

**CASE REPORT**

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Successful treatment of a patient with herbal drug-induced immune thrombocytopenic purpura using freshly donated blood

Marcellinus Uchechukwu Nwagu***ABSTRACT****BACKGROUND**

Drug-induced thrombocytopenia (DITP), which also includes thrombocytopenia induced by beverages, foods, and herbal remedies, is an important clinical problem for haematologists. Drug-induced thrombocytopenia is often misdiagnosed as immune thrombocytopenic purpura with resulting inappropriate treatment. Immune thrombocytopenic purpura (ITP) is a clinical disorder that leads to easy bruising (purpura), excessive bleeding or extravasation of blood from capillaries into skin and mucous membranes (petechiae). The bleeding tendency is due to decreased number of circulating platelets (thrombocytopenia). There is production of antibodies against the platelets by the patient's immune system. This case report was conducted to introduce the effectiveness of freshly donated blood and steroids on patients with immune thrombocytopenic purpura (ITP) after ingestion of herbal drugs.

CASE DESCRIPTION

DT was a 30-year old female who presented with bleeding per vagina, gum bleeding and weakness. The patient did not have any systemic disease that would cause any spontaneous hemorrhage. The patient was referred to a hematologist urgently and her thrombocyte count was found to be 2000/ μ L. Other test results were in normal range. Full blood count revealed severe thrombocytopenia. Freshly donated whole blood was given to the patient and then the changes in her general condition were analyzed, as well as the blood test results.

CONCLUSION

In the absence of platelet concentrate especially in rural settings and resource-poor countries, freshly donated whole blood can be used in the management of a case of severe thrombocytopenia from ITP.

Keywords: Freshly donated whole blood, immune thrombocytopenic purpura, herbal drugs

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is an acquired haematological disorder characterized by platelet destruction mediated by auto-antibody. The resultant clinical manifestations include purpuric lesions of the skin, mucosa and other sites.⁽¹⁾ There are usually two distinct clinical syndromes namely, an acute condition in children and a chronic condition in adults. The acute type follows an infection and has a spontaneous resolution within few months while chronic immune thrombocytopenia usually persists more than six months with an unknown specific cause.⁽²⁾ The antibodies implicated are immunoglobulin G (IgG) directed against platelet membrane antigens, specifically glycoproteins Ib-IX or IIb-IIIa. These immunoglobulins can be detected in about 60% of cases.⁽³⁾ The coating of the platelets by these auto-antibodies makes them to be opsonised and removed both by the splenic macrophages and hepatic Kupffer cells. The destruction of megakaryocytes by these antibodies is also thought as one of the mechanisms of platelet destruction. Impaired production of thrombopoietin has also been demonstrated as a contributor to thrombocytopenia. This has led to the development of thrombopoietin receptor agonists.⁽⁴⁾ The activity of the abnormal T-lymphocytes leads to stimulation of the auto-antibody production.⁽⁵⁾ These T-lymphocytes are also affected by drugs which are targeted against B-lymphocytes such as rituximab.⁽⁶⁾

If the platelet count falls below 20,000 per μL , any of these signs and symptoms may occur, namely, formation of spontaneous petechiae (tiny bruises) on the limbs, bleeding from the gums/nostrils and menorrhagia. A platelet count of below 10,000 per μL may result in oral and mucous membrane haematomas. There is prolonged bleeding time from minor cuts or lacerations.⁽⁷⁾ At extremely low platelet counts (<5,000 per μL) there may be serious complications such as subarachnoid and intracerebral bleeding, gastrointestinal haemorrhage and various types

of internal bleeding following blunt abdominal injury, eg following a car crash. Normally, there is no enlargement of the spleen despite destruction of platelets by splenic macrophages. An enlarged spleen should lead to finding other causes of the thrombocytopenia.

Diagnosis of ITP is made by exclusion. It must be established that there are no other blood disorders apart from thrombocytopenia and no other physical findings except bleeding. About 5-10% of cases are caused by secondary factors which must be excluded. Such secondary causes include leukemia, medications (heparin, quinine), hepatitis C, HIV, lupus erythematosus and antiphospholipid syndrome. Other secondary causes include cirrhosis, antiphospholipid syndrome and Von Willebrand factor deficiency.^(7,8) Usually the bleeding time is prolonged. However, the use of bleeding time in making a diagnosis of ITP is discouraged by American Society of Hematology guidelines,⁽⁹⁾ a normal bleeding time does not exclude platelet disorder. Bone marrow examination is performed when the diagnosis is in doubt or for patients who are not responding to treatment.⁽⁸⁾ Examination of the bone marrow shows increased megakaryocytes. Analysis of anti-platelet antibodies has about 80% specificity and hence its clinical usefulness not universally accepted. Its use is a matter of choice by the physician.⁽⁸⁾

Indication for treatment is not based on just platelet counts except in rare situations. Currently, the guidelines on treatment are based on severity of bleeding. However, there are different indications of treatment in both adults and children.⁽¹⁰⁾ Steroids are usually the first line of treatment. These steroids are medications which suppress the immune system. The determinants of mode of administration and dose include the platelet count and severity of bleeding. In urgent situations and in cases of severe bleeding, infusions of methylprednisolone or dexamethasone may be used. In less severe cases, oral prednisone may suffice. Once there is improvement in platelet counts, the dosage of steroids is reduced while looking out for the possibility of relapse. About

