A Great Masquerader: Chronic Active Epstein-Barr Virus for the Rheumatologist

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Chronic active Epstein-Barr virus (CAEBV) infection is an EBV-associated lymphoproliferative disease defined by (1) illness lasting > 6 months; (2) infiltration of tissues with lymphocytes; (3) elevated EBV DNA, RNA, or proteins in affected tissues; and (4) the absence of any other immunosuppressive condition[1,2]. It has 2 forms: EBV-associated T/natural killer (NK) cell proliferation, and EBV-associated B cell proliferation[3]. In addition to chronic mononucleosis symptoms, the clinical spectrum includes mucocutaneous disease, uveitis, encephalitis, vasculitis, myocarditis, and hemophagocytosis, thus potentially mimicking rheumatic disease[1,2,3,4,5].

A 9-year-old girl presented with recurrent angioedema and mouth ulcers following 6 months of perioral rash, fevers, night sweats, headaches, and weight loss. Examination revealed periorbital edema, tongue and lip swelling, and diffuse oral mucosal ulceration (Figure 1), tachycardia, hepatomegaly, and bilateral anterior uveitis. Echocardiography revealed coronary aneurysms, but further testing was not suggestive of vasculitis. Infectious investigation revealed high EBV viral load > 58,000 copies/ml peripheral blood, indicating active EBV infection despite serology consistent with past exposure. A mucosal biopsy reviewed by the National Institutes of Health confirmed CAEBV by demonstrating increased EBV-positive cells that were CD3+ and CD20– on double-staining, consistent with the T/NK cell subtype.

Given the progressive, life-threatening natural history of CAEBV, the patient underwent a hematopoietic stem cell transplant 7 months following diagnosis. Unfortunately, she died shortly thereafter of posttransplant complications.

CAEBV has multiple manifestations that overlap with

Figure 1. Mucosal irritation and edema.

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autoimmune and inflammatory conditions, including vasculitis[4,5]. Rheumatologists should consider this rare diagnosis when evaluating patients with complex clinical presentations. CAEBV causing angioedema has not been previously reported.

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