

CLINICOPATHOLOGIC CONFERENCE

Gingival ulceration and exposed bone

Benedicta E. Beck-Broichsitter, MD, DMD,^a Wolfram Klapper, MD,^b Andreas Günther, MD,^c Jörg Wiltfang, MD, DMD,^d and Stephan T. Becker, MD, DMD,^a Kiel, Germany

CLINICAL PRESENTATION

A 53-year-old woman presented to our Department of Oral and Maxillofacial Surgery with a complaint of continuous painful ulcerations for the preceding month on the attached oral mucosa, especially covering the hard palate and mandibular anterior. The lesions were becoming progressively larger. She did not report general symptoms, such as fever or night sweats, but had a weight loss of 4 kg within the preceding 6 months. She denied regular alcohol and tobacco consumption.

Her systemic lupus erythematosus and osteoporosis were treated with prednisone, mycophenolate mofetil, cholecalciferol, calcium, pantoprazole, and alendronic acid.

Clinical examination revealed gingival ulcerations of the hard palate and anterior upper jaw (Figure 1) and mandibular right anterior gingiva. In addition, exposed bone was visible following local deep scaling and root planing in the region of the lower left molars, which had been done 2 weeks before (Figure 2). Dental x-ray examinations showed no signs of bone loss. Ultrasound imaging of the head and neck region did not reveal any lymphadenopathy. Leukocyte count in blood was 6.27/nL (12.5% lymphocytes, 79.2% neutrophils), hemoglobin was 11.1 g/dL, and platelet count revealed 346/nL. Immunophenotyping by flow cytometry indicated a mild lymphocytopenia affecting B cells (42/ μ L) as well as T cells (393/ μ L). No viral Epstein–Barr virus (EBV)-associated DNA copies were detectable in the

blood by polymerase chain reaction or any viral copies of human immunodeficiency virus.

DIFFERENTIAL DIAGNOSIS

After inspection, our hypothesis was that the patient suffered from 2 different afflictions. The first complaint (lower jaw) resembled an osteonecrosis of the jaw after local deep scaling and root planing in the region of the lower left molars. Pharmaceutical agents like bisphosphonates may induce an osteonecrosis of the jaws in the context of the treatment of bone metastases or osteoporosis. Clinically, exposure of necrotic bone after extraction of teeth or minor periodontal interventions occurs. Most of these cases are associated with intravenous drug application of zoledronic acid or pamidronate.^{1,2}

The second complaint, even more burdensome for the patient, was painful ulcerations of the oral mucosa. Ulcerations are a common complaint for patients presenting to dentists and oral surgeons. Several possible differential diagnoses have to be considered.

The most common cause for oral ulcerations results from infections or from trauma of denture sores and can be treated easily. Trauma, such as physical damage, caustic chemicals, and repeated vomiting may induce oral ulcerations. In our case, the patient did not have dentures and denied previous trauma.

Dental examination revealed no evidence of gingivitis or periodontal disease. Dental x-ray examinations showed no bone loss, as mentioned previously. In conclusion, a dental origin remained unlikely.

Painful lesions of the oral mucosa can also arise from a primary infection with herpes simplex virus type 1 (HSV-1). After a period of incubation of 3 to 10 days, herpes vesicles converting into mucosal erosions can appear all over the oral cavity. Patients usually feel very sick and show lymphadenopathy of the neck.³ Ultrasound imaging did not reveal any sign of lymphadenopathy in this case, and lesions had been present too long to be an HSV-1 infection.

Oral manifestations of tuberculosis are rare in northern Europe, although in the past few years the incidence is increasing, especially in immunocompromised patients. Initially the mucosa appears with edema and redness. Finally, a nonhealing ulceration develops, es-

^aAssistant Doctor, Department of Oral and Maxillofacial Surgery, Christian Albrechts University, Kiel, Germany.

^bUniversity Professor, Attending, Department of Pathology, Hematopathology Section and Lymph Node Registry, Christian Albrechts University, Kiel, Germany.

^cAttending, Department of General Medicine, Stem Cell and Immune Therapy Section, Christian Albrechts University, Kiel, Germany.

^dUniversity Professor, Head of Department, Department of Oral and Maxillofacial Surgery, Christian Albrechts University, Kiel, Germany.