60-90% of patients will experience relapse following dosage reduction or cessation.^(8,9) Steroids are avoided being used for a prolonged period due to its potential side effects and complications which include osteoporosis and cataract.⁽¹⁰⁾ Apart from steroids, there is increasing use of steroid-sparing agents such as azathioprine. In chronic refractory cases vinca alkaloids may be used,⁽¹¹⁻¹³⁾ and chemotherapeutic agents such as vincristine may be tried.^(14,15) Other treatment options include use of intravenous immunoglobulins, thrombopoietin receptor agonists, anti-D immunoglobulin, surgery (splenectomy) and the use of rituximab, which is however very expensive.⁽¹⁶⁾ Treatment with platelet transfusion alone is not usually successful in producing a long-term increase in platelet count, hence it is not usually recommended except in an emergency due to severe bleeding. The explanation is that the underlying autoimmune mechanism that is destroying the patient's platelets will also destroy donor platelets.⁽¹⁷⁾

CASE REPORT

Miss DT is a 30-year old single lady who presented to the Accident and Emergency (A & E) section of Delta State University Teaching Hospital Oghara, south-south Nigeria. Her presenting complaints were seven months history of irregular prolonged vaginal bleeding, two months duration of gum bleeding and one week of general body weakness. The prolonged vaginal bleeding was said to have been provoked by the ingestion of herbal drugs, Chukatrin herbal powder, which she mixed with lime for treatment of severe dysmenorrhea. On ingesting the medication, she developed the bleeding which progressively worsened with passage of clots. Physical examination revealed a young fair lady not in any obvious distress, she was pale, anicteric and not febrile to touch. There were petechial haemorrhages on the abdomen, chest, and the anterior parts of both upper and lower limbs. There were also blood clots in the buccal cavity. Her pulse was 96 beats per minute, blood pressure

was 100/80 mmHg and there was neither splenomegaly nor any enlarged organ in the abdomen. A preliminary diagnosis of bleeding disorder was made.

Series of laboratory investigations were requested and the results were as follows: 1) full blood count showed haemoglobin 8.72g/dL; white blood cell count 5,740/ μ L; and platelet count 1,650/ μ L. Urine analysis showed presence of red blood cells (haematuria). Clotting profiles were normal as well as the electrolytes, urea and creatinine. The erythrocyte sedimentation rate (ESR) was also within normal range. The peripheral blood film was remarkably normal except for the presence of very few platelets. Our centre does not have the facility to detect platelet auto-antibodies.

The final diagnosis was adult (chronic) thrombocytopenic purpura. The line of management was as follows: the patient was admitted and the offending herbal preparation was stopped forthwith. The hospital does not have an aphaeresis machine to prepare platelet concentrates. Alternatively, she was commenced on fresh whole blood (transfused within six hours of donation). Her relations and well-meaning individuals donated blood for her. She received a total of eight units of freshly donated whole blood while on admission, which raised the platelet count to 27,000/ μ L during the four weeks of admission. This stopped all forms of bleeding and she became better clinically. In addition to blood transfusion products, she was placed on injections of methylprednisolone 500mg daily. The platelet count has been above 25,000 per μ L for a period of two weeks after the last blood transfusion and the bleeding per vagina, petechiae and gum bleedings have stopped. She was discharged home on oral prednisolone 60mg daily and was given a one-week appointment for a follow up visit at the haematology clinic.

Two months later, her platelet count was normal (375,000 per μ l) and all the presenting complaints were no longer present. The prednisolone was reduced to 30mg daily and was given a four-week follow up. She was seen

again one month later and her platelet count was 392,000 per μL . This case report was reported per the tenets of the Declaration of Helsinki and was approved by the institutional review board and ethical committee of my university. I obtained written informed consent from the patient.

DISCUSSION

Immune thrombocytopenic purpura (ITP) is rare among Africans and people of African descent living in other countries compared to Caucasians. The overall prevalence rate in Nigeria is 0.005% of hospital cases.⁽¹⁸⁾ No case has ever been reported in the Niger-Delta region of Nigeria. There is no clear cause of ITP in most cases of the disease. However, only 5-10% of cases are linked to secondary factors or causes,^(7,8) None of these secondary causes was associated with native preparations as in this case. This patient ingested an aloe vera product named Chukatrin which elicited her immune reaction and ITP. Nigeria is one of the countries where the use of various native/herbal preparations is rampant and has been on the increase.⁽¹⁹⁻²¹⁾ These herbal preparations are not without harmful effects. Some of these harmful effects are not even reported because of the high cost of western healthcare. Many cases do not present to the hospital. Worse still, marketers of these herbal drugs make lots of claims in the media and public places without being checked by constituted authorities and thereby endangering lots of our populace.

The role of freshly-donated blood is emphasized in this case. Severe thrombocytopenia is preferably treated using platelet concentrate or platelet-rich plasma. However, the development of component therapy is still rudimentary in our hospital setting and we resorted to using freshly-donated blood to salvage the thrombocytopenia in this patient. A freshly-donated blood one unit of platelet concentrate from aphaeresis or pooled leucocyte depleted would be expected to

increase the platelet count of a 70kg adult by 20,000-40,000 per μL . In this case 8 units of fresh blood raised the platelet count to about 25,350 per μL , giving an average of 3,000 per unit of fresh whole blood. The exact mechanism by which fresh blood assists in ITP is unclear. However, the dilutional effect of the freshly donated blood on the circulating anti-platelet antibodies may play a significant role.

CONCLUSION

This is the first reported case of successful management of severe thrombocytopenia using freshly donated whole blood transfusion rather than platelet concentrate. It is being recommended that in the absence of platelet concentrate, fresh whole blood can be of benefit. Government and constituted authorities should discourage public promotion of herbal preparations especially when the efficacy and safety of the use of such products have not been verified.

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CONFLICT OF INTEREST

The author confirms that this article content has no conflict of interest.



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