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How Safe is It to Prescribe Cephalosporins in Patients with Infectious Mononucleosis? Implications for Clinical ENT Practice

Letter to the Editor

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Dear Editor,

Infectious mononucleosis is an acute self-contained disease, mostly caused by the Epstein–Barr virus (γ-subfamily herpes virus), and not rarely by cytomegalovirus (β-subfamily herpes virus). Clinical manifestations in the head and neck area include fever and cervical lymphadenopathy, as well as exudate in the faucial tonsils and pharyngitis. The latter manifestations frequently prompt an Ear, Nose & Throat (ENT) assessment. ENT surgeons, in contrast, are traditionally trained not to prescribe amoxicillin in cases of suspected infectious mononucleosis because of the risk of developing antibiotic-induced skin rash. Hence, they often resort to prescribing cephalosporins in doubtful cases, which are believed not to carry such a risk (1).

Nevertheless, the latter notion does not appear to be entirely accurate. Indeed, the maculopapular skin eruption, associated with the administration of amoxicillin in the course of infectious mononucleosis, is considered to represent a delayed-type hypersensitivity reaction (type IV allergic reaction). During this reaction, Th2 T cells are activated and secrete interleukins 4, 5, and 13, resulting in eosinophilic inflammation (1). In addition, the aforementioned reaction may be accompanied by the secretion of IgE and IgG4 from B-cells, thus linking the type IV to a potential immediate allergic reaction (type I allergic reaction) (2).

From a chemical perspective, penicillins have a β-lactam ring attached to a thiazolidine ring with one side chain. IgE-mediated penicillin allergy (type I allergic reaction) is likely to include all β-lactam ring-containing antibiotics. However, it is suspected that non-IgE mediated penicillin allergy is often related to the side chain and may be one source of delayed nonurticarial rashes (3, 4). Conversely, cephalosporins have a β-lactam ring attached to a dihydrothiazine ring with two side chains. Allergic reactions to cephalosporins are increasingly attributed to the antigenic action of the side chain and not the β-lactam ring itself (5). In addition, the side chain of older cephalosporin members (e.g., cephalothin, cephaloridine, and cefamandole) is similar to that of penicillin (5) thus increasing the risk of cross-reactivity and type IV allergic reaction with penicillin and its derivatives.

Taking the aforementioned together, and considering the fact that drug sensitization in patients with infectious mononucleosis develops during the infection (type IV allergic reaction), we propose that the standard practice of favoring administration of cephalosporin over amoxicillin in cases of potential infectious mononucleosis by virtue of its safety only holds true for newer cephalosporins (1). Given also the risk of developing immediate type I reaction, which is universal to all β-lactam ring-containing antibiotics, cephalosporin administration per se should be advocated with caution in such patients, and if possible, avoided altogether. Clarithromycin and clindamycin may be suitable alternatives, should the clinician decide to prescribe antibiotics, with infectious mononucleosis being included in the differential diagnosis.

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