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Refractory localized "periodontitis"

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CASE REPORT

A 61-year-old male patient presented to his family dentist with a painful and loose tooth, #24, associated with localized gingival enlargement, for several weeks' duration. Besides heavy tobacco and alcohol use, his medical history was otherwise unremarkable. Initial radiographic examination showed a radiolucency with irregular, poorly defined borders in the interproximal area between teeth #24 and #25 (Fig 1, *A*). The dentist suspected localized inflammatory periodontal disease. Local scaling and root planning were performed, and the patient was placed on strict oral hygiene measures. Two weeks later, increased tooth mobility was noted with lateral extension of the area of gingival enlargement to include teeth #23 and #25. Tooth #24 was extracted, and the patient was prescribed amoxicillin (500 mg, 1 tablet every 6 hours for 7 days). Three weeks later, the extraction site of tooth #24 remained unhealed (Fig 1, *B*), and teeth #23 and #25 were mobile. Both teeth were extracted with surgical removal of the enlarged gingival tissue, and the patient was placed on a second course of amoxicillin. At the postoperative visit, an ulcerative process involving the anterior mandibular alveolar ridge was seen (Fig 2). The ulcer had rolled borders with extension into both the floor of the mouth and the mucolabial fold. Radiographic examination showed a 2.5-cm osteolytic defect in the anterior mandibular ridge with irregular and ill-defined borders. The patient was then referred to the School of Dentistry at the Medical College of Georgia for evaluation.

Differential diagnosis

Initially, the radiographic and clinical features in this case were thought to be consistent with localized, inflammatory periodontal disease. Yet, despite local debridement and antibiotic therapy, evidence of a destructive lesional process was noted. In the differential diagnosis, specific infection, eosinophilic granuloma, squamous cell carcinoma, lymphoma, and metastatic disease were considered. A specific infection, such as mycobacteria or deep fungal forms, was a possible suspect. These types of infection may cause significant bone destruction, mobility of teeth, and necrotic ulceration. Although typically a disease of young individuals, with more than 50% of cases arising during the first two decades, eosinophilic granuloma (monostotic Langerhans cell disease) may be seen over a wide age range. In the jaws, eosinophilic granuloma often appears as an irregular, noncorticated radiolucency of the tooth-bearing alveolar ridge. With proliferation of the gingival soft tissue and tooth mobility, the clinical presentation of eosinophilic granuloma can be reminiscent of local periodontal disease. Squamous cell carcinoma, originating either from the gingival or sulcular surface epithelium or centrally from odontogenic epithelium, was also considered. Squamous cell carcinoma in these locations may cause bone destruction, root resorption, and mobility of teeth. Radiographically, lesions often appear as an ill-defined, moth-eaten radiolucency with irregular borders. Extranodal lymphoma was included in the differential. Lymphoma may be present in the jaws with irregular bony destruction and may be associated with soft tissue mass and tooth mobility, mimicking periodontal disease. Finally, although the patient reported no history of cancer, the possibility of metastatic disease from unknown primary was also considered.

Diagnosis

An incisional biopsy was performed at the periphery of the ulcerative process. Routine histopathologic examination showed a diffuse, cellular infiltrate of large and smaller-sized, round to oval cells (Fig 3). The large neoplastic cells had prominent basophilic nuclei and abundant cytoplasm that varied from eosinophilic to optically clear (Fig 4). A plasmacytoid morphology was noted focally within the population of smaller cells. Nuclear hyperchromatism and atypical mitotic figures were readily identified. The neoplastic cells were strongly positive for CD45 (leukocyte common antigen) and CD20, a B-cell marker (Fig 5), but negative for T-cell

