tumors presented as solid masses with few ductiform structures. Tumor cells had basaloid appearance with large pleomorphic and prominent nuclei or densely hyperchromatic with scant cytoplasm. Frequent mitotic figures and comedolike necrosis were seen. Tumor infiltration was detected in the perineurial region of the inferior alveolar nerve and within bone medula. In one case, tumor cells has spread to the dental pulp. Immunohistochemically, tumor cells in one case were positive for CK7, 34BE1, CD117, Ki67 (>5 in 10hpf) and negative for p63 and CK5/6.

Conclusion: Two rare cases of mandibular extension of a parotid gland ACC through the mandibular foramen is presented. Computed tomography and magnetic resonance confirmed primary ACC in the parotid gland, suggesting access of tumor cells through mandibular canal. Meticulous clinical and radiographic analysis were essential to detect primary tumor for an appropriate therapy.

DIFFERENTIAL MAST CELL POPULATION IN SUBTYPES AND METASTATIC ORAL SQUAMOUS CELL CARCINOMA.

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Tumor microenvironment is a dynamic network, orchestrated by neoplastic, non-neoplastic cellular, and non-cellular components in tumorigenesis, cancer progression, and metastasis. Mast cells (MCs) can modulate tumor cell activity during angiogenesis and extracellular matrix degradation in breast and lung cancers. MCs are distinguished according neutral proteases like tryptase (MCT), tryptase/chymase (MCTC), and chymase only (MCC). Its role in oral cancer remain controversial. Oral squamous cell carcinoma (OSCC) represents 90% of cases of head and neck cancer with considerable mortality and morbidity.

Objectives: To identify MC population in two topographic regions among OSCC subtypes.

Material and methods: Immunohistochemical study of mast cell tryptase and mast cell chymase was performed in 54 cases of OSCC. Positive cells were counted in 10 consecutive fields at 400X magnification in peritumoral and intratumoral regions. Negative control was considered at the surgical margin histologically negative.

Results: Overall MC density increased 6.3 times in OSCC. MCTC density was significantly higher than MCT ($p<0.001$) mainly in the peritumoral region. High density of MCTC was associated with smokers ($p<0.046$) and metastatic tumors ($p<0.048$). Interestingly, mast cell phenotype of degranulation was registered only in chymase-positive MCs. MCTdensity was low in the periphery of basaloid SCC and higher in less differentiated tumors.

Conclusion: MC population is highly increased in OSCC predominantly with MCTC.High density of chymase-positivity cells suggests a subset of MC chymase only in OSCC and its expression may be related to tobacco consumption, metastasis, local invasion, and differentiation.

SECRETED PROTEINS AS POTENTIAL BIOMARKERS IN ADENOID CYSTIC CARCINOMA OF THE SALIVARY GLANDS.

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Secreted proteins are involved in several physiological mechanisms. In solid tumors, it can be used as diagnostic and prognostic tools. Human anterior gradient 2 (AGR2) and CD10 are proteins secreted in body fluids in prostate cancer. The main of this study was to evaluate expression of the secreted proteins AGR2 and CD10 in adenoid cystic carcinoma (ACC) of the salivary gland. A total of 20 cases of ACC of the salivary glands were examined by immunohisto-chemistry method. Female was more affected (70%) with age varying from 10 to 79. Tumor sizes ranged from 1.3 to 9 (mean 2.7 cm), located mostly in minor salivary glands and submandibular gland. Eleven cases showed neural invasion. AGR2 was typically citoplasmatic and focally expressed in 75% of cases. Its expression was observed in all solid subtype, followed by tubular (88.8%) and cribiform (55.5%). Interestingly, half of ACC exhibited AGR2 expression in the extracellular space or inside ductiform structures. Clinically, neural invasion, nodal involvement, and systemic metastasis were associated to AGR2 expression. The surface protein CD10 was also focally expressed mainly in ductal structures in solid and tubular subtypes. Interestingly, its expression was restricted only to stroma in cribriform subtype. This secreted protein was also found freely inside ductiform structures. Furthermore, peripheral nerves involved in the tumor significantly expressed CD10 ($p = 0.029$) in the tubular subtype.

Conclusion: Neural invasion may involve participation of CD10 in ACC of the salivary gland. Further studies should confirm if extracellular AGR2 and CD10 represent potential biomarkers for salivary detection as diagnostic and prognostic tools in the clinic.

METASTATIC NEUROENDOCRINE PROSTATE CANCER, AN AGGRESSIVE PROSTATE MALIGNANCY: A REPORT OF TWO CASES WITH ORAL MANIFESTATIONS.

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Objectives: Neuroendocrine prostate cancer (NEPC) is a lethal prostate malignancy with a median survival of less than 1 year from time of detection. NEPC can occur de novo or more commonly as a treatment emergent phenomenon (t-NEPC). t-NEPC occurs in a subset of patients with metastatic-castration resistant prostate cancer. Two cases of t-NEPC with oral manifestations are presented highlighting the pathologic features and the varied clinical context in which these lesions presented.

