service of Baylor College of Dentistry. We analyzed the data as to histologic type, location, presence of clinical pigmentation, and configuration, as well as patient age, gender, and race. Intracanalicular nevus was the most common type (57.1%), followed by common blue nevus (23.8%), compound nevus (8.3%), and junctional nevus (3.6%). Combined nevus and cellular blue nevus were extremely rare (2.4% each). The hard palate was the most commonly affected site (38.1%), followed by the buccal mucosa (17.8%), vermilion border (17.8%), and gingiva (11.9%). We also report a case of intramucosal nevus with lipo- matous-like changes and nevrotization on the gingiva. In addition, we report 2 cases of junctional dysplastic nevus, one on the vermilion border of the lip and the other on the hard palate. OMN and early developing melanoma can be clinically indistinguishable; therefore, all unexplained pigmented lesions of the oral cavity should be biopsied. Melanocytic lesions presenting dysplastic or atypical changes should be completely excised.


Introduction. Sjögren syndrome (SS) is a rare autoimmune dyscrasia. Primary SS (pSS), or Sicca syndrome, affects salivary and lacrimal glands predominantly, whereas secondary SS (sSS) occurs in conjunction with other autoimmune connective tissue disorders. In addition to reduced salivary and lacrimal function, serious systemic aspects of the disease are recognized. Care for SS patients is palliative, because no established therapies target the immune dysfunction directly. Initially, T cells were considered to be key mediators of disease; currently an important role for B cells is emerging, because B-cell abnormalities are seen systemically and within salivary glands. However, the contribution of B cells to SS is poorly understood. For B cells to function most effectively, they must be recruited to specific sites where they interact with other cells and secrete mediators to orchestrate immune responses. CXCL13 is a B-cell chemokine that is elevated in many autoimmune diseases. Accordingly, we hypothesized that CXCL13 is up-regulated during SS progression and may serve as a valuable biomarker of disease.

Study design. We quantified CXCL13 by real-time polymerase chain reaction and enzyme-linked immunosorbent assay at various disease time points using pSS and sSS models.

Results. CXCL13 transcript and protein levels increased with disease severity in salivary tissue and serum, respectively. Moreover, CXCL13 colocalizes with lymphocytes in salivary tissue, and serum CXCL13 correlates with saliva levels during late-stage disease.

Conclusion. These data indicate that CXCL13 in salivary tissue and/or sera may be pathogenetically involved in SS disease and may serve as a marker of SS progression and severity. Therapeutic targets of CXCL13 may provide an innovative approach in the management of this debilitating disease.


Kaposi sarcoma (KS) is an enigmatic vascular tumor thought to be a consequence of dysregulated expression of the human herpesvirus 8–encoded G protein–coupled receptor (vGPCR). Indeed, transgenic animals expressing vGPCR in just a few cells manifest vascular tumors histologically identical to human KS through a remarkable paracrine mechanism. Both human and vGPCR experimental KS lesions are characterized by prominent angiogenesis and vascular permeability attributed to the paracrine release of angiogenic mediators, most notably vascular endothelial growth factor (VEGF). To date, the relative contribution of these paracrine mediators to the angiogenic and exudative phenotype of KS lesions remains unclear. Here we show that vGPCR up-regulation of the VEGF/KDR conduit is not sufficient to explain the potent angiogenesis and vascular permeability observed in KS. Rather, we demonstrate that vGPCR up-regulation of angiopoietin-like 4 (ANGPTL4) plays a prominent role in promoting the angiogenic and exudative phenotype of this tumor. Inhibition of ANGPTL4 effectively blocks vGPCR promotion of angiogenesis and vascular permeability in vitro and tumorigenesis in vivo. These observations suggest that ANGPTL4 is a previously unrecognized target for the treatment of patients with KS. Because angiogenesis and increased vessel permeability are common themes in all solid tumors, these results may have a broad impact on our understanding and treatment of cancer.


Bisphosphonates are commonly used pharmaceutical agents in the management of diseases involving high bone turnover. Intravenous bisphosphonates are associated with a high incidence of bone necrosis in the jaws, also called bisphosphate-related osteonecrosis (BRON). Only ~2%-3% of the patients with BRON take the oral preparations. As a major referral center, we have accumulated detailed information on 34 patients with this complication and with funding from Merck and Co. have initiated a study to create a detailed database of these patients. We use the American Academy of Oral and Maxillofacial Surgeons guidelines for defining the disease (exposed necrotic bone in the oral cavity for 6–8 weeks and unresponsive to therapy in a patient on any of the high-potency bisphosphonates). We document the radiographic changes associated with BRON and any changes that may precede bone exposure (preosteonecrosis). Triggers such as extractions, presence of lobulated tori, prominent mylohyoid ridge, and so on are examined. Importantly, the time of initiation of oral bisphosphate therapy, duration of therapy, the presence of periodontal disease, and the onset of osteonecrosis have been documented.


