

tient), despite the fact that the risk of permanent disability in such patients is very low.<sup>2</sup> These problems with the diagnostic criteria for multiple sclerosis and the entry criteria for clinical trials need to be addressed.

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## A Relapsing Inflammatory Syndrome and HHV-8

**TO THE EDITOR:** The case of human herpesvirus 8 (HHV-8) reported by Dagna et al. (July 14 issue)<sup>1</sup> is considered to be distinct from HHV-8–associated multicentric Castleman’s disease owing to the absence of typical histologic findings and elevated plasma levels of interleukin-6. The histopathology of HHV-8–associated multicentric Castleman’s disease is variable, as compared with the classic descriptions of HHV-8–negative Castleman’s disease<sup>2-4</sup> and would encompass the changes described in the report, especially in the context of cytotoxic treatment before biopsy. In HHV-8–associated multicentric Castleman’s disease, the HHV-8–infected B-lineage cells can be seen either within the B-cell follicles or in the interstitium of many tissues, including bone marrow<sup>4,5</sup> and lymph nodes, as seen in this case. Phenotypically, these cells resemble the plasmablasts in the follicles and the plasma cells in the interstitium. The infected cells secrete viral interleukin-6, which triggers an autocrine feedback loop involving human interleukin-6,<sup>3</sup> as reflected by the elevated plasma levels of interleukin-6, particularly at the time of the biopsy.

The downstream effects of interleukin-6 are probably the cause of the clinical syndrome, which is indistinguishable from HHV-8–associated multicentric Castleman’s disease. We feel that this case report represents an HHV-8–associated multicentric Castleman’s disease, rather than a newly recognized HHV-8–associated inflammatory syndrome.

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**THE AUTHORS REPLY:** It seems to us that the issue raised by Dogan and colleagues is one of definition. From the clinical standpoint, severe symmetric arthrosynovitis (hardly ever observed in patients with HHV-8–associated multicentric Castleman’s disease) was the referring symptom. Our patient had anemia of chronic inflammatory disease but none of the hematologic abnormalities and bone marrow features characteristically associated with HHV-8–associated multicentric Castleman’s disease.<sup>1,2</sup> On only two occasions was the level of human interleukin-6 increased; rather, it remained normal throughout the follow-up, regardless of disease activity.<sup>3</sup> Although there is some variability in the features of Castleman’s disease, some of which is apparently related to the HHV-8 infection,<sup>1,4</sup> Castleman’s disease remains primarily a morphologic diagnosis: a minimum set of criteria must be

met or else the diagnosis ceases to have meaning. The microscopical appearance of the lymph nodes (including one excised before treatment) did not bear even a remote resemblance to any recognized type or variant of Castleman's disease. For these reasons, we do not believe that our patient should be given the diagnosis of Castleman's disease, but we do acknowledge the likelihood of a shared etiologic factor and pathogenesis.

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## A Fractured Diagnosis

**TO THE EDITOR:** Cukierman et al., in their Clinical Problem-Solving article (Aug. 4 issue),<sup>1</sup> affirm that "the clinical picture suggests primary Sjögren's syndrome because of the lack of clinical features associated with rheumatoid arthritis or other autoimmune disorders," according to the revised European criteria.<sup>2</sup> The more recent American-European Consensus Group classification<sup>3</sup> establishes as exclusion criteria for primary Sjögren's syndrome the presence of infection with hepatitis C virus (HCV) or the human immunodeficiency virus (HIV). Were HCV and HIV infection considered in this patient? Is there another fragment in the fractured diagnosis?

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**THE AUTHORS REPLY:** The revised American-European Consensus Group classification scheme requires that before the diagnosis of primary Sjögren's

syndrome be made, the following conditions must be ruled out: infection with HCV or HIV, lymphoma, sarcoidosis, graft-versus-host disease, and the use of anticholinergic drugs.

Our patient was tested for HCV and HIV and was negative for both. Therefore, the diagnosis of primary Sjögren's syndrome is still plausible. Despite this fact, it is possible that longer follow-up might reveal another underlying diagnosis.

An increasing body of evidence supports a strong association between HCV infection and a Sjögren's syndrome-like condition. In one study, 12 percent of patients with Sjögren's syndrome were HCV-positive.<sup>1</sup> In another study, 25.9 percent of people with chronic HCV infection met the European criteria for Sjögren's syndrome.<sup>2</sup> Clinically, primary Sjögren's syndrome may be differentiated from Sjögren's syndrome associated with HCV infection by the absence of neuropathy, vasculitis, or liver involvement, as well as by the much higher frequency of antibodies to Ro and La.<sup>1</sup>

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