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Sulfamethoxazole-trimethoprim Induced Thrombocytopenia: A report of two cases and a literature review

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Sulfamethoxazole-trimethoprim-Induced Thrombocytopenia

A Report of Two Cases and Literature Review

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ABSTRACT

Sulfamethoxazole-trimethoprim (ST) is a sulfonamide derivative antibiotic that interferes with bacterial folic acid synthesis and growth by blocking dihydrofolic acid formation from para-aminobenzoic acid. A potential side effect of sulfamethoxazole-trimethoprim is thrombocytopenia. Thrombocytopenia is a blood disorder characterized by a decreased number of circulating platelets.

We present two cases of ST-induced thrombocytopenia where the oral manifestations were the first indication of the low platelet count, leading to life-saving interventions. Our aim is to educate dentists about the oral manifestations of thrombocytopenia and its association with ST, as their examination may be instrumental in directing treatment.

Bactrim (sulfamethoxazole-trimethoprim [ST]) is a sulfonamide derivative antibiotic that interferes with bacterial folic acid synthesis and growth by blocking dihydrofolic acid formation from para-aminobenzoic acid. A common and concerning side effect of sulfamethoxazole-trimethoprim is thrombocytopenia.[6] We present two cases of ST-induced thrombocytopenia that presented first in the oral cavity.

Case Reports

Case 1 occurred in a 69-year-old male who presented to his oral surgeon with the chief complaint of "blisters" in his mouth after being seen by his dentist. His medical history was significant for Graves disease, hypertension, prostate cancer and the corresponding treatment (radiation therapy, hormone therapy and gynecomastia surgery). Ten days post-gynecomastia surgery, he had a fever and was given sulfamethoxazole-trimethoprim by his surgeon. Clinically, the oral surgeon visualized a large purpura of the left buccal mucosa (Figure 1). The patient was on Bactrim for eight days before developing oral lesions.

Case 2 occurred in a 75-year-old female who presented to her dentist with the chief complaint of developing "blood blisters" in her mouth after having difficulty swallowing her sulfamethoxazole-trimethoprim pill the night before. At the visit with her dentist, she reported that her blisters were "improved" that morning, but that she also had "mosquito bites" on her arms. Clinically, the patient presented with purpura and petechiae of her right buccal mucosa and labial mucosa and petechiae of the dorsal tongue and forearms (Figures 2-6). The patient was on Bactrim for 10 days before developing oral lesions.

After consultation with oral pathologists, both patients were sent to the hospital with suspected drug-induced thrombocytopenia. Patient one was admitted with a platelet count of 1,000; patient two was admitted with a platelet count below 5,000. Both patients were instructed to discon-

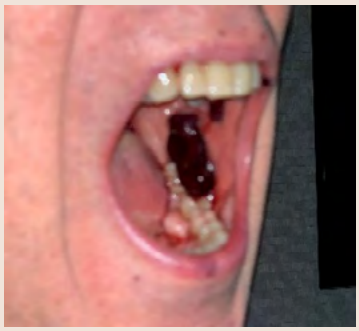

Figure 1. Case 1: Purpura of buccal mucosa.

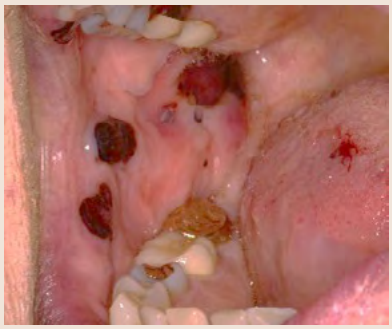

Figure 2. Case 2: Purpura and petechiae of right buccal mucosa and dorsal tongue.

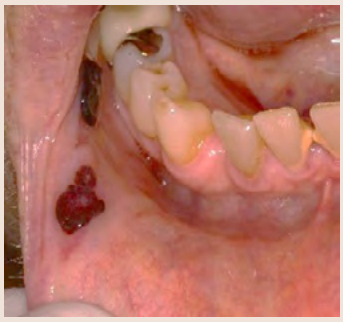

Figure 3. Case 2: Purpura and petechiae involving labial mucosa.

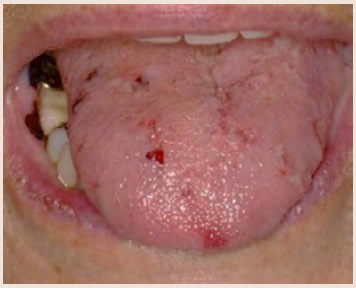

Figure 4. Case 2: Petechiae involving tongue.