Of the 4 commonly speculated mechanisms for bisphosphonate-related osteonecrosis of the jaw (BRONJ), namely, repetitive microtrauma, primary osteoclastic dysfunction, angiogenetic effects, and a primary bacterial infection from oral commensal microflora, the osteoclastic dysfunction and antian-

Background. During the early stages of bisphosphonate-related osteonecrosis (BRON), areas of reduced uptake of technetium-99 methylene diophosphonate on scans are consistent with the decreased level of vascularity of the bone. With disease progression, scintigraphy is able to show areas of radionuclide uptake representative of osteoblastic hyperactivity. Increased uptake of technetium-99 in the scintigraphy of the jaws of patients who receive bisphosphonates should always be considered as an indicator of probable BRON.

Objective. The purpose of this retrospective study was to correlate nuclear medicine study findings with rate of inflammation and bone activity before dispensing any intravenous bisphosphonates and to identify any potential confounding or evolving changes thereafter.

Study design. This retrospective study involved a review of a patient’s previous medical record and bone scintigraphies which were images made for initial metastatic workup and subsequently compared with images after the commencement of any bisphosphonate regimen to establish a baseline for further readings. Review of all available follow-up images was also carried out. The amount of uptake of the radiotracer was graded as 0 (no uptake), 1 (mild), 2 (moderate), or 3 (intense).

Results. The study showed base grade and cumulative dose to have statistically significant results. A 3-way correlation to see the effect of base grade and cumulative dose on the jaw showed that it is twice as likely to see changes in mandible than maxilla. The presence of preexisting “hot-spots” in the jaws before bisphosphonate therapy makes future identification of BRON difficult. It was also seen that a series of scintigraphs of the same subject showed changes and the possibility of predicting BRON.

NONINVASIVE DETECTION OF ANEUPOID CELLS CAN PREDICT THE MALIGNANT POTENTIAL OF ORAL LICHEN PLANUS. A. Hirshberg, N. Yaron, T. Shani, I. Kaplan, M. Vered, G. Rechavi, N. Amariglio, L. Trakhtenbrot. Tel Aviv U School of Dental Medicine, Tel Aviv, Rabin Medical Centre, Petah-Tiqva, Chaim Sheba Medical Center, Tel-Hashomer, Israel.

The malignant potential of oral lichen planus (OLP) has been the subject of controversy in the literature. The present study aimed to evaluate the presence of chromosomal numeric aberrations in cells collected by brush sampling from OLP patients for early detection of potentially malignant cells even before cytologic changes are apparent by traditional histopathology. Brush samples from affected and nonaffected mucosa of 57 patients with OLP and 41 control subjects were simultaneously analyzed for morphology and fluorescent in-situ hybridization (FISH) using chromosomes 2 and 8 centromeric probes. In 14 OLP patients (24.5%) >2% and in 10 (17.5%) >5% of the cells were aneuploid. ACs were also detected in the normal-looking mucosa in 7 patients. Three patients developed squamous cell carcinoma in 5 years’ follow-up; the brush sample of these patients contained a significant number of ACs. In the control group, >2% ACs were detected only in 3 subjects (7%). OLP carries an increased risk for chromosomal instability. Identifying aneuploid cells in a brush sample and the combined morphologic and FISH analysis can increase the specificity in predicting the malignant potential of OLP.


Over the past 3 decades, our understanding of the histopathology of ischemic bone disease has dramatically improved, but a classification system has not been well established. We present current concepts of chronic ischemic bone disease (CIBD) histopathology and propose a useful disease classification. This summary is based on review of a convenience sample of >11,000 jawbone marrow samples from a large archival oral pathology database, an extensive literature review, and collaboration with well known medical experts in osteonecrosis. Ischemic bone death is represented by focal (not scattered) loss of osteocytes and is not found in most jaw CIBD. Marrow changes include: wispy (not dense) ischemic myelofibrosis streaming between adipocytes; variation in adipocyte size; dilated marrow capillaries, typically with few remaining erythrocytes and with passive endothelial cells; few, if any, chronic inflammatory cells; occasional mast cells; oil cysts; granular cytosol in nonivable adipocytes; fatty microvesicles; intramedullary cavitation; frequent intravascular thrombi; focal hemorrhage (microinfarction); plasmoastosis (serous oozes); and calcific/proteinaceous detritus. Although microscopic features are similar, a distinction between inflammation and CIBD can usually be made, and some lesions will show both diseases. A suggested CIBD classification system includes: avascular necrosis, bone marrow edema, regional ischemic osteoporosis, ischemic myelofibrosis, ischemic osteosclerosis, ischemic marrow atrophy (honeycombed bone), intramedullary fibrous scar, and ischemic cavitation. The microscopic parameters are distinct enough to allow a confident diagnosis of CIBD and distinguish it from inflammatory marrow changes. A classification system is proposed.