

A case of wet purpura due to etoricoxib induced thrombocytopenia



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Submitted: 20-03-2016

Revised: 21-05-2016

Published: 01-09-2016

ABSTRACT

Etoricoxib is a selective cyclo-oxygenase-2 inhibitor, commonly used in treatment of rheumatoid arthritis, gout and back pain. Pretibial edema and erythema, gastric irritation and risks of cardiovascular and cerebrovascular thrombotic events are some of the reported adverse effects due to etoricoxib. This case report is regarding a patient who presented with wet purpura following etoricoxib intake. Drug induced thrombocytopenia is an unreported side effect of etoricoxib.

Key words: Etoricoxib, Drug induced thrombocytopenia, Wet purpura

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v7i5.14674

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Etoricoxib is a cyclo-oxygenase-2 (COX-2) inhibitor, which works to relieve pain and inflammation. It is used to treat painful conditions such as arthritis, back pain and gout. The risk of stroke and myocardial infarction have been reported with COX-2 inhibitor usage.^{1,2} Other adverse events include gastric irritation and pretibial oedema.^{3,4} However, a drug induced thrombocytopenia by etoricoxib has rarely been reported.

CASE REPORT

The patient being reported is a 51 year old male, shopkeeper, who presented to the Medicine OPD with one episode of bleeding from the mouth. While he was watering his garden in the morning, he blew through the pipe hose to remove a block and recognised a bloody taste in his mouth. On looking in the mirror, he noticed bleeding from his tongue. He did not give any history of fever or any other bleeding manifestations. He was taking tablet etoricoxib 90 mg twice daily for the past 7 days, as over the counter medication, for his lower back pain. He had been prescribed this drug for 3 days by an orthopaedic surgeon, about 1 year ago, for back pain. He is not a diabetic or hypertensive, and is not on any regular medications.

On examination, he was moderately built and nourished; conscious, oriented and afebrile. His vitals were stable, with heart rate of 70 beats/minute, blood pressure of 110/70 mmHg with no postural drop and respiratory rate of 20 breaths/minute. His tongue had a blackish discoloration, suggestive of wet purpura (Figure 1). There were petechial rashes and ecchymosis over upper and lower limbs (Figure 2). His systemic examinations were normal.

His complete blood count showed platelets of 8000/ μ L (150,000–450,000) and Hb 11 g% (12–15), but no leucopenia. His electrolytes, renal and liver functions were normal. Prothrombin time and activated partial thromboplastin time were normal. Dengue serology, malarial smear and blood cultures were negative. Peripheral smear showed severe thrombocytopenia with normal platelet and red blood cell morphology, with no evidence of haemoparasites and abnormal cells. Viral markers for hepatitis B, hepatitis C and HIV were negative. Serology for *Helicobacter pylori* was negative. Antinuclear antibody and anti dsDNA, Coombs' test (direct and indirect) and serum protein electrophoresis were also negative. His IgA levels were normal. His chest Xray, ECG and ultrasound abdomen were normal. Urine microscopy did not showed any evidence of hematuria.

Based on the history of development of symptoms following 7 days of etoricoxib intake and history of its usage in the past,

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Figure 1: Wet purpura over the tongue



Figure 2: Petechiae and ecchymosis over lower limb

the diagnosis of drug induced immune thrombocytopenia was considered. In view of severe thrombocytopenia, he was given 4 units of platelet transfusion. He was also put on twice daily dose of injection pantoprazole. On day 3, in spite of the transfusions and withholding of etoricoxib, his platelet increased only to 9000/ μL . He was given another 4 units of platelets the next day, but his platelet count continued to be almost the same. He did not have any new bleeding manifestations following admission. He was given intravenous methylprednisolone for 2 days. On day 5, his platelet counts increased to 13,000/ μL . He was started on tablet prednisolone 1 mg/kg once daily. Over the next 5 days, his platelet levels normalized without any need for further transfusions. His wet purpura disappeared and petechial rash and ecchymosis also started subsiding. He was discharged on tapering doses of prednisolone and reviewed after 1 week and 3 weeks of stopping prednisolone. His complete blood count was perfectly normal on both occasions. Since the patient had only thrombocytopenia, which had normalized, in response to steroids, bone marrow examination was avoided.

DISCUSSION

Platelets play a key role in maintaining hemostasis. The average life span of platelets is 7-10 days.⁵ Thrombocytopenia is defined as a platelet count less than 150,000/ μL .⁶ It is caused either due to decreased bone marrow production or sequestration or increased platelet destruction. A platelet count of 5000 to 10,000 is required to maintain the vascular integrity of microcirculation. