOB), <sup>C</sup> HOSPITAL METROPOLITANO ODILON BEHRENS (HMOB), <sup>D</sup> SCHOOL OF DENTISTRY OF THE UNIVERSIDADE FEDERAL DE MINAS GERAIS (UFMG)/ HOSPITAL METROPOLITANO ODILON BEHRENS (HMOB), <sup>E</sup> SCHOOL OF DENTISTRY OF THE FACULDADE DE ESTUDOS ADMINISTRATIVOS DE MINAS GERAIS (FEAD)/ HOSPITAL METROPOLITANO ODILON BEHRENS (HMOB)**

This study presents a case of a 29-years old male patient with immunosuppression-associated Kaposi's Sarcoma (KS) caused by the medicines for the leprosy treatment. The patient was presented to the stomatology service of the Hospital Metropolitano Odilon Behrens, Brazil, with a tumoral growth in the rights side of the lip commissure, with no history of local trauma. He was previously diagnosed with borderline leprosy, cataract and glaucoma and was under regular use of 100mg prednisone for 1 year and 6 months for treatment of leprosy complication. At the clinical examination it was possible to observe an erythematous tumoral growth in the lip commissure, right side, with necrosis on the surface measuring approximately 12mm. In view of the diagnostic hypothesis of non-neoplastic proliferative lesion and neoplasia of mesenchymal origin, an incisional biopsy of the lesion was performed. Microscopic findings and immunohistochemical examination of the lesion led to a final diagnosis of KS. The patient was submitted to the rapid serology test for human immunodeficiency virus (HIV), which proved to be negative, a result confirmed by the fourth-generation test. The patient was referred for surgical evaluation of the lesions and for reevaluation of the systemic steroid dosage. Faced with the infeasibility of reducing corticoid dosage, the patient underwent surgical excision of the lesions and was free of recurrence of the disease for 2 years. So, this case shows the importance of including KS in the differential diagnosis of oral cavity lesions in patients who use chronic immunosuppressant drugs.

#### SYMMETRICAL PALATAL FIBROMATOSIS

(SPF) – 5 NEW CASES AND A LOGICAL DIAGNOSTIC NAME FOR A RARE LESION

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**Objective:** To present 5 new cases of a lesion reported fewer than 20 times in the literature, under a dozen different names, and to recommend the most appropriate name.

**Methods:** 5 new SPF cases are clinically and microscopically characterized, with a literature review.

**Findings:** 5 cases (3F & 2M) presented in patients 20-39 years of age. All presented as bilateral, symmetrical, asymptomatic, sessile, moderately firm or soft (n=2) masses of the lateral posterior hard palate; 2 were isolated to the tuberosities. All masses were normal in color, with smooth, nonulcerated surfaces and occasional broad surface nodularity. One case had bilateral secondary, anterior extensions. Underlying bone was radiographically normal, and adjacent teeth were asymptomatic. All masses seemed to originate from tissues over the palatal bone, only secondarily extending to gingivae and/or crestal tuberosity bone, i.e. this does not appear to be a gingival entity, as previously thought. Cases had been present 2-15 years, with no familial or environmental etiologies identified. Histopathologically, masses were comprised of dense, avascular fibrous connective tissue with scattered thick bands of collagen and occasional slight surface nodularity. Surface epithelium showed regions with long, pointed and/or thin rete processes, and subepithelial stroma contained scattered large, angular fibroblasts, sometimes with multiple nuclei, sometimes with a "smudged" appearance, consistent with those in giant cell fibroma; melanin

granules were not present. Conservative surgical excision affected cure in all cases.

**Conclusion:** The present investigators propose SPF as the most accurate name for this chronic, presumably rare and certainly unique entity. It fits the definition of fibromatosis more than reactive fibrous hyperplasia, and the presence of giant fibroblasts in the stroma is a unique, possibly required, histopathologic feature. Conservative surgical excision is the recommended treatment, with no recurrences reported to date.

#### SCREENING OF B-CATENIN INHIBITOR FROM MEDICINAL PLANT EXTRACTS FOR INTRACTABLE RECURRENT ORAL CANCER.

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**Objectives:** Recent progress in malignant tumors has revealed cancer stem cells (CSC) can be the key contributors in tumor ignition, progression, and chemoradiotherapy recurrence. CD133 is a prognostic marker of survival in squamous cell carcinoma (SCC) including OSCC. CD133 can physically associate as a ternary complex with HDAC6 and the central molecule of the canonical Wnt signaling pathway,  $\beta$ -catenin. This association stabilizes  $\beta$ -catenin and leads to activation of  $\beta$ -catenin signaling targets in colon and ovarian cancer cell lines. Therefore, given that CD133 marks progenitor cells and strongly related with  $\beta$ -catenin activation, targeting  $\beta$ -catenin may be a means to treat multiple cancer types in CD133+ CSC-like cells. In this study, we confirmed that b-catenin was also overexpressed in KBCD133+ cells which acquired CSC-like characteristics than KB cells. Therefore we hypothesized a natural extract capable of inhibiting the activity of  $\beta$ -catenin can effectively inhibit the cancer progression of OSCC which acquired CSC-like characteristics.

**Findings:** We measured  $\beta$ -catenin activity of 54 plant extracts to select new candidates with  $\beta$ -catenin inhibitory effect. We have found 5 candidates showed significant inhibited  $\beta$ -catenin activities and Raphanus sativus L. seed (RSLs) extracts effectively induces cell apoptosis in KB as well as KBCD133+ cells. We also investigated that RSLs has strong inhibit nuclear localization of  $\beta$ -catenin, EMT via Axin/GSK-3 $\beta$ / $\beta$ -catenin pathway.

**Conclusions:** We propose that RSLs can be used as a new alternative chemotherapeutic for the treatment of intractable recurrent oral cancer.

#### OSTEOSARCOMA OF THE JAWS DURING PREGNANCY: CASE REPORT AND REVIEW OF THE LITERATURE.

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Osteosarcoma of jaw bones represents less than 1% of all head and neck malignancies. Malignancy in pregnant women is also an uncommon event, and occurs in a ratio of one case per 1000 deliveries. The aim of this study is to report a rare case of maxillary osteosarcoma in a pregnant woman, and to review the previous cases published in English literature. A 29-year old woman, in the 33rd week of gestation, presented with a 2.5 cm