


The Authors’ Reply

The interesting case presented by Pagni and colleagues serves to further describe the spectrum of human herpesvirus-8 (HHV-8)–related plasmablastic proliferations in the setting of multicentric Castleman disease (MCCD). These were reviewed in the context of the 2009 Society of Hematopathology/European Association for Haematopathology Workshop on the Spectrum of Immunoproliferative Disorders and the Border Between B-Cell Lymphoma and Plasma Cell Neoplasms.1 The presented case of MCCD demonstrates an exuberant proliferation of HHV-8+ plasmablasts (IgM+, λ+, EBER–) within newly formed germinal centers in the mesenteric fat rather than within the lymph node microanatomy. Such newly formed germinal centers, which can be seen in nodal HHV-8+ MCCD in the perinodal adipose tissue but also during bone marrow involvement, do not necessarily indicate a higher risk of disease.2

As noted in our review, the biologic and pathologic features of progression from MCCD with collections of HHV-8+ plasmablasts and HHV-8+ large B-cell lymphoma have not been well characterized, and it was suggested that the presence of sheets of plasmablasts outside follicles that distort architecture might be sufficient for the diagnosis of bona fide large B-cell lymphoma.1 One objective criterion for large-cell transformation is the presence of a clonal immunoglobulin (Ig) rearrangement. The plasmablasts in MCCD are polyclonal for Ig rearrangement despite expressing monotypic Ig λ light chains. So-called microlymphomas tend to be oligoclonal, whereas HHV-8+ large B-cell lymphoma is monoclonal.3 In the case of Pagni et al, the illustrations clearly show HHV-8+ plasmablasts present in collections that fulfill the description of a microlymphoma but not necessarily a large B-cell lymphoma. No IGH@-MYC or copy number abnormalities of chromosomes 8 and 14 were present, and so no positive evidence of genetic abnormalities was demonstrated. Unfortunately, no Ig rearrangement studies were performed. This information both for the whole process and for individual germinal centers would be important for assessing the clinical risk. Although a detailed clinical history is not provided, such as human immunodeficiency virus status or other prognostic features, such as performance status, the authors allude to a regression of unknown duration with immunochemothepapy.

In the context of the spectrum of HHV-8+ MCCD and HHV-8+ plasmablastic lymphomas, this case may represent the transition in which uncontrolled proliferation of these cells is beginning. However, it appears that standard treatment regimens for aggressive B-cell lymphomas were able to effectively eliminate this proliferation. Whether this is due to direct effects on the HHV-8+ plasmablasts alone or in combination with the immunomodulating effects on the background of MCCD is uncertain. Additional informative cases such as this are needed, with clinical and pathologic description and application of tools such as microdissection and gene rearrangement, or perhaps high-resolution single-nucleotide polymorphism array karyotyping or next-generation sequencing. These studies may help us define key genetic aberrations, elucidate the borders between neoplastic and nonneoplastic proliferations, and inform treatment choices.

Eric D. Hsi, MD
Department of Clinical Pathology
Cleveland Clinic
Cleveland, OH

Ahmet Dogan, MD, PhD
Department of Anatomic Pathology
Mayo Clinic
Rochester, MN

References

