Case Report

Hormonal Contraceptive Induced Immune Thrombocytopenic Purpura

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Abstract

Immune thrombocytopenic purpura (ITP) is an acquired disorder of platelets that clinically manifests with mucocutaneous bleeding. There are several causes of ITP, but its association with hormonal contraceptive implants has not been widely reported. A 39-year-old Para 10+0 7 alive presented to the Yobe State University Teaching Hospital with complaints of nasal bleeding, gum bleeding, purpura, and menorrhagia, which were noticed a month after insertion of a Levonorgestrel – containing hormonal contraceptive implant, at a Primary Healthcare facility. Complete blood count, peripheral blood film, and bone marrow aspiration cytology led to the diagnosis of ITP. Epistaxis was managed conservatively. The patient was placed on prednisolone with a noticeable increase in platelet count and remarkable improvement in the clinical state. ITP is a complication of the hormonal contraceptive implant. Clinicians should be aware of the possible association of contraceptive implants and ITP.

Keywords: Hormonal contraceptive implants, immune thrombocytopenic purpura, mucocutaneous bleeding, prednisolone

Introduction

Immune thrombocytopenic purpura (ITP) is an acquired hematological disorder in which antiplatelet antibodies cause accelerated destruction of platelets by the cells of the mononuclear phagocytic system.[1] The disorder affects both children and adults. Adult-type ITP is insidious in onset and often pursue a protracted course.[1] The incidence of ITP in adults is estimated to be between 1.6 and 3.9 per 100,000 per year.[1] As with most autoimmune disorders, adult-type ITP commonly occurs in females: The prevalence in males and females between the ages of 18 and 64 years is 16.6 and 27.2 per 100,000, respectively.[1] The prevalence increases significantly after the age of 65 years. Chronic infections, bacterial and viral, vasculitides, and some drugs, are implicated in the etiopathogenesis of ITP.[1-3] Thrombocytopenia following insertions of hormonal contraceptive implants was reported by the United States Food and Drug Administration in 6 women between 1991 and 1993.[4]

Studies in Nigeria and other parts of the world have shown that bleeding disorder constitutes one of the most comon reasons for discontinuation of contraceptive implants with documented evidence of thrombocytopenia among the study population.[5,6] However, the mechanism of thrombocytopenia has not been explained in these studies. The thrombocytopenia may be as a result of immune-mediated destruction by antiplatelet antibodies. As women are becoming empowered to make an informed decision about family size, levonorgestrel-containing contraceptive implants have become the preferred method of contraception.

Here, we report the occurrence of ITP in association with a hormonal contraceptive implant in a newly established tertiary health facility in the North-East geopolitical zone of Nigeria.

Case Report

Patient U. F. A, a 39-year-old P_{10}^{+0} 7 alive presented to the Yobe State University Teaching Hospital, Damaturu,

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Yobe State, North-Eastern Nigeria, with a 4-month history of epistaxis, gum bleeding, purpura and bleeding per vagina. Symptoms commenced 4 weeks after the insertion of levonorgestrel–containing hormonal contraceptive implant, at a Primary Healthcare facility. Epistaxis was said to be spontaneous, recurrent, and bilateral. She noticed gum bleeding on brushing her teeth. Bleeding per vagina presented as spots with no significant clots. No previous history of menstrual irregularities or use of contraceptives and no history of intrapartum or postpartum hemorrhage. There was no fever, weight loss, night sweats, bone pain, abdominal swelling, or jaundice. No history of bleeding from orifices before the use of the contraceptive implant. She was diagnosed with hypertension during her last pregnancy. She was not a known diabetic. She had five units of blood transfused before the presentation.

On examination, she was acutely-ill, not dehydrated, moderately pale, anicteric with a conjunctival hemorrhage in the right eye [Figure 1]. No significant peripheral lymphadenopathy. Purpuras were present on the antecubital fossae. No pedal edema. Her weight and height were 46.9 kg and 1.55 m, respectively.

The cardiovascular system was remarkable for tachycardia (pulse rate of 108 bpm), and hypertension (blood pressure [BP] 217/135 mmHg). There was mucosal ulceration in the little's area on the right nostril and hematoma in the gums [Figure 2]. The abdominal examination was unremarkable. She had normal external female genitalia, with the vulva moderately stained with blood.

