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Foreign body gingivitis (FBG) has been previously described as a localized inflammatory reaction associated with the presence of foreign material in gingival tissues. However, among the gingival biopsies submitted to the Pacific Oral Pathology Laboratory (POPL) for diagnosis, we have identified foreign material in lesions that are markedly keratinized and described clinically as white plaques rather than inflamed lesions.

**Objectives:** To evaluate the clinical and histopathological features of 86 gingival biopsies containing foreign material retrieved from the POPL archives and to identify the composition of these particles by energy-dispersive x-ray spectroscopy (EDX). Further, primary human gingival fibroblasts (HGF) were stimulated with silica (SiO<sub>2</sub>) microparticles to investigate the production of COL-1, MMP2 and inflammatory cytokines.

**Findings:** Foreign material was most commonly found in women (61%), in the 6th or 7th decade of life, and the clinical lesions were most frequently described as white plaques involving posterior mandibular gingiva. Interestingly, histopathological examination identified verrucous hyperplasia in 60.5% of the cases and epithelial dysplasia in 28.5% of the cases. EDX microanalysis revealed that Si (94%) followed by Ca (85%) and Al (66%) were the most frequently detected elements in the foreign particles. Silica microparticles induced higher COL-1 expression and increased MMP-2 activity in HGF, and higher levels of pro-inflammatory cytokines such as IL-6, IL-8 and TGF- in a micro-particle-concentration-dependent manner.

**Conclusions:** Our study demonstrates that there is a strong association between the presence of foreign material in gingiva and clinically and microscopically demonstrable hyperkeratotic verrucous plaques. Moreover, we found that the most common element in the foreign material is Si which is usually found in the Earth's crust as silica. Our in vitro findings demonstrate the importance of silica-mediated effects on gingival fibroblasts, suggesting that the presence of silica in gingival biopsies could modulate the host inflammatory response and should be further investigated.

**ODONTOGENIC KERATOCYST - THE ROLE OF PTCH1 AND HEDGEHOG SIGNALING IN ITS PATHOGENESIS. PROF. TIEJUN LI, MR. JIANYUN ZHANG. PEKING UNIVERSITY SCHOOL OF STOMATOLOGY**

**Objectives:** Mutations in PTCH1 gene, a receptor in the Hedgehog (Hh) signaling, are responsible for Gorlin syndrome (GS) and are related in tumors associated with this syndrome. The aims of this series of studies were to determine the role of PTCH1 mutation and misregulation of the Hh signaling in the pathogenesis of GS-related and sporadic odontogenic keratocysts (OKCs).

**Findings:** Based on screening of 73 sporadic and 30 GS-related OKCs, we identified PTCH1 mutations in 35.6% (somatic, 26/73) of sporadic cases and 83.3% (germ-line, 25/30) of GS-related OKCs. However, a much higher mutation rate (79%, 30/38) in sporadic OKCs was detected by analyzing epithelial samples separated from the fibrous capsules. The previously underestimated mutation rate in sporadic cases might be due to the masking effect of the attached stromal tissues. Mutations in other genes of the Hh signaling such as PTCH2, SUFU, and SMO were rare and their pathologic roles in OKC were uncertain. Using whole-exome sequencing (WES), we further characterized the mutational landscape of 5 OKC samples lacking PTCH1 mutation and revealed 22 novel mutations, among which two significantly altered genes (CDON and MAPK1) were predicted to affect Hh signaling activity in two cases. However no recurrent mutations were identified in the WES samples and validation cohort of 10 OKCs. Functional analysis revealed that PTCH1 mutations activated Hh signaling and resulted in aberrant cell proliferation via both classical and non-canonical Hh pathways.

**Conclusions:** Our data confirmed the high PTCH1 mutation rate in both GS-related and sporadic OKCs. In PTCH1-negative cases, other genetic alterations were rare, but could also be related to Hh signaling. These results suggested that an inhibitor of the Hh pathway may be effective for the treatment of OKCs.