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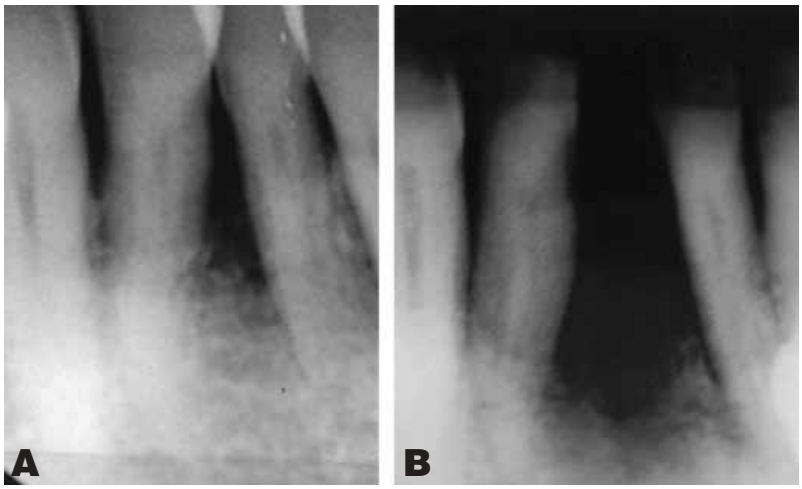

Fig 1. **A**, Preoperative radiograph showing interproximal radiolucency. **B**, Periapical film showing a crater-shaped radiolucency with irregular borders 3 weeks after extraction of tooth #24.

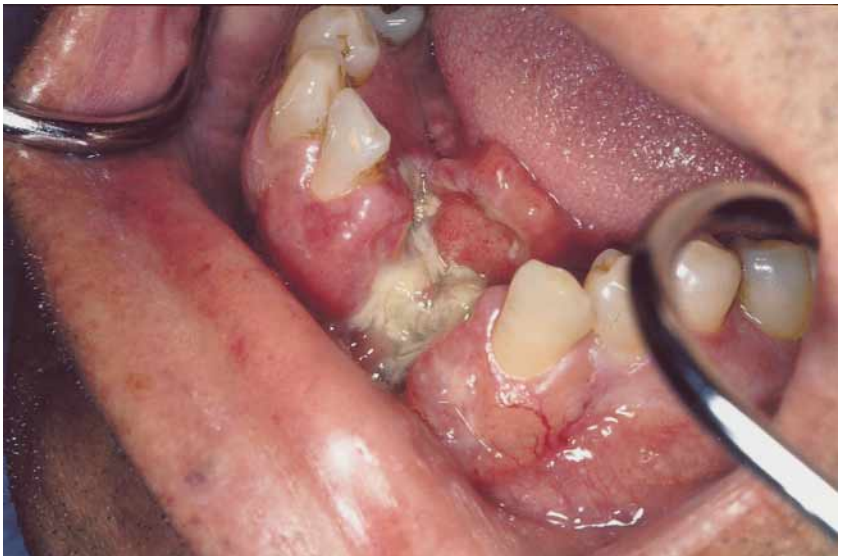

Fig 2. Large ulcer involving the anterior mandibular alveolus, floor of mouth, and mucolabial fold.

markers. Probes for α and λ light chains showed kappa light chain restriction.

The final diagnosis was immunoblastic lymphoma, B-cell type.

Management

On hospital admission, extensive patient workup including complete physical examination, complete blood count with differential, blood chemistry, and bone marrow aspiration showed no additional abnormal findings. The patient received 4 cycles of multiple-drug chemotherapy consisting of Cytoxan 750 mg/m^2, adriamycin 50 mg/m^2, vincristine 1.4 mg/m^2 intravenously, and prednisone 100 mg/m^2 orally. After the first 2 cycles, the patient developed pharyngitis, laryngitis, and epigastric distress but tolerated the remaining treatments reasonably well. The oral lesion totally resolved before completion of chemotherapy. Posttreatment evaluation of the patient's head and neck with computed tomography and gallium scans was negative for tumor. The patient was subsequently lost to follow-up.

DISCUSSION

Immunoblastic lymphoma (IBL) is a high-grade neoplasm that comprises less than 5% of all lymphomas. According to the recently updated REAL (Revised European-American classification of lymphoid neoplasms) system, IBL remains included within the morphologic subtypes of diffuse, large B-cell lymphomas (DLBCLs).[1-4] Immunohistochemical

