reactions, infectious diseases (fungal or bacterial), sarcoidosis, and Crohn's disease. Here we review CGIR seen over ten years and attempt to clarify their etiologies with the hope that this data will yield information which will allow us to better guide clinicians in the evaluation and treatment of their patients. A review of all cases of CGIR from New York Presbyterian/Queens between 2007-2016 was performed. After eliminating all lesions where foreign material or fungal organisms could be seen, 120 cases of CGIR were identified. Additionally, cases seen in conjunction with a lichenoid inflammatory infiltrate were excluded from the review as they warrant further, separate study. Using relevant clinical information submitted as well as responses to a ten-question survey sent to doctors which included questions regarding the etiology of the CGIR, medical work up, the presence of additional lesions, treatment, progression and recurrence, we identified the following information. Of the 120 cases, 56 were male and 64 were female. The age range was 3−88 years old. 122 sites were identified as some cases had multiple lesions. Only 13 of the 122 lesions were central in bone. The most striking findings was that 9 cases occurred under the age of 18 and all these were in males. Two of these patients had intrabony lesions. In this group, Crohn's disease was found to be the commonest etiology, seen in 5 patients. Therefore, the finding of granulomas, especially intrabony, in a young male warrants a gastrointestinal work up prior to an extensive medical evaluation.

IN VITRO EVALUATION OF THE ANTINEOPLASTIC EFFECT OF METFORMIN ON ORAL SQUAMOUS CELL CARCINOMA.

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Metformin is one of the most commonly prescribed drugs worldwide for the management of diabetes. Oral Squamous cell carcinoma is a public health problem worldwide and very little has been achieved regarding survival rates since the 1980s, despite some advancement in traditional treatment options. Metformin has demonstrated a citotoxic effect on neoplastic cells by inhibiting anabolism and stimulating catabolism. AMPK lead to inhibition of the mTOR pathway, thus reducing global protein translation and, therefore, slowing tumor progression.

Objectives: To evaluate the effect of metformin on viability and proliferation of oral squamous cell carcinoma cells in vitro.

Methods: Three cell lines were used, namely CAL27, HaCat and SCC4 (ATCC). The cutures were treated with a single dose of metformin at 10 mM and 20 mM. Cell proliferation and viability were evaluated at 24h and 48h using flow cytometry. Annexin V-FITC and propidium iodide (PI) were used to establish the rate of apoptosis and cell death, respectively.

Results: metformin proved cytotoxic with increased rates of apoptosis and cell death and in the HaCat (24.5% and 43%, respectively) and SCC4 lines (55% and 35%), especially at 20mM and 48h of treatment, except for the CAL27 line, which did not respond to the treatments.

Conclusion: Metformin caused cell death via apoptosis in oral squamous cell carcinoma cultures in vitro in a dose and time dependent manner.

PERICORONAL LESIONS OF UNERUPTED TEETH: EXPERIENCE IN 25 YEARS.

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Objectives: The aim of this study was to determine the epidemiology and clinical concordance of pericoronal lesions of unerupted teeth in biopsies of the Oral Pathology Laboratory of Universidad Peruana Cayetano Heredia (1991-2015).
A retrospective study was performed. Request forms for anatomical-pathological examination and histopathological slides were assessed. Data registered included: Age, sex, dental piece, presumptive and definite diagnosis. The WHO Classification (2017) was used for cysts and odontogenic tumors

Findings: 270 pericoronal lesions were found (1.69% of the total). There was relationship between the diagnoses and association to teeth (p=0.021), but not with position of the teeth and sex. It was present more in second and third decade of life (range: 5-80 years). The main histopathological diagnoses were dentiger cyst (40%) and normal dental follicle (23.7%). About pericoronal lesions, they mainly were located in inferior third molars (35.93%) and superior canines (21.85%). The concordance between presumptive and definitive diagnosis is low (Kappa=0.2536).

Conclusion: No concordance was found between presumptive and definitive diagnosis, it is the reason why the histopathological study in pericoronal lesions is very important.

A NEW HIGH-RESOLUTION INVASION TEST (HIT) CAN PREDICT MALIGNANT TRANSFORMATION IN ORAL EPITHELIAL DYSPLASIAS.

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Rationale: Detecting the earliest signs of invasion and predicting transformation in oral potentially malignant lesions (OPMLs) can facilitate earlier treatment of oral squamous cell carcinoma (OSCC) and decrease morbidity and mortality. Here we described a new test to diagnose early invasion and predict malignant transformation in OPML.

Methods: Fluorescent immunohistochemist and multichannel colocalization were used to identify invadopodia markers FISH, cortactin and MMP14 in OSCC and OPML. The presence of invadopodia markers was calculated using 3-channel colocalization analysis based on a custom algorithm developed using Volocity Software. The threshold for colocalization was determined by linear least-square fit of the channel intensities and the product of the difference of the means was (PDM) was used to compare the area of colocalization (HIT score). This algorithm was applied to 80 cases (10 cases of non-dysplastic hyperkeratosis, 22 cases of epithelial dysplasias (ED), 20 cases of OSCC and 28 cases from patients who progressed from ED to OSCC) to determine the overall validity of the approach and establish cut off values.