Patients and Methods: Case 1) A 79 year-old man with a history of prostate adenocarcinoma undergoing hormone treatment presented with a fungating mass of the right maxilla and palate, clinically suspicious for squamous cell carcinoma. Biopsy revealed a high grade neuroendocrine carcinoma. Case 2) A 76 year-old man with a history of metastatic prostate adenocarcinoma receiving zoledronic acid and denosumab treatment for bony metastases, presented with mandibular fracture. A segmental resection without reconstruction with debridement

was performed with a clinical diagnosis of medication-related osteonecrosis of the jaw (MRONJ). The pathology revealed a high grade neuroendocrine cell tumor. Both cases were positive for neuroendocrine markers chromogranin, synaptophysin, and CD56, and stained negative for prostate specific antigen (PSA) and prostate specific acid phosphatase (PSAP). Both tumors demonstrated a proliferative index (Ki-67) of 60-70%. An extended panel of immunostains appeared to eliminate other entities from consideration.

Conclusions: Awareness of t-NECP is of importance to correctly diagnosis the entity, recognizing that tumor markers such as PSA and PSAP are negative, and standard serum markers for prostate carcinoma may be stable or show no increase with progression of disease. Neuroendocrine carcinoma in the setting of medication related osteonecrosis of the jaw in a patient with prostate carcinoma needs to be included in the differential diagnosis.

DRUG SCREENING OF ORAL CARCINOMA CELL LINES USING PLASTIC, MOUSE OR HUMAN TUMOR DERIVED MATRICES.

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Objectives: Oral squamous cell carcinoma (OSCC) is the sixth most common cancer worldwide. Traditionally, cancer cell lines cultured in 2D are used to predict the efficacy of new anti-cancer compounds. However, this method has low predicting value for efficacy since more than 80% of the cancer drugs, which have promising effect in pre-clinical studies, fail in Phase II clinical trials. Our group has developed human matrix based product, Myogel, which is extracted from leiomyoma tissue. Our hypothesis is that Myogel represents better the in vivo condition compared with the 2D plastic wells, or even wells coated with mouse derived Matrigel®.

We selected 12 OSCC cell lines and 19 anti-cancer compounds, targeting mTOR and epidermal growth factor receptor (EGFR) signalling pathways. The High Throughput Drug Screening method with five different conditions were used: cells in 2D plastic wells; on top and within Matrigel® or Myogel. Additionally, the morphology of OSCC cells and EGRF location were studied using immunofluorescence staining and confocal microscope.

Findings: Cancer cells on top and within Myogel were less responsive to EGFR inhibitors compared to cells cultured in 2D plastic or Matrigel®. However, in case of mTOR inhibitors, similar efficacy of the drugs in all conditions was seen. The morphology of the carcinoma cells differed depending on the matrix. Within Matrigel, the cells formed isolated round-shaped organoids, whereas the cells within Myogel were stellate-shaped. Immunofluorescent staining revealed that in 2D and Matrigel, EGFR was located primarily on the cell membranes, while in Myogel, the staining was mainly in the cytoplasm.

Conclusions: Carcinoma cells showed different behaviours and responses to anti-cancer compounds depending on the testing conditions. Comparison between clinical data and our in vitroresults are still needed to reveal the most reliable condition for cancer drug testing.

ORAL MANIFESTATIONS AID IN THE DIAGNOSIS OF COWDEN SYNDROME: ROLE OF AN ORAL DIAGNOSTICIAN.

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Cowden Syndrome, also referred to as Multiple Hamartoma Syndrome or PTEN Hamartoma Tumor syndrome (PHTS), is an autosomal dominant disorder with a broad clinical spectrum and wide degree of penetrance. This rare disorder causes an increased predisposition to the development of numerous malignancies, and benign hamartomas and neoplasms. The oral manifestations have also been well documented and are present in nearly all affected individuals by the third decade of life.

Objective: To describe the role of an Oral Diagnostician in the preliminary diagnosis of Cowden Syndrome. We report a case of a patient who presented with pathognomonic oral signs of Cowden Syndrome. Upon further review of her medical and family history, she was referred to her family physician and genetic counselor where the diagnosis of Cowden syndrome was confirmed through genetic testing.

Findings: A 31 year old female presented to the dental clinic at University of Colorado for a routine dental evaluation. The patient was noted to have multifocal papules affecting the gingiva, tongue and buccal mucosa, and multiple papular skin lesions. She reported a history of a thyroid tumor and a family history of breast and uterine cancer. Based on the review of the medical history, family history and oral mucosal findings, a diagnosis of Cowden syndrome was considered. The patient was referred to her family physician and genetic counselor where the diagnosis of Cowden syndrome was confirmed through genetic testing (PTEN mutation). Additional clinical findings included macrocephaly, trichilemommas and thyroid goiter.

Conclusion: The NCCN guidelines list multifocal or extensive oral papules as one of the major criteria in the diagnosis of Cowden Syndrome. The Oral Diagnostician can play a crucial role in the diagnosis. Early diagnosis of patients affected with Cowden syndrome can facilitate early screening, detection and management of benign and malignant neoplasms.

A UNIQUE PRESENTATION OF METASTATIC DISEASE IN A PATIENT WITH AN OCCULT HISTORY OF BREAST CARCINOMA.

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Metastatic disease to the oral cavity is relatively rare and constitutes approximately 1% of all oral cavity malignancies. Skeletal involvement predominates over soft tissue presentations and the posterior region of the mandible is frequently affected. Pain, swelling and sensory alterations have been reported and may mimic periodontal or periapical disease or osteomyelitis. We present a case of a 63-year-old female with a complaint of progressive dysthesia for three months. Panoral and 3D imaging revealed widening of the PDL and loss of lamina dura affecting most of the mandibular teeth, which all tested vital. The patient's