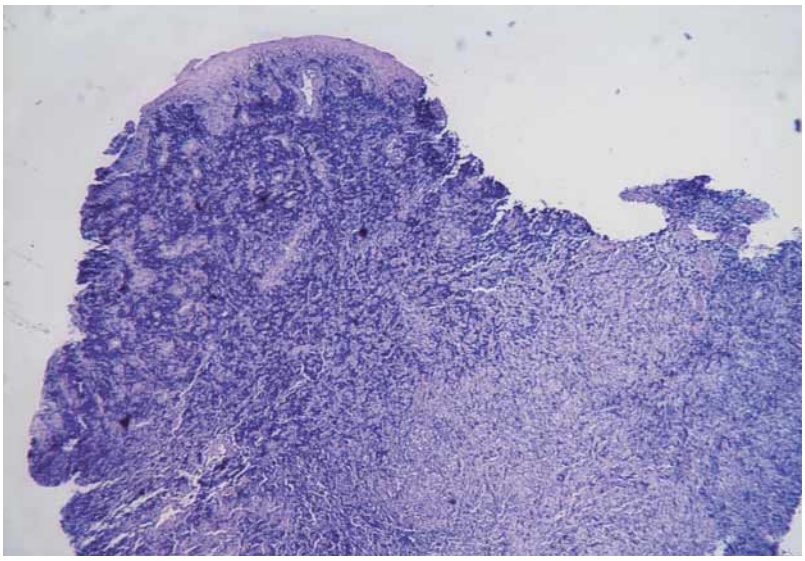

Fig 3. Low-power photomicrograph of the gingival biopsy showing heavy subepithelial infiltration of lymphoid cells (hematoxylin-eosin stain; original magnification ×20).

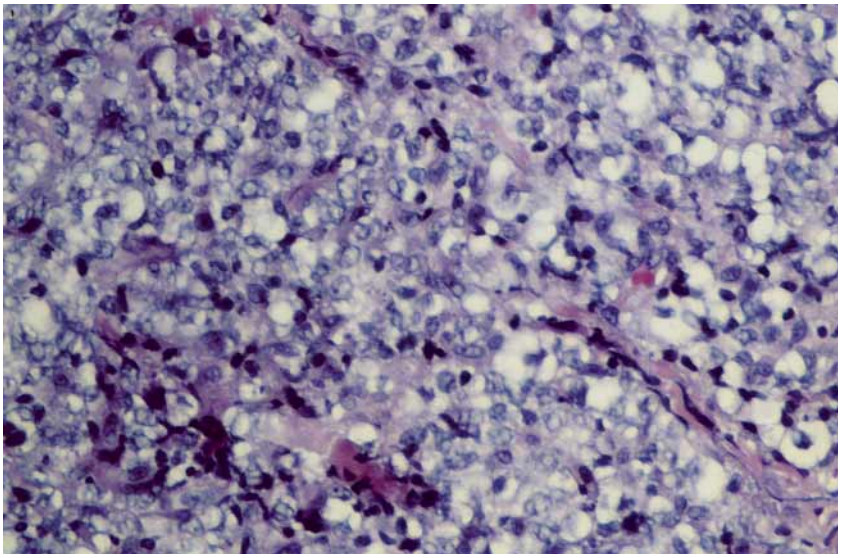

Fig 4. Medium-power photomicrograph illustrating large and small neoplastic lymphoid cells (hematoxylin-eosin stain; original magnification ×200).

evidence suggests that DLBCLs arise from cleaved and noncleaved cells within the germinal centers of lymph nodes.[2,5] Several subtypes of DLBCLs, including centroblastic, IBL, and anaplastic large cell (CD30+), have been described.[2,4] Although IBL was previously thought to develop from reticulum cells or histiocytes, it is now believed to arise from antigenically activated or transformed lymphocytes known as immunoblasts.[5] This was reflected by the morphologic classification scheme proposed by Schneider et al[6] in 1985, who designated these cases as immunoblastic sarcoma.

