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RANITIDINE INDUCED THROMBOCYTOPENIA: A CASE REPORT

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ABSTRACT

Introduction: Thrombocytopenia is defined as a platelet count of 100,000/mm3 or >50% drop in the platelet count from baseline. Ranitidine causes thrombocytopenia by an idiosyncratic reaction. **Case Report:** A 60-year-old female, a case of psoriasis, presented in dermatology department with multiple pustules over lower extremities, associated with fever and vomiting with the history of diabetes mellitus type-2 and hypertension as co-morbidity from the past six years. Initially the platelet count of patient was 1.85 × 109 /dL. Hb was 9 g%. Patient was started on azithromycin 250 mg BD, paracetamol 500 mg BD, IV ranitidine 50 mg BD and IV domperidone. Hematological investigations repeated after 3 days revealed thrombocytopenia with platelet count of 71 × 109/dL and WBC count of 2500 cells/mm3 with neutropenia and Hb 9.2 g%. Repeated blood picture showed further decrease in platelet count to 28,000 × 109/dL and WBC count to 1500 cells/mm3. Important causes of pancytopenia were ruled out. The drug was withdrawn and after 48 hours a considerable improvement in the hemogram was noticed with Hb 9.7 g%, WBC count of 4800 cells/mm3 and platelet count of 80 × 109/dL. The patient had recovery without incident and was discharged ten days later with normal blood counts. **Conclusion:** In cases of severe thrombocytopenia in critically ill patients, a pharmacological cause must be suspected, including H2-receptor antagonist such as in our case it was ranitidine induced thrombocytopenia. Alternative drugs for prophylaxis of stress ulcer should be considered.

KEYWORDS: Thrombocytopenia, H2-receptor antagonist, Ranitidine, Adverse drug reaction.

INTRODUCTION

Nowadays inclusion of H2-receptor antagonist in the dose regiment during the treatment of patient in his hospital stay for prophylaxis of stress ulcer has become a common medical practice. In this class ranitidine drug is widely prescribed. Though it is an safe drug with minimal side effects however it can cause some rare adverse drug reactions such as thrombocytopenia. Thrombocytopenia is usually defined as a platelet count of 100,000/mm3 or >50% drop in the platelet count from baseline.[1] Severe thrombocytopenia is defined as platelet counts of <50,000/mm3, involves an increased risk of bleeding during invasive procedures. Platelet counts of <10,000/mm3 may have serious bleeding consequences and may even result in patient mortality.[2,5] Ranitidine causes thrombocytopenia by an idiosyncratic reaction associated with an increase in platelet-induced immunoglobulins and its later clearance by the phagocytic system.[6] The H2-receptor antagonists are typically the first medication to be implicated and substituted with an alternative anti-secretory agent. Many health care providers assume that the H2 antagonists are a well-established cause of thrombocytopenia. Even though other medications such as phenytoin and cephalosporins are also related to thrombocytopenia.[7,8] Thus, it is important to differentiate between H2-receptor antagonist-associated thrombocytopenia and H2-receptor antagonist-induced thrombocytopenia in order to assess the risk-to-benefit ratio of the continuation of H2 antagonist administration. The diagnosis of this condition is mainly dependent on the objective evidence hence if detected on time it can be life saving for critically ill patients.

CASE REPORT

A 60-year-old female, a case of psoriasis, presented in dermatology department of tertiary care hospital with multiple pustules over lower extremities, associated with fever and vomiting. The patient had diabetes mellitus type-2 and hypertension as co-morbidity from the past six years. Routine hemogram on admission revealed WBC count of 4500 cells/mm3 (N: 69, L: 21, E: 4, B: 1) and platelet count of 1.85 × 109 /dL. Hb was 9 g%. Patient was started on azithromycin 250 mg BD, paracetamol 500 mg BD, IV ranitidine 50 mg BD and IV domperidone. Hematological investigations repeated after 3 days revealed thrombocytopenia with platelet count of 71 × 109/dL, WBC count of 2500 cells/mm3 with neutropenia and Hb 9.2 g%. Important causes of pancytopenia like malaria, leptospirosis, dengue, autoimmune disorders, and sepsis were ruled out. Repeated blood picture showed further decrease in platelet count to 28,000 × 109/dL and WBC count to 1500 cells/mm3; however, there was no spontaneous bleeding. Bleeding time, clotting time and INR were normal. With other causes

ruled out realistically and the patient being clinically asymptomatic, it was concluded that a drug may be the possible cause of thrombocytopenia. Ranitidine-induced thrombocytopenia in critically ill patients has been reported. The drug was without delay withdrawn and after 48 hours a considerable improvement in the blood picture was noticed with Hb 9.7 g%, WBC count of 4800 cells/mm3 and platelet count of 80 × 109/dL. The patient had recovery without incident and was discharged ten days later with normal blood counts.

DISCUSSION

There are three possible mechanisms by which a drug causes decrease in platelet count: failure of production by bone marrow, immune destruction and platelet aggregation in circulating blood.[9] Mainly the antigenic stimulus for the production of platelet associated antibodies probably depends on the drug binding to either platelets or plasma proteins, which then act as haptens. The antibody or antibody-drug complex subsequently produced coats circulating platelets, and possibly developing megakaryocytes, resulting in increased destruction or decreased formation and release.[10,11] Ranitidine are normally only weakly bound to plasma proteins and any complex formed is probably only weakly antigenic. Several drugs have been implicated in causing acute immunologically mediated thrombocytopenia.[12] The diagnosis of thrombocytopenia is based on clinical suspicion. In our case, in order to confirm the causality of ranitidine leading to thrombocytopenia, we applied the WHO-UMC system for standardized case causality assessment[13] which suggested a "certain relationship" between ranitidine and thrombocytopenia though we could not subject the patient to a rechallenge. Drug-induced thrombocytopenia can usually take weeks or months to appear but may appear within 12 hours of drug intake in a sensitized individual.[14,18] Typically, the platelet count falls to 75-80% of the normal and thrombocytopenia may be associated with neutropenia and anemia. In our case, there was anemia and pancytopenia which considerably improved after withdrawal of ranitidine. Review of literature shows that this rare adverse drug reaction due to H2 receptor antagonist such as ranitidine is more common in critically ill patients mostly patients admitted in Intensive Care Unit (ICU). Hence, preventative measure should be taken before putting these patients on medication for ulcer prophylaxis.

CONCLUSION

In cases of severe thrombocytopenia in critically ill patients, a pharmacological cause must be suspected, including H2-receptor antagonist such as in our case it was ranitidine induced thrombocytopenia. Alternative drugs for prophylaxis of stress ulcer should be considered.

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