Complete blood count (CBC) was as follows: Packed cell volume 32%, total white blood cell count was 4.0×10^9 (Neutrophils 57%, Lymphocytes 34%, Eosinophils 2.0%, Monocytes 7.0%). The platelet count was 23.0×10^9/L (Local reference range is 100–400 $\times 10^9$/L). Peripheral blood film examination showed microcytic hypochromic red cells with target and pencil cells. There were no fragmented red cells. Platelets were markedly reduced with few giant forms on film.

Bone marrow aspiration (BMA) cytology showed a normocellular marrow for age with trilineage haematopoiesis but with reduced megakaryocytes. Erythropoiesis was predominantly micronormoblastic. The myeloid series was unremarkable [Figure 3]. The direct antiglobulin test (DAT) was negative. Fasting blood glucose was 4.3 mmol/L. Electrolytes, urea, and creatinine were within reference limits. Viral screening for HIV, Hepatitis B, and C was negative.

We made a diagnosis of ITP secondary to hormonal contraceptive implant and hypertensive emergency. We controlled the elevated BP with intravenous (IV) Hydralazine and Tablets Alpha-Methyldopa and placed her on tablets prednisolone at a dose of 1 mg/Kg body weight (15 mg tid) and hematinics. Anterior nasal packing was done and also placed on Tabs Dicynone 500 mg tid for 10 days. We counselled her on the removal of the implant and the use of alternative

Figure 1: Conjunctival haemorrhage in the patient's right eye

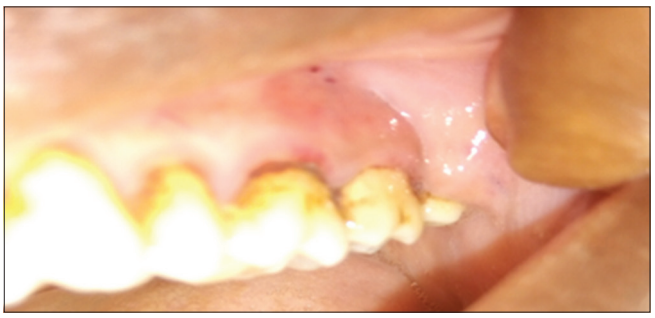

Figure 2: Haematoma in the patient's gum

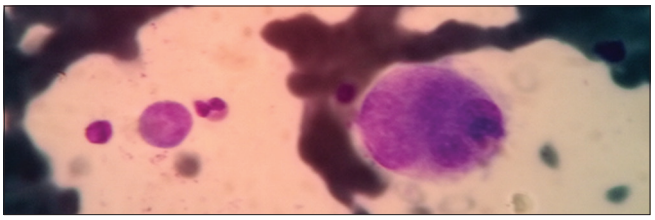

Figure 3: Bone marrow aspiration cytology film (×100), showing a megakaryocyte

forms of contraceptive. On the 3rd day of prednisolone, the platelet count increased to 67.0×10^9/L, and bleeding ceased. On the 4th day of admission, a two-rod contraceptive implant was removed under aseptic condition. On the 6th day, platelet count increased to 87.0×10^9/L, and she was discharged home on drugs.

On her first follow-up visit, the platelet count increased to 109×10^9/L. Two weeks later, she came back with facial swelling and a Platelet count of 110×10^9/L. We explained to her the reason why she had the facial swelling (moon face). We reduced the dose of prednisolone to 10 mg tid. She was, however, lost to follow-up for 3 months. The patient, however, returned with mucocutaneous bleeding of 1-week duration. She stopped taking drugs for the past 3 months that she defaulted follow-up citing financial constraints as the main reason. Her platelet count dropped to 20.0×10^9/L. Prednisolone was recommenced at a dose of 10 mg bid. At follow-up, the platelet count increased to 404.0×10^9/L. We tapered the dose of prednisolone to 5 mg bid, and the platelet count remained at 173.0×10^9/L.

Discussion

The occurrence of ITP after insertion of hormonal contraceptive implant is uncommon, the diagnosis of ITP in our patient confirmed and added to these rare complications.