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Fig. 1. An ulcer covered by fibrin is located on the attached gingiva of the right maxilla and is even much more pronounced on the palatal mucosa.



Fig. 2. Exposed bone can be observed between the lower left molars instead of a dental papilla. Furthermore, the attached gingiva of the lower anterior teeth on the right side of the mandible shows an ulceration covered with fibrin, which is less distinctive in comparison with the palatal ulcer.

pecially in the region of the tongue.⁴ Our patient met several criteria, such as her migration background (former Soviet Union), immunosuppressive therapy, and the pain. Clinical signs suggested tuberculosis as a suspected diagnosis. To verify the diagnosis, either a QuantiFERON test or tuberculin skin test has to be performed.

Furthermore, potential differential diagnoses include Crohn's disease, Wegener granulomatosis, pyoderma gangrenosum, traumatic eosinophilic ulcer, and syphilis.⁴⁻⁹ If one of the previously mentioned diagnoses is considered, then an interdisciplinary cooperation may be advisable (e.g., general medicine).

The most often observed malignant processes in the oral cavity are squamous cell carcinomas. Their predilection site is the floor of mouth and the lateral border of the tongue, as an exophytic or endophytic variant. Rarely, metastatic tumors with a primary tumor in the lung,¹⁰ prostate,¹¹ or kidney¹² appear in the oral cavity.

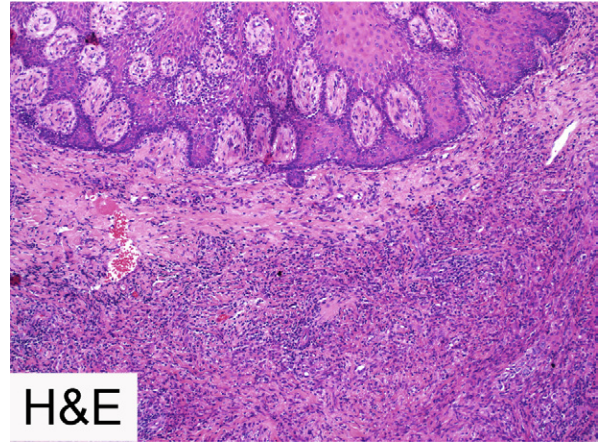


Fig. 3. A polymorphic infiltrate composed of lymphocytes, plasma cells, histiocytes, and blasts was detectable in the tissue adjacent to the palatal ulceration (hematoxylin-eosin [HE], original magnification $\times 400$).

Some cases of plasmacytoma originating from the jaw are described in the literature leading to lesions of the oral mucosa.¹³ Neoplasia arising from the hematopoietic system may be considered, as well. The presented patient was lacking any risk factors for carcinoma (nonsmoker, little consumption of alcohol). Furthermore, the patient was suffering from painful ulcerations at 2 major sites at the same time, making a diagnosis of metastasis unlikely. To exclude malignancy and to confirm diagnoses, in lesions without tendency to heal, a biopsy has to be taken.

In the presented case, the patient was suffering from systemic lupus erythematosus and received mycophenolate mofetil for immunosuppression. Ulcerations of the skin and mucosa are potential side effects of immunosuppressive medications.

Gathering the anamnestic information and clinical observations led to 2 major assumptions: these ulcerations were caused by lupus erythematosus, or were attributable to immunosuppression.

DIAGNOSIS AND MANAGEMENT

Biopsies of the maxillary ulcerations were obtained, showing a regular squamous epithelium with focal ulceration. Immunohistochemistry was performed for CD20, CD3, CD30, CD15, LMP1, EBNA2, Zebra, and Ki-67 (self-generated antibodies, Neomarkers, Lab Vision, Cheshire, UK, and Dako, Hamburg, Germany). In addition, detection of EBV-encoded RNA (EBER) was done by EBER in situ hybridization (Leica Bond; Leica Microsystems, Wetzlar, Germany). In the tissue adjacent to the ulceration, a polymorphic infiltrate composed of lymphocytes, plasma cells, histiocytes, and blasts was detectable (Figure 3). Occasionally, the blastic cells resembled Hodgkin or Reed-Sternberg cells,

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