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Bactrim-induced Severe Thrombocytopenia in Pregnancy

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Authors' contributions

This work was carried out in collaboration between all the authors. Author WG designed the study. Author SH managed the literature search and wrote the first draft of the manuscript. Author MA wrote the second draft with assistance from authors RT and MG. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

A 29-year-old Caucasian woman at 30 weeks' gestation presented with severe and asymptomatic thrombocytopenia with a platelet count of 17 × 10^9/L after completing 9 days out of a 10-day course of Bactrim DS for a nasal abscess. Upon further investigation, Bactrim-induced thrombocytopenia was diagnosed. After discontinuing this medication, her laboratory abnormalities immediately improved without any additional interventions.

Keywords: Drug-induced thrombocytopenia; Trimethoprim/sulfamethoxazole; steroids; platelet count; gynecology/obstetrics.

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1. INTRODUCTION

Thrombocytopenia is a common finding in hospital patients, and drug-induced thrombocytopenia is well-documented but is often unrecognized by clinicians. The condition can be asymptomatic, but it can also lead to life-threatening bleeding [1]. In pregnant patients, thrombocytopenia is the second most common hematologic abnormality. Therefore, it is even more challenging to differentiate drug-induced thrombocytopenia from thrombocytopenia secondary to gestational conditions, such as pre-eclampsia or gestational thrombocytopenia [2]. Trimethoprim/sulfamethoxazole (TMP/SMX) is one of the first-line antibiotic agents available for methicillin-resistant staphylococcus aureus in soft tissue infections [3]. TMP/SMX is among the drugs that are often implicated in drug-induced thrombocytopenia [4].

2. CASE PRESENTATION

A 29-year-old G6P5 female who was 30 weeks pregnant presented to the ED complaining of worsening lower leg pain and fevers of three-day duration. The patient was a housewife. After undergoing a negative workup for a deep venous thrombosis, she was found to be severely thrombocytopenic with a platelet count of 17 × 10^9/L. 4 weeks earlier her platelet count was 220 x 10^9/L. Upon further questioning, she stated that she was prescribed Bactrim DS for a nasal abscess and completed 9 of the 10-day course. Trauma to her nasal bone led to nasal hematoma, which got infected and resulted in nasal abscess. She was recently diagnosed with gestational diabetes, but she otherwise had no significant medical history and denied any previous episodes of thrombocytopenia during her prior pregnancies. She visited her obstetrician regularly for prenatal care, and her other prenatal laboratory results were unremarkable. Her family and social history were non-contributory. The only medication she took besides Bactrim DS was a once daily prenatal multivitamin.

She denied any history of recent bleeding, bruises, or rashes, and a ten-point review of systems was negative. There was no history of previous episodes of fever, weight loss, weakness, fatigue, rash, inflammatory arthralgia or synovitis suggesting any autoimmune disease. On admission, her blood pressure was 128/76, heart rate was 82 beats per minute, respiratory rate was 18 per minute, and her temperature was 97.8 Fahrenheit. Her physical exam was unremarkable. Her complete blood count was normal except for a decreased platelet count of 17× 10^9/L. The blood smear showed normal morphology for both RBC and platelets. The PT was normal and the fibrinogen level was elevated (512). The liver function test, serum creatinine, blood urea nitrogen (BUN), and estimated glomerular filtration rate (eGFR) were all normal. Her tick borne disease panel was negative for babesiosis, lyme, anaplasmosis, and ehrlichiosis. The hepatitis viral panel was non-reactive for antibodies against hepatitis A, B, or C. HIV test and non treponemal antibodies was also negative.

The patient was hospitalized with suspected drug-induced thrombocytopenia. Bactrim DS was immediately discontinued, and the patient was started on a normal saline infusion while continuing to be worked up for other possible causes of thrombocytopenia. Her leg pain and fever was resolved on next day of admission and no etiology was found for it. The platelet count was monitored daily throughout the patient's three-day stay in the hospital. After initially dropping to 12 × 10^9/L, her platelets slowly began to rise, and she was discharged with a platelet count of 42 × 10^9/L. A follow up complete blood count was completed one day after discharge and showed a platelet count of 105 × 10^9/L (Fig. 1). There was no further episode of thrombocytopenia throughout the pregnancy. She never developed hypertension for the rest of the pregnancy and post-delivery, and all workup was negative for preeclampsia.

3. DISCUSSION

Thrombocytopenia in pregnancy is defined as a platelet count of less than 150,000/μL or platelet count lower than 2.5th percentile (116,000/μL) in pregnant women. Mild thrombocytopenia is defined as platelet count of 100,000-150,000/μL, moderate is between 50,000-100,000/μL, and severe is platelet count less than 50,000/μL. It is estimated that about 6-15% of pregnant women have mild thrombocytopenia during third trimester, but in most cases it is resolved spontaneously postpartum without treatment [2,5,6].

