Severe immune-mediated adverse drug reactions and previous history of drug allergy

A 10-year-old boy, who previously suffered an anaphylactic reaction to penicillin, presented to a paediatric hospital with a severe adverse reaction to cotrimoxazole. He had a fever, a few mouth lesions, nonpurulent conjunctivitis and some erythematous spots on the body. He was diagnosed with Stevens-Johnson syndrome (SJS) and was admitted to hospital for supportive care. He deteriorated shortly thereafter and was transferred to intensive care, where he was mechanically ventilated for five days. Serological testing for *Mycoplasma pneumoniae* IgM was reactive. Of note, two other boys of different ethnicities, who were between the ages of 10 and 15 years and were also known to be allergic to penicillin with skin rashes, were admitted in the same year with severe reactions due to cotrimoxazole. One had SJS and the other was diagnosed with drug hypersensitivity syndrome. Mycoplasma screening was negative for both patients. The mean length of stay for the three patients was nine days (range two to 16 days).

LEARNING POINTS

- Severe immune-mediated adverse drug reactions (ADRs) are among the most severe of all ADRs affecting children, often leading to hospitalization and even death.
- These reactions are poorly documented and under-reported by most surveillance programs. In patients 18 years of age or younger, surveillance of suspected ADRs to cotrimoxazole reveals the following:
  - From January 1, 1996, to September 30, 2006, the Canadian Adverse Drug Reaction Monitoring Program (CADRMP)* at Health Canada received eight reports of SJS, erythema multiforme or toxic epidermal necrolysis.
  - In 2004 and 2005, the CPSP received one report of vasculitis.
  - In 2005, the Genotype-specific Approaches to Therapy in Childhood (GATC) surveillance network† documented two reports of SJS and one report of drug hypersensitivity syndrome.
- SJS has been associated with different infections, including *Mycoplasma pneumoniae* in the absence of drug therapy. Food and, less commonly, vaccines are other possible etiologies, and in some circumstances no clear etiology is identified.
- Patients with a history of sulfonamide allergic reactions should not receive sulfonamide-containing agents and should be monitored closely during therapy with other antibiotics, because they are known to have an increased risk of reaction to penicillins.
- It is essential, upon diagnosis of possible immune-mediated bullous exfoliative rash, to immediately discontinue the causative agent because this can potentially limit the severity of the reaction.

*CADRMP caveat: The CADRMP is a spontaneous reporting system that is suitable to detect signals of potential health product safety issues during the postmarket period. The data have been collected primarily by a surveillance system in which adverse reactions to health products are reported on a voluntary basis. Each report represents the suspicion, opinion or observation of the individual reporter. Under-reporting of adverse reactions is seen with both voluntary and mandatory spontaneous surveillance systems <www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/index_e.html>; †The GATC ADR surveillance network includes clinicians at eight of Canada's major paediatric hospitals, who are identifying and documenting ADRs as part of a national pharmacogenomic project <www.popi.ubc.ca>

The Canadian Paediatric Surveillance Program (CPSP) is a project of the Canadian Paediatric Society, which undertakes the surveillance of rare diseases and conditions in children. For more information, visit our Web site at <www.cps.ca/cpsp> or <www.cps.ca/pcsp>. This article has been peer reviewed.