ITP is an acquired hematological disorder associated with antibody-mediated shortening of platelets' lifespan. Platelets have a normal lifespan of about 7–10 days in the circulation but, this is shortened to a few hours in ITP.[1,2] The marrow response in patients with ITP cannot keep pace with the rate of peripheral destruction, leading to thrombocytopenia. Implicated autoantibodies are predominantly of the immunoglobulin G class; the remainders are immunoglobulin M and immunoglobulin A.[2] In most cases, the antiplatelet autoantibodies target the glycoprotein IIa/IIIb on the platelets membrane, leading to the destruction of the antibody-coated platelets in the spleen.[2] Cellular immunity and complements have also been implicated in the pathogenesis of ITP.[2] Available knowledge also attributed thrombocytopenia to platelet underproduction as a result of immune-mediated destruction of megakaryocytes.[1] Consistent with ITP, our patient presented with marked thrombocytopenia with mucocutaneous bleeding. A review of the BMA cytology of our patient revealed that although megakaryocytes were present, they were reduced in number. This finding further confirmed earlier observations of immune-mediated suppression of megakaryopoiesis in some cases of ITP.

The contraceptive implant used by our patient, contains the synthetic hormone, levonorgestrel. It is a two-rod implant, and each rod contains 75 mg of the progestin, levonorgestrel.[7] It works mostly by suppressing ovulation, thickening of cervical mucus, slowing ovum movement through the fallopian tubes, and alteration of the endometrium.[7] Injectable contraceptives such as deport medroxyprogesterone acetate have also been associated with ITP.[8] When we consider the onset of bleeding, it seemed likely that the hormonal contraceptive implant used by our patient, was causally associated with the thrombocytopenia.

The diagnosis of ITP is based on the exclusion of other causes of thrombocytopenia.[1,2] Clinically, ITP may present with mucocutaneous bleeding, a reflection of perturbed primary hemostasis. Laboratory findings in support of ITP on CBC include thrombocytopenia without anemia and leucopenia. The diagnosis of ITP in our patient was based on the finding of thrombocytopenia on full blood count and the presence of megakaryocytes without morphological evidence of dysplasia on BMA cytology. The diagnosis of ITP was further strengthened clinically by the absence of splenomegaly, and therapeutically, by the observed increase in platelet count with the commencement of a corticosteroid. The microcytic hypochromic anemia seen in our patient could be as a result of iron deficiency from the combination of chronic blood loss for over 4 months, increased iron demands of lactation, and the background poor socioeconomic status. Evans Syndrome, a close differential of ITP, was ruled out by negative DAT and the absence of schistocytes on peripheral blood smear. The role of BMA in the diagnosis of ITP has been debated.[9] However, BMA can help to rule out other causes of thrombocytopenia. The hallmark of the diagnosis of ITP is the demonstration of antiplatelet antibodies. However, routine tests for the implicating anti-platelets antibody in clinical practice are not advocated because of low sensitivity.[1]

The American Society of Hematology Guidelines 2011 recommended that treatment be administered for patients with platelets count $<30 \times 10^9$/L.[10] Our patient presented with a platelet count of 23.0×10^9/L with mucocutaneous bleeding, therefore justifying the commencement of treatment. Corticosteroids, with or without IV immunoglobulin, are the first-line treatment for newly diagnosed ITP.[1,2] Prednisolone monotherapy at a dose of 1 mg/kg was used in our patient with significant improvement in platelet count and cessation of bleeding.

Conclusion

With the increasing awareness of the need for child-spacing, the hormonal contraceptive implants have become a preferred choice of contraceptives in Nigeria. This report, therefore, seeks to create awareness among clinicians about the possible causal association between hormonal contraceptives and immune-mediated thrombocytopenia. Clinicians may need to serially or periodically monitor platelets count of their clients on hormonal contraceptives.

Limitations

An assay that can detect and quantify antiplatelet antibodies is the gold standard for the diagnosis of ITP. However, such an assay is unavailable in our center.

Ethical consideration

Consent of the patient was obtained that permitted us to use her photographs in this report.

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Conflicts of interest

There are no conflicts of interest.

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