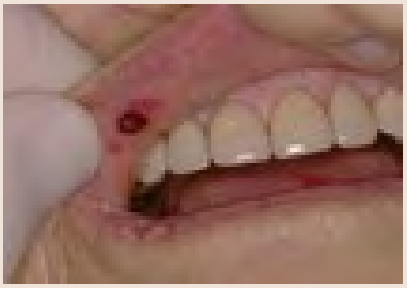

Figure 5. Case 2: Petechiae of upper labial mucosa.

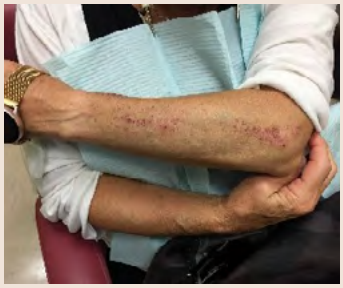

Figure 6. Case 2: Widespread petechiae of arms of patient.

tinue the sulfamethoxazole-trimethoprim and were given IV immunoglobulins and steroids during their hospital stay. Patient one was given three platelet transfusions while admitted. Both patients recovered and are doing well.

Discussion

These two case reports demonstrate the oral manifestations of drug-induced thrombocytopenia (DITP), a concerning possible side effect of sulfamethoxazole-trimethoprim. A normal platelet count is generally considered to be between 150,000 and 450,000 cells per microliter.[3] When the platelet count drops below 150,000 cells per microliter, the patient is thrombocytopenic.[4] Clinically, patients with drug-induced thrombocytopenia may demonstrate lightheadedness, chills, fever, nausea, vomiting, purpura and petechiae.[4] Risk of severe bleeding, including CNS hemorrhage, hematuria, melena and hematemesis, increases as the platelet count drops below 10,000 cells per microliter.[4]

There are many causes of thrombocytopenia, including conditions that cause trapping of platelets in the spleen, conditions that cause a decrease in platelet production and conditions that cause an increase in platelet destruction.[1] Drug-induced thrombocytopenia falls under the category of increased platelet destruction. There have been at least six different mechanisms identified in which drug-induced antibodies can promote platelet destruction.[1]

Of the six different mechanisms proposed for DITP, sulfamethoxazole-trimethoprim falls in the "quinine type" immune pathogenesis category.[2] This quinine-type DITP occurs when the drug, in this case sulfamethoxazole-trimethoprim, induces an autoantibody to bind to a membrane protein only in the presence of the drug. It is hypothesized that while the autoantibody and the platelet glycoprotein are always present, the reaction between them without the drug is too weak. The presence of the drug improves the structural affinity of the autoantibody and platelet glycoprotein, causing a binding.[1] Other drugs that fall into the quinine mechanism of action category include quinine, other sulfonamide antibiotics and nonsteroidal anti-inflammatory drugs.[2]

A study performed in the Eastern United States estimated that DITP occurred in persons treated with sulfamethoxazole-trimethoprim at a rate of 36 persons per million per week of exposure.[1] The onset of DITP is variable. It typically presents 5 to 10 days after the first exposure to the causative drug and within hours of the second exposure of the drug.[2] Oral manifestations of drug-induced thrombocytopenia may be the first indication to the patient that they are having an adverse reaction to their medication. Our cases document the timeline of two patients prescribed sulfamethoxazole-trimethoprim and their subsequent drug-induced thrombocytopenia.

The best treatment for drug-induced thrombocytopenia is discontinuation of the causative agent. Platelet transfusions are not usually indicated due to the continued platelet destruction in the presence of the drug.[2] Howev-

er, transfusions can be helpful for patients with a platelet count <20,000/ mm³ after discontinuation of the drug. Both case report patients were admitted with platelet counts well below 20,000, and patient one received three platelet transfusions during his hospital stay to aid in his recovery.

While platelet transfusions are not always indicated, they can be necessary to control overt hemorrhage.[5] Steroids are often administered in the hospital because at admission, immune thrombocytopenic purpura cannot be ruled out. The first line of treatment for immune thrombocytopenic purpura is administering corticosteroids to decrease circulating autoantibodies.[5] Recovery from drug-induced thrombocytopenia usually starts within one to two days after stopping the causative agent, and complete recovery usually takes place within a week.[1] The antibodies created during the drug exposure can linger for years, making it imperative to confirm drug-induced etiology, so that the patient can avoid the drug in the future.[1]

Conclusion

Knowledge of drug-induced thrombocytopenia is of paramount importance when evaluating a patient with new onset petechiae and purpura. Oral healthcare professionals may be the first people patients seek out when they notice the intraoral signs. Awareness of the presentation of thrombocytopenia can aid our patients in receiving proper and potentially lifesaving care.

Queries about this article can be addressed to Dr. Griffin at leigh.griffin@tufts.edu.

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