Immunophenotypically, IBL may be separated into T- or B-cell types.[5,7] The T-cell type is an aggressive neoplasm with a poor prognosis that usually develops in the lymph nodes and is now considered to be among the category of peripheral T-cell lymphomas.[4,7,8] By contrast, IBL B-cell type develops more frequently in extranodal sites including mediastinum, stomach, neck, lung, diaphragm, testis, and bone, with less frequent origin in the lymph nodes or spleen.[6,7] IBLs often arise in patients with autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis,

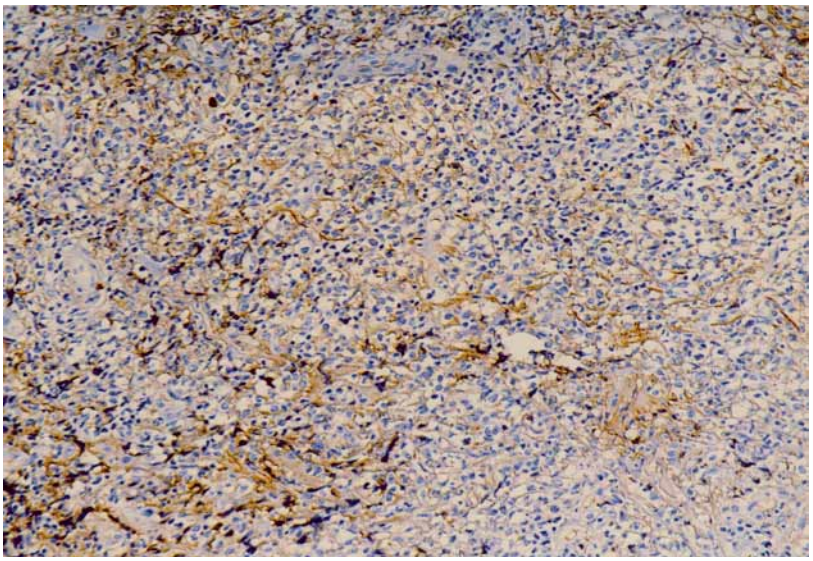

Fig 5. Photomicrograph showing positive reaction of neoplastic cells to the B-cell marker, CD20 (immunoperoxidase ×100).

Hashimoto thyroiditis, and Sjögren's syndrome.[7,9-11] In one study, a history of immunologic disease was noted in 36% of patients with IBL B-cell type and in 16% of patients with T-cell type.[7] Benign or low-grade lymphoproliferative conditions, including angioimmunoblastic lymphadenopathy, chronic lymphocytic leukemia, Waldenstrom macroglobulinemia, and well-differentiated lymphocytic lymphoma, may also precede the onset of IBL.[10,12,13] This feature was reportedly more common with the T-cell type (26%) than with B-cell type cases (13%).[7] In addition, IBL is one of several lymphoproliferative disorders reported to occur in patients with congenital immune deficiencies, immunosuppressed transplant recipients, as well as patients with acquired immune deficiency syndrome (AIDS).[14-16] These disorders share several common features, including origination in or involvement of extranodal sites, diffuse aggressive histopathologic features, B-cell lineage or differentiation, association with Epstein-Barr virus, and rapid clinical progression.[17]

Immunoglobulin (Ig) production, a characteristic feature of terminal B-cell (plasma cell) differentiation, is determined by rearrangement and expression of the genes encoding the heavy and light Ig chains.[18] Strauchen et al[19] reported Ig expression in 254 of 345 (74%) B-cell lymphoma cases. Ig was most frequently expressed by small lymphocytic, small cleaved and noncleaved cell histologic types and occurred less frequently in lymphomas of the large cell (cleaved and noncleaved) and immunoblastic histologic types.

IBL of the oral cavity is extremely uncommon. A search of the literature yielded 12 cases, all of which occurred in AIDS or human immunodeficiency virus (HIV)–infected patients.[20-23] Takahashi et al[24] reported an additional 12 cases of IBL among 70 (17%) cases of primary extranodal non-Hodgkin's lymphomas of the oral region. Unfortunately, information regarding HIV-positivity or immunologic status of their patients was not provided. In the current case, IBL developed in the anterior mandibular alveolus in a patient with no known underlying immunologic disorder and without evidence of nodal involvement. Despite clinical similarity to localized, inflammatory periodontal disease, the lack of responsiveness to conventional therapy warranted careful exclusion of a more aggressive, possibly neoplastic condition. Even so, the patient underwent 2 separate extraction procedures without the benefit of biopsy of the associated, abnormal soft tissue. The delay in diagnosis and treatment of our patient is yet another reminder that histopathologic evaluation and diagnosis of clinically abnormal tissues are critical, even in cases of refractory "periodontitis."

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