Editorial Comment: Plasmablastic Lymphoma—A Diagnostic and Therapeutic Puzzle

Oral cavity lymphoma occurs frequently in HIV-positive patients, often with a poor prognosis. Ortega and colleagues present an enlightening case of a destructive oral plasmablastic lymphoma in a 43-year-old HIV-positive man. Similar to another recently reported case, this lymphoma was their patient's first manifestation of his underlying HIV infection.

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Plasmablastic lymphoma is a unique AIDS-related lymphoma, which was first described in the jaws and oral cavity of HIV-infected persons about a decade ago. Awareness of this distinctive lymphoma can prevent misdiagnosis by the clinician (eg, as odontogenic cellulitis) or the pathologist (eg, as a nonlymphoid malignancy). Since the original reports of plasmablastic lymphoma, it has been described in several other sites, including the GI tract (particularly the anorectum), omentum, lung, nasal and paranasal regions, testes, bones, soft tissue, lymph nodes, bone marrow, skin, and CNS. Plasmablastic lymphoma has also been documented to arise from long-standing sacrococcygeal cysts in HIV-positive persons. Plasmablastic lymphoma accounts for 2.6% of all HIV-related non-Hodgkin lymphomas. This lymphoma has also been reported in HIV-negative persons, particularly those who have immunosuppression. Plasmablastic lymphoma usually develops in middle-aged adults, with the age at onset in one large series varying from 35 to 55 years, but it can also occur in the pediatric age group. There are 3 recognized categories of plasmablastic lymphoma. The first type is plasmablastic lymphoma of oral mucosa. Such lymphomas contain a monomorphic population of plasmablasts with no or minimal plasmacytic differentiation. They are found largely in the oral mucosa but also may occur in other extranodal or nodal sites. The second type is plasmablastic lymphoma with plasmacytic differentiation. These extraoral lymphomas are composed predominantly of plasmablasts but exhibit more differentiation to mature plasma cells than is seen in the first type. The third kind is plasmablastic lymphoma associated with Castleman disease, which is typically nodal or splenic.

Plasmablastic lymphoma is listed in the World Health Organization 2001 classification as a variant of diffuse large B-cell lymphoma. The histological findings of a diffuse infiltrative growth pattern, brisk mitotic activity, and necrosis, along with the fact that they are rapidly growing destructive tumors, supports their designation as a high-grade malignant lymphoma. Based on a similar morphology and behavior, plasmablastic lymphoma needs to be distinguished from the immunoblastic variant of diffuse large B-cell lymphoma, classic (body cavity-based) and solid (extracavitary) variants of primary effusion lymphoma, Burkitt lymphoma with plasmacytoid differentiation, and extramedullary plasmablastic tumors secondary to multiple myeloma or plasmacytomas. Plasmablastic lymphoma is characterized by immunoblastic morphology and plasma cell phenotype. In other words, plasmablasts are lymphoid cells that morphologically resemble B-cell immunoblasts but have acquired a plasma cell immunophenotype (ie, loss of B-cell markers and surface immunoglobulin with the acquisition of plasma cell surface markers). Thus, unlike immunoblasts, plasmablasts fail to express CD45 (leukocyte common antigen) as well as the B-cell marker CD20 and are only variably immunoreactive for CD79a—a broader-spectrum B-cell marker. They are also negative for pan–T-cell markers. Positive staining for plasma cell markers such as VS38c, CD38, MUM-1, and CD138 indicates a phenotype akin to plasma cells. Newer B-lineage markers (eg, OCT.2 and BOB.1) may prove useful in determining a B-cell origin in plasmablastic lymphomas.
While it is established that most plasmablastic lymphomas are positive for Epstein-Barr virus (EBV), the role of human herpesvirus 8 (HHV8) in their lymphomagenesis remains somewhat unresolved. Like EBV, HHV8 is a lymphotrophic gammaherpesvirus. Originally, it was reported that plasmablastic lymphomas were negative for HHV8 using immunohistochemistry, and this was confirmed by subsequent studies. However, other investigators have detected HHV8 RNA in oral plasmablastic lymphomas by using polymerase chain reaction methods. The association of plasmablastic lymphoma with HHV8 certainly helps explain why, over time, some of these tumors arise from the HHV8-related plasmablastic variant of Castleman disease seen in HIV-infected patients. Documentation of the development of Kaposi sarcoma, Castleman disease, and plasmablastic lymphoma simultaneously in patients suggests a critical role of HHV8 as a common denominator in the pathogenesis of all of these diseases.

The growing body of literature dealing with the clinical outcome and treatment of plasmablastic lymphoma is puzzling. Published data indicate that these are aggressive tumors, frequently resistant to therapy, and often rapidly fatal. Moreover, in the setting of HIV infection, plasmablastic lymphoma has been shown to evolve into plasmablastic leukemia. Available data from the pre-HAART era showed that plasmablastic lymphoma carried a poor prognosis, with a dismal median survival of about 5 months. Therefore, it is unclear why in certain immunodeficient hosts, spontaneous regression or prolonged survival has been reported. Ortega and colleagues treated their patient with antiretroviral therapy; however, we do not know the outcome. To date, there have been very few case reports suggesting that the prognosis of plasmablastic lymphoma may be improved following antiretroviral therapy. Hopefully, there will be larger trials investigating the potential beneficial role of antiretrovirals in treating this novel lymphoma.

Liron Pantanowitz, MD
Assistant Professor of Pathology
Baystate Medical Center
Tufts University School of Medicine
Springfield, Mass

Bruce J. Dezube, MD
Associate Professor of Medicine
Beth Israel Deaconess Medical Center
Harvard Medical School
Boston

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