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Cutaneous Eruptions Associated with Antimicrobials in Patients with Infectious Mononucleosis

To the Editor:

An 8-year-old boy with fever, sore throat, and abdominal pain received penicillin. Within 2 days he developed a red, nonpruritic, maculopapular rash, spreading caudally (**Figure**). Throat swab was negative for group A *Streptococcus*; Epstein-Barr Virus Capsid Antigen was immunoglobulin M positive. Diagnosis was cutaneous eruption associated with antimicrobials in acute infectious mononucleosis.

Filatov[1] described mononucleosis in 1887 as "idiopathic adenitis." Pfeiffer[2] called it "drüsenfieber" (glandular fever) in 1889, and in the 1920s it was called "acute benign lymphoblastosis" or "infectious mononucleosis."[2-4] Henle et al[5] "named Epstein Barr virus … after the cell lines in which it was first observed." Skin rashes (seen in 5%-15%) were not in these early descriptions, and it wasn't until the 1960s that acute infectious mononucleosis and antimicrobial rashes were linked[6-10]:

Rashes were the most frequent (95%) in the 19 patients who received ampicillin. In this group the rash was invariably extensive, maculopapular, pruritic, and accompanied by slight or moderate pyrexia. It appeared usually seven to ten days after the patient had started ampicillin and the drug had usually been discontinued for a few days before the rash disappeared. The incidence of rashes in patients treated with penicillin alone was 43% … Only 2 of the 17 patients treated with tetracycline developed rashes.[11]

The mechanism of antimicrobial rash in mononucleosis is unclear.[12] Epstein-Barr virus causes polyclonal B cell activation, increased immunoglobulins, and increased atypical lymphocytes (CD8+ T cells). Hypersensitivity is unlikely because there are no antibodies against ampicillin, and drug re-challenge elicits no reaction.[13-16] Polyclonal antibodies may form immune complexes with drugs, deposit in the dermis, and damage tissue.[17] Alternatively, activated CD8+ lymphocytes may react with drug antigens because skin biopsies show CD8+ lymphocytic infiltrates.[18]

The antimicrobial rash associated with Epstein-Barr virus occurs 2-10 days after antimicrobial exposure. In 95% the rash is exanthematous, and in 5% it is urticarial. It is more extensive than the rash of Epstein-Barr virus alone, often involving the face, neck, trunk, mucous membranes, and sometimes palms and soles, and resolves within a week of discontinuing the antimicrobial.[12,19]

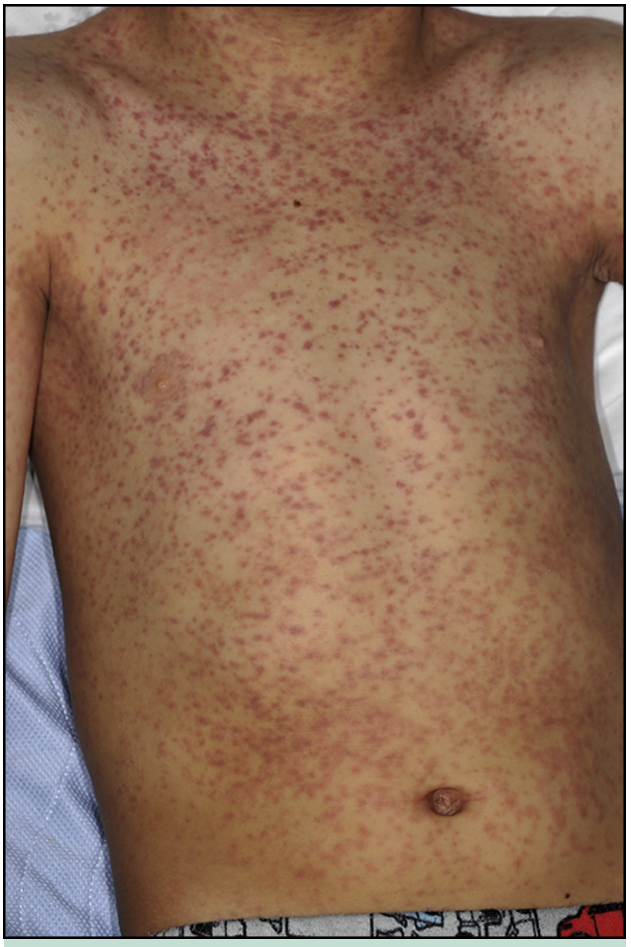

Figure An 8 year old boy with acute infectious mononucleosis caused by Epstein-Barr virus developed this cutaneous eruption two days after starting penicillin for presumed bacterial pharyngitis. The cutaneous findings resolved within a few days after discontinuing the antimicrobial.

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