Results: There was a significant and progressive increase in the colocalization of invadopodia markers (HIT score) in dysplasias and OSCC compared to control. The results

showed that the HIT score could detect lesions that transformed to OSCC independently of the histopathological diagnosis with a sensitivity of 84% and specificity of 61.76%, PPV= 0.61 and NPV=0.84, AUC= 0.7653, likelihood ratio of 2.1, $p<0.005$. The HIT score was also able to distinguish transforming from non-transforming dysplasias with a sensitivity of 63.4% and specificity of 73.9%, PPV=0.7, NPV=0.68, likelihood ratio of 2.4, $p<0.01$.

Conclusion: The HIT scores can predict malignant transformation in oral biopsies independent of the histopathological diagnosis. Larger prospective studies are needed to validate and assess the applicability of this test in combination with conventional histopathology.

GRANULAR CELL TUMOR S-100 NEGATIVE VARIANT.

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Granular cell tumor is a benign mesenchymal lesion that occurs more often in the oral cavity and skin. Its cell origin is controversial, including muscle, fibroblasts, neural crest, neural sheath and histiocytes. Granular cell tumors composed of larger and polygonal cells with abundant eosinophilic granular cytoplasm. Classic granular cell tumor shows positive immunostaining for S-100 and vimentin, and in some cases, positive CD68 staining is also reported positive. However, three cases of S100 negative granular cell tumor in oral mucosa and several cases in skin have also been reported in the literature recently. Therefore, the purpose of this study is to report a case of oral S100 negative granular cell tumor to increase the awareness of this entity. A 79-year-old female patient presented with a small asymptomatic, circumscribed mass lesion in the posterior lateral aspect of the palatal torus. Histologically, the specimen was covered by keratinized stratified squamous epithelium showing no pseudoepitheliomatous hyperplasia. The lamina propria consisted of fibrous connective tissue with chronic inflammation and cluster or sheet of large polygonal cells with granular cytoplasm. Immunohistochemistry showed that the granular cells stain positive for CD68 but negative for S100. Currently there is no difference in recommended treatment or in prognosis of S100 negative from S100 positive granular cell tumor. However, it is important to be aware of this rare variant of granular cell tumor for stablishing correct diagnosis.

CALCIFYING ODONTOGENIC CYST PRESENTING ODONTOGENIC KERATOCYST-LIKE AREAS.

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Odontogenic cysts showing features of two or more distinct types of cysts are rare. Particularly, calcifying odontogenic cyst (COC) associated with odontogenic keratocyst (OKC)-like areas have been not reported. The patient, an 81-year-old man, was referred for diagnosis of a mandibular radiolucent lesion of unknown duration. On cone-beam computed tomography, sagittal views revealed a well-delimited, unilocular, and hypodense lesion located in the right edentulous mandibular body, which caused enlargement of the buccal and lingual cortical bone. Panoramic reconstruction revealed that there was thinning of the superior cortical bone. Residual radicular cyst was the clinic-radiographic diagnosis. Under local anesthesia, an incisional biopsy was performed. Microscopically, a cystic cavity lined by ghost cells was observed, with basal cells showing reverse nucleus polarity. Solid areas were also noted. Moreover, there were cystic cavities lined by epithelium presenting a corrugated parakeratin surface and prominent basal cells disposed in a palisaded fashion. Cytokeratins 14 and 19 were positive in both areas, COC and OKC. However, bcl-2 was positive only in COC areas. Thus, the diagnosis was of COC with OKC-like areas. The lesion was excised, confirming these histopathological findings. Currently, the patient is under follow-up, without clinical or imaging signs of recurrence after 2 years of treatment. In conclusion, COC with OKC-like areas is rare and this association seems present a good prognosis.

RARE INFECTIONS OF THE HEAD AND NECK: A CASE SERIES.

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Protozoal, invasive fungal and mycobacterial infections in the head and neck region are exceedingly rare in the developed world. However, in developing countries, endemic infections may involve the oral mucosa or facial skin. Here we present three unusual infections involving these sites. Case 1: A 48-year-old male presented with difficulty in swallowing for a couple of months. Intraoral exam showed ulceration on the palate extending down to the oropharynx. Although a malignant diagnosis was favored initially, that was ruled out since a destructive lesion involving the left auricle and helix was also present. Histopathologically the case was diagnosed as leishmaniasis following identification of small oval organisms in macrophages which was confirmed with Giemsa stain. Case 2: A 38-year-old female presented with multiple nodules on the temporal skin that had been progressively enlarging over the past 2 years and hypo-pigmented skin patches. A prior biopsy was inconclusive. The repeat biopsy of the largest nodule showed presence of bright red colored bacilli on Fite staining confirming a diagnosis of leprosy. Case 3: A 19-yr-old male presented with a one year history of an extra-oral draining sinus after extraction of mandibular posteriors. Following a radiographic diagnosis of osteomyelitis, multiple courses of antibiotics were administered with no resolution and increase in the size of sequestrum. During surgical removal of sequestrum, a soft tissue mass was also noted in the vicinity. Sections from the necrotic bone and tumor-like mass showed chronic granulomatous inflammation along with septate hyphae, consistent with aspergillosis. All patients were referred to an infectious disease expert for further care. Each of this case enforces the need for histopathological awareness of infectious entities, so that appropriate treatment can be rendered.