Diagnosis: Epstein-Barr virus acute infectious mononucleosis.
Laboratory testing revealed a positive heterophile antibody, a positive Epstein-Barr virus (EBV) viral capsid antibody immunoglobulin M, a negative EBV viral capsid antibody immunoglobulin G, and a serum EBV DNA load of 2597 copies/mL.
Additional laboratory testing for human immunodeficiency virus (HIV) (including an HIV antibody and RNA polymerase chain reaction), syphilis, measles, enterovirus, varicella zoster virus, herpes simplex virus, human herpesvirus 6, human herpesvirus 8, Neisseria gonorrhoeae, Chlamydia trachomatis, cytomegalovirus, and rickettsiae were all negative.
The histopathological exam of the lesions demonstrated superficial perivascular dermatitis with extravasation of erythrocytes and lichenoid inflammation with focal vacuolar interface alteration, few individual necrotic keratinocytes in the epidermis, and a sparse, deep perivascular inflammatory infiltrate. Immunohistochemical staining demonstrated a mixture of CD4+ and CD8+ T lymphocytes. These findings were consistent with a viral exanthem.
Of note, in situ hybridization for EBV-encoded RNA and immunohistochemical staining for latent membrane protein 1 (LMP-1) were negative, indicating there was no evidence of latent EBV infection in the skin. In addition, the lesions were negative for EBV BZLF1 (EBV immediate-early protein expressed during virus replication), indicating there was no evidence of EBV replication in the skin. Taken together, these findings suggested that the rash was most likely from immune activation rather than a direct cytopathic effect of EBV in the skin.
The patient was treated symptomatically for acute infectious mononucleosis (AIM), his rash gradually resolved over the course of 2 weeks, and he made a complete recovery.
Fever, pharyngitis, hepatitis, and cervical lymphadenopathy are the most common manifestations of AIM [1]. Historically, a rash has been reported in about 5% of cases of AIM in the absence of penicillin derivatives, but more recent accounts suggest that it may be more common than previously noted [2, 3].
Several different rashes have been reported in the setting of AIM including an “ampicillin rash,” a spontaneous rash, the Gianotti-Crosti syndrome (found only in children), erythema multiforme, urticaria, and non-sexually related acute genital ulcers [2–7].
The appearance of this patient’s skin lesions and his clinical history make it difficult to categorize his rash into one that is typically reported in the setting of AIM (Figure 1). Regardless, it is important for providers to consider the diagnosis of AIM when evaluating a patient with a febrile syndrome and rash.

**Notes**

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