**CLINICAL HISTORY:**

A 70-year-old male presented to a dental clinic for a one-year history of non-healing necrotic gingival ulcer, 1.2 cm in greatest dimension, after dental work for poor dentition. The clinical differential diagnosis included necrotic ulcerative periodontitis versus squamous cell carcinoma.

The patient has a 12-year history of chronic lymphocytic leukemia (CLL) with observation only. A PET/CT showed scattered lymphadenopathy without significant increase in SUV, consistent with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and without concern for transformation. A bone marrow biopsy in the past year demonstrated a hypercellular bone marrow predominantly comprised of CLL/SLL (~90%). Other notable history includes a non-melanoma skin cancer of lip (excised) and a recent decline in peripheral blood white count to 12.9 x 103 cells/µL with an absolute neutrophil count of 0.4 x 103 cells/µL.

**MICROSCOPIC DESCRIPTION:**

Microscopic examination of the gingival lesion biopsy demonstrates four tissue sections having oral mucosa with ulceration and a dense lymphoid infiltrate. Underlying the necrotic ulcer base is an atypical lymphoid population comprised of intermediate to large cells including scattered Hodgkin-Reed-Sternberg (HRS)-like cells.

The atypical population expresses CD20 and PAX5, with a subset of the large cells expressing CD30. The cells of interest also express BCL6 and MUM1; CD10 is negative. EBER in situ hybridization marks a significant subset of the B cell population, with appropriate controls. The HRS-like population appears negative for CD15 and CD45. CD3 and CD43 stains a loose band of small T cells at the ulcer base and intermixed with the B cell population. The T cells predominantly express CD4 with fewer scattered cells expressing CD8.

**DISCUSSION:**

Epstein-Barr Virus-positive mucocutaneous ulcer (EBVMCU) presents as a solitary (occasionally regionally multifocal), well-circumscribed, and non-mass-forming ulcer at mucosal or cutaneous sites. Patients are often older (> 70 years), have immunodeficiency/immunocompromise, autoimmune disease, HIV infection, or post-organ transplantation. A subset of patients have chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) or are under chronic immunosuppression (e.g., methotrexate). After ruling out other systemic lymphoproliferative disease, therapy may include withdrawal of immunosuppressive agents or localized therapy (e.g. radiotherapy). EBVMCU may have a relapsing/remitting disease course, but without progression.

Histopathologic evaluation demonstrates a polymorphous lymphoid population, immunoblasts, and scattered atypical large cells with features of Hodgkin-Reed-Sternberg cells. Background cellularity includes histiocytes, plasma cells, and eosinophils. Thrombosis, angioinvasion, and necrosis are often present. Pseudoepitheliomatous hyperplasia may be present in overlying epithelium. The lesion is often rimmed by a dense population of small, mature T cells. The polymorphous lymphoid population is a mixture of B and T cells with a predominance of CD8-positive T cells in some cases. The HRS-like cells have B cell character, expressing CD20 (variable), PAX-5, CD30 (variable), and EBV antigens. CD15 is rarely expressed.

Excluding diagnoses with overlapping features, especially EBV-positive diffuse large B cell lymphoma (EBV-DLBCL) and classic Hodgkin lymphoma (CHL), may be challenging. Establishing the correct clinical context for EBVMCU including immune deficiency/dysregulation and lack of a mass or evidence of systemic disease is essential, as EBVMCU treatment is typically more conservative than for EBV-DLBCL or CHL. Clonal immunoglobulin heavy chain and T cell receptor gene rearrangements are identified in more than 30% of cases and does not aid in distinguishing from lymphoma.

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