To the Editor:

Plasmablastic lymphoma (PL) is an uncommon variant of diffuse large B-cell lymphoma first described by Delecluse et al.\(^5\) in 1997. It tends to be located in the oral cavity of patients with human immunodeficiency virus (HIV) infection.\(^2\) PL is highly malignant, and Epstein–Barr Virus (EBV) is believed to be implicated in its pathogenesis.\(^3\) The cells have an immunoblastic appearance, and are characterized by the loss of mature B-cell antigens, such as CD20, and the acquisition of plasma cell markers, such as CD38 and CD138.\(^4\) Treatment includes chemotherapy and highly active antiretroviral therapy, but response rates are low.

The patient was a 43-year-old woman referred to us for evaluation of painful progressive nodular lesions. Examination of the patient revealed firm subcutaneous nodules of between 1 cm and 3 cm in diameter on the trunk and lower limbs (Figure 1), adherent to the deep planes, and with a violaceous contusiform appearance of the overlying skin.

Relevant details of the patient’s history include previous parenteral drug use, hepatitis B virus (HBV) (surface antigen positive), hepatitis C virus (HCV), and HIV (stage B3) infection; she was on treatment with methadone and antiretroviral therapy (tenofovir, lamivudine, ritonavir, and atazanavir).

Blood tests included complete blood count, coagulation studies, biochemistry, serology, and tumor markers. The important results were CD4 counts of 377 cells/µL, abnormal liver function (aspartate aminotransferase, 87 U/L; alanine aminotransferase, 78 U/L; alkaline phosphatase, 177 U/L; and γ-glutamyltransferase 89), elevated β2-microglobulin of 4184.5 mg/L, and serological confirmation of HIV, HBV, and HCV infection, and markers for past infection by EBV.

Biopsy revealed the presence of a diffuse hypodermic tumor infiltrate made up of lymphoplasmacytoid cells with marked pleomorphism and numerous macrophages (Figures 2 and 3).

Immunohistochemistry was negative for CD20, multiple myeloma-1, B-cell lymphoma-6, CD3, terminal deoxynucleotidyl transferase, and Human herpesvirus (HHV)-8. However, tumor cells were positive for plasma cell markers such as CD138, and there was a high proliferation index. The Epstein–Barr virus encoded RNA (EBER) marker of EBV was positive using in situ hybridization techniques. A diagnosis of PL was made based on these results.
A study of disease extension was requested, including a whole body computed axial tomography that confirmed tumor infiltration of the spleen, lymph nodes, and kidneys. The study was completed with a bone marrow aspiration and biopsy that showed reactive plasmacytosis and normocellularity in the three cell lines, ruling out tumor infiltration. The lymphoma was classified as stage IV-A.

Chemotherapy was started with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), and prophylactic intrathecal chemotherapy was also given. However, the patient died after the first cycle due to treatment-related complications.

According to the WHO-EORTC classification, PL is a diffuse large B-cell lymphoma with terminal differentiation. In 1997, Delecluse et al. described a series of 16 patients with oral PL; 15 were HIV-positive men, and 11 were homosexual. Morphologically, the tumor presented characteristic features of diffuse large B-cell lymphoma, but proved negative for the leukocyte common antigen and for CD20. Meanwhile, there was very clear presence of plasma cell markers, such as CD38 or CD138, and EBV infection was detected in 9 of 15 patients using EBER in situ hybridization.

Barely 40 cases of PL have been published in the short time since the condition was first described. Most cases present as oral lesions in HIV-positive patients; extraoral disease is extremely uncommon. Extraoral sites include the nasal mucosa, lymph nodes, stomach, lungs, and skin, and, although very rare, they present the same clinical-pathologic characteristics. Tavora et al. have recently published a review of the cases of extraoral PL reported in English-language journals.

Pathologic study characteristically reveals a proliferation of large, round or oval B lymphocytes with a large volume of eosinophilic cytoplasm and an eccentric nucleus with a prominent nucleolus. Macrophages are usually present, producing a “starry sky” appearance, and there is a high mitotic rate. Immunohistochemical analysis is positive for plasma cell markers such as CD38 and CD138.

The pathogenesis of PL is also associated with EBV (latency type 1 pattern), and positive results are commonly found for virus markers such as, latent membrane protein, or EBER. Initial studies on HHV-8 involvement in PL pathogenesis have been inconclusive, and it is currently considered to be a coincidental infection.

PL is highly malignant and prognosis tends to be poor despite chemotherapy. The most common chemotherapeutic regimen is CHOP; this achieves the best response rates. Recently, complete remission from cutaneous PL was reported in a patient with HIV infection who was treated with CHOP chemotherapy in association with highly active antiretroviral treatment.

Finally, recent studies indicate that large B-cell lymphomas with terminal differentiation could include a greater number of diseases than was initially thought; these diseases have different clinical-pathologic and phenotypic characteristics and include “buccal mucosa” type PL, PL with plasmacytoid differentiation, and PL secondary to multiple myeloma or plasmacytoma, among others.

References