Bactrim-induced severe thrombocytopenia is a rare adverse effect with an estimated incidence of 38 cases per 1 million Bactrim users per week [7]. Typical symptoms in drug-induced thrombocytopenia range from asymptomatic

thrombocytopenia to life-threatening hemorrhage, thrombotic thrombocytopenia purpura (TTP) and hemolytic-uremic syndrome (HUS) have been associated in severe cases. Typically a patient has to take the offending medication consistently for a week or intermittently over a longer period of time to present symptoms of thrombocytopenia. Very rarely a patient with pre-existing antibodies can experience thrombocytopenia within one or two days of starting the causative agent. The onset is often rapid, and the platelet count is usually below 20× 10^9/L. Discontinuing the medication can improve the symptoms within one to two days, and the platelet count can increase to normal range within a week [1,8].

Fig. 1. Platelet count pattern during patient's 3-day stay in the hospital

The initial treatment is to discontinue the medication that is causing thrombocytopenia. This is by reviewing the medication needs of the patient and determining which medication should be substituted [1,9,10]. Most patients can recover without additional treatment after they stop taking the medication. With myelo-suppressive medications, thrombocytopenia is managed with platelet transfusion. However, with immune mediated drug-induced thrombocytopenia, the drug must be discontinued, and it generally takes about a week for the platelet count to return to normal range [1,11]. In patients with life-threatening bleeding, second-line treatment, such as intravenous immune globulin and/or steroids and plasmapheresis, can be administered but have not proved to be effective [12]. However, these measures have not been proven effective [12]. Platelet transfusion is used when the severity of the thrombocytopenia carries a high risk of spontaneous hemorrhage, or when the patient is showing signs of hemorrhage [1,12,13].

The mechanisms behind drug-induced thrombocytopenia can be divided into decreased platelet production and increased platelet destruction. Most medications accelerate platelet destruction through immune or less commonly non-immune mediated reaction. In the case of sulfamethoxazole, it is hypothesized that the immune system, in the presence of the causative agents, generates platelet-specific antibodies targeting glycoprotein IIb/IIIa and Ib/V/IX, which serve as receptor sites for fibrinogen and von Willebrand factor [1,12].

In this case, the severity of the thrombocytopenia limited our differential diagnoses. Due to the patient's gestational stage, pre-eclampsia, HELLP syndrome and Primary Immune Thrombocytopenia (Primary ITP) were among the top differentials. However, because of the absence of new-onset hypertension, hemolysis, normal renal and liver function, and proteinuria, preeclampsia and HELLP syndrome were ruled out. Additionally, while gestational thrombocytopenia is common, the condition is typically mild and the platelets usually remain above 70 × 10^9/L [2,5]. This patient never had abnormal platelet count in this or any previous pregnancy, which made gestational thrombocytopenia unlikely. Microangiopathic hemolytic anemia (MAHA) can be caused by conditions such as thrombotic thrombocytopenia purpura (TTP), hemolytic-uremic syndrome (HUS), or disseminated intravascular coagulation (DIC) all of which can present with thrombocytopenia [2,5]. However, the lack of schistocytes on blood smear as well as the elevated fibrinogen ruled out these conditions. Primary ITP is a diagnosis of exclusion so we didn't measure antithrombocyte antibodies, as is our case drug was a possible cause of thrombocytopenia.

The diagnosis of drug-induced thrombocytopenia is made only after other causes have been excluded in this patient. The treatment for drug-induced thrombocytopenia is the cessation of the causative agent, so we mainly provided the patient with supportive care. The patient remained asymptomatic throughout the hospital stay so we hold platelet transfusion unless the platelet count dropped below 10 × 10^9/L. Since therapy with Bactrim preceded thrombocytopenia (Criteria 1), the quick recovery of the platelet count after the discontinuation of Bactrim (Criteria 2), Bactrim was the only drug used before the onset of thrombocytopenia (Criteria 2), and other causes were ruled out (Criteria 3), level of evidence 2 (criteria 1-2) was fulfilled in evaluating causative relationship in

drug-induced thrombocytopenia [1]. Therefore, this is a probable case of drug-induced thrombocytopenia. The patient was advised to avoid TMP/SMX in the future for antimicrobial treatment.

4. CONCLUSION

This is a case of a 29-year-old Caucasian woman at 30 weeks' gestation with severe and asymptomatic Bactrim induced thrombocytopenia. The patient's gestational age complicated the possible differentials of thrombocytopenia, but after extensive laboratory workup and careful history taking other causes were ruled out. After discontinuing this medication, her laboratory abnormalities immediately improved without any additional interventions. This case emphasizes the importance of including drug-induced thrombocytopenia into the differentials of new-onset thrombocytopenia.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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