

Type II hypersensitivity and trimethoprim-sulfamethoxazole

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Abstract

Type II hypersensitivity reaction is an unusual response to trimethoprim-sulfamethoxazole. We discuss a case of rash and pancytopenia immediately following the use of trimethoprim-sulfamethoxazole in an adolescent female.

Key words: Drug eruptions, Hypersensitivity, Pancytopenia, Sulfamethoxazole

Introduction

Trimethoprim-sulfamethoxazole (Septra) is a widely used antibiotic world-wide. The clinical use has been increasing in the pediatric population [1].

Septra has been associated with a broad array of drug associated reactions including gastrointestinal complaints, cutaneous reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis and cytopenias including immune mediated thrombocytopenia [2].

Adverse reactions occur in 6-8% of patients. In the pediatric patient hospitalized for an adverse drug reaction prior exposure to Septra is found in 75% of patients [3]. In the case presented we describe a cutaneous reaction to Septra clinically consistent with a Type 2 hypersensitivity reaction with associated pancytopenia. Idiosyncratic reactions such as Type 2 hypersensitivity have rarely been reported with Septra exposure. These adverse drug reactions have infrequently been reported to be fatal [4]. With the increasing use of Septra for the management of community acquired methicillin resistant *Staphylococcus aureus* of skin and soft tissue infections [5] clinicians will need to recognize this clinical complication.

Case Report

A 16-year-old female presented with rash. Two weeks prior to presentation she had a foot abscess drained and received cephalexin. Five days later she was switched to trimethoprim-sulfamethoxazole (Septra). Five days prior to presentation she developed pruritic 'small, red bumps' diffusely over her body. The day before presentation, she developed fever, chills, nausea, and headache. At presentation, she was febrile (103°F) and had facial redness and swelling. At the time of presentation she had been on trimethoprim-sulfamethoxazole twice daily for 6 days and reported having missed 2-3 doses. This was her first known exposure to trimethoprim-sulfamethoxazole. The patient received a 125 mg dose of methylprednisolone (Solumedrol) and a hemogram demonstrated pancytopenia. She was referred to our institution for further management.

On arrival, the hemogram showed: WBC 2,000/ μ L (78% neutrophils), ANC 1,600; hemoglobin 11.5 g/dL; and platelets 115,000/ μ L. Reticulocyte count was 0.3%. Screening for a possible hemolytic anemia demonstrated the Lactate dehydrogenase was 373 U/L and uric acid was 2.7 mg/dL. The patient was clinically stable. Physical examination revealed a generalized rash involving the upper and lower extremities, abdomen, chest, and back with no involvement of the palms or soles. The rash was

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characterized by petechiae most prominently on the legs (Figure 1) but also on the palate. The drained abscess was noted to have a well-healing incision site, mild erythema and swelling, but no fluctuance or expressible pus. A 5 cm by 5 cm hard, nontender nodule was palpable behind the right ear; no other

lymphadenopathy was present. Based on the clinical characteristics of the rash we concluded the patient demonstrated a type II hypersensitivity reaction to trimethoprim-sulfamethoxazole. The drug was discontinued at admission.

Figure1: Characteristic rash involving lower extremities



Table1: Complete blood counts at admission and three days following discharge.

	Admission Date	Post-Discharge Day 3
WBC ($10^3/\mu\text{L}$)	2.0	4.6
Hemoglobin (g/dL)	11.5	12.4
Platelets ($10^3/\mu\text{L}$)	115	186

The patient remained in the hospital for two days, during which time she had modest clinical improvement. A hemogram three days after discharge indicated the patient's bone marrow to be recovering (Table 1). She was contacted 13 days after discharge and reported that the rash was resolved, she was afebrile, and she had required no further treatment.

Discussion

The patient's recent exposure to Septra, stable condition, and the characteristic pruritic maculopapular rash led us to believe that drug hypersensitivity was the most likely explanation of her symptoms. The petechial nature of the rash was concerning and not entirely consistent with the relatively minor degree of thrombocytopenia. Our diagnosis for this patient was a type II hypersensitivity reaction, however other severe and potentially life-threatening diagnoses were considered, including rickettsial disease, (endemic in our region) and hematologic malignancy. As there was no eosinophilia noted we did not feel this represented a

drug reaction with eosinophilia and systemic symptoms (DRESS syndrome).

The normal lactate dehydrogenase and uric acid levels ruled out a hemolytic process or tumor lysis. The reticulocyte count at 0.3% indicated bone marrow suppression. Uncommonly, neutropenia/agranulocytosis has been associated with trimethoprim-sulfamethoxazole [6].

Conclusion

Cutaneous reactions to Septra have been well described and include urticarial, maculo-papular and papular exanthems. Rarely Stevens Johnson Syndrome and

Toxic Epidermal Necrolysis have been reported [7]. Most drug hypersensitivity reactions are types I and IV; types II and III are less common and associated with a higher dose or prolonged therapy with the offending drug. The case presented here demonstrated features of a type II hypersensitivity reaction. Common hematologic manifestations of type II drug reactions are neutropenia, hemolytic anemia, and thrombocytopenia; characteristic features of this case. Symptoms usually do not appear until at least 5 to 8 days following administration of the drug, as was true in this case [8]. Idiosyncratic reactions may occur including agranulocytosis and sepsis like hypersensitivity syndrome [9] which are rarely fatal. The physician needs to be aware of the wide range of cutaneous and systemic manifestations associated with

exposure to Septra; while these are rarely fatal, the extent and characteristics of the drug reaction may represent a poor outcome [4]. Close follow-up with the patient including serial blood counts is important to ensure normalization of the blood counts. In this case with the discontinuation of the drug the patient returned to her normal state of health with normalization of the hematologic parameters.

Conflict of Interest:

Shelby Allen reports no conflict of interest

Sean Ervin reports no conflict of interest.

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