Published in final edited form as:

Pediatr Blood Cancer. 2015 May ; 62(5): 922–923. doi:10.1002/pbc.25430.

Immune Thrombocytopenia due to Trimethoprim-Sulfamethoxazole; Under-Recognized Risk in Children?

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Keywords

Platelets; ITP; Thrombocytopenia; Immune thrombocytopenia

Drug-induced immune thrombocytopenia (DITP) is often unrecognized; failure to diagnose this condition can result in unintended re-exposure to the drug and bleeding risk.[1] Here we report three children with DITP due Trimethoprim Sulfamethoxazole (TMP/SMX) dependent, platelet-reactive antibodies. With the increased use of TMP/SMX over the past several years, these cases highlight the need for heightened awareness of this potential adverse reaction in children.

The pathogenesis of ITP in most cases is immune-mediated destruction secondary to autoantibodies directed against platelets. Medications may induce drug dependent antibody formation and result in DITP[1]. This association is often not recognized and relatively few cases of DITP are reported in children. In a recent review, TMP-SMX was the most commonly identified cause of drug-dependent, platelet-reactive antibodies in pediatric patients; however the clinical course of these patients are not reported[2]. Here we describe the clinical course of three children who presented to our institution in a single year (2012) with DITP due to TMP-SMX.

Case 1 is a previously healthy 15-year-old female who presented with a platelet count of $5 \times 10^9/L$ and a 2 day history of petechiae and gum bleeding. She was treated with TMP-SMX two weeks prior for pharyngitis. Case 2 is a 7 year old previously healthy female who presented petechiae, ecchymosis, and mucosal hemorrhages and a platelet count of $6 \times 10^9/L$. She was treated with TMP-SMX for a UTI 2 weeks prior. Case 3 is a 10 month old male with a history of spina bifida, hydrocephalus and neurogenic bladder. He was started on TMP-SMX 3 weeks prior for UTI prophylaxis. He had a one day history of petechiae and

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There are no financial relationships relevant to this article to disclose. There are no conflicts of interest to disclose.

ecchymosis with a platelet count of $6 \times 10^9/L$ and an ANC of 970/uL. All three patients had an otherwise unremarkable peripheral blood smear. TMP-SMX was discontinued and one dose of IVIG (1gm/kg) was given for all patients. The platelet counts improved within several days and normal platelet counts were sustained. In all patients, SMX-dependent antibodies were detected by flow cytometry (Figure 1A).

A significant increase in TMP-SMX prescribing for children has been reported in the United States; this trend may be driven by the increasing incidence of community acquired Methicillin resistant *Staphylococcus Aureus* (CA-MRSA) infections [3] [4]. At the Johns Hopkins hospital, the doses of TMP-SMX dispensed to inpatients increased from 2,252 doses in 1999 to 6,569 doses in 2012. Similarly, the doses of TMP-SMX dispensed from the Johns Hopkins Pediatric Emergency Room have increased. (Figure 1B) At the Platelet and Neutrophil Immunology lab, Blood Center of Wisconsin, an increase in the number of TMP-SMX-dependent platelet antibodies detected in sera of patients less than 18 years were noted from 2011-2012 (Figure 1C); whether these observations reflect an increased rate of TMP-SMX associated ITP or increased recognition of the condition is not known.

The clinical course for our patients was typical for ITP and all improved with IVIG and discontinuation of TMP-SMX. Our experience should raise awareness of this potential adverse event to this increasingly used medication.

Reference

1. Aster RH, Bougie DW. Drug-induced immune thrombocytopenia. *N Engl J Med*. 2007; 357(6):580–587. [PubMed: 17687133]
2. Reese JA, Nguyen LP, Buchanan GR, Curtis BR, Terrell DR, Vesely SK, George JN. Drug-induced thrombocytopenia in children. *Pediatr Blood Cancer*. 2013; 60(12):1975–1981. [PubMed: 24038783]
3. Goldman JL, Jackson MA, Herigon JC, Hersh AL, Shapiro DJ, Leeder JS. Trends in adverse reactions to trimethoprim-sulfamethoxazole. *Pediatrics*. 2013; 131(1):e103–108. [PubMed: 23209098]
4. Lee MC, Rios AM, Aten MF, Mejias A, Cavuoti D, McCracken GH Jr, Hardy RD. Management and outcome of children with skin and soft tissue abscesses caused by community-acquired methicillin-resistant *Staphylococcus aureus*. *Pediatr Infect Dis J*. 2004; 23(2):123–127. [PubMed: 14872177]

Figure 1.

A)) Flow cytometry results for case 1 demonstrate TMP-SMX specific drug dependent antibodies binding the patient platelets only in the presence of drug similar to results with positive control. In the negative control there is no antibody binding both with and without drug. B) Increase in use of TMP-SMX at Johns Hopkins Hospital. Number of dispensed doses per 10000 visits at the Johns Hopkins Pediatric Emergency Room from 2002-2012. C) Increase in number of TMP-SMX dependent, platelet-reactive antibodies from samples sent to the Platelet and Neutrophil Immunology lab at the blood center of Wisconsin, the referral laboratory for antibody testing. Samples were from patients less than 18 years of age. Case 1-3 are included in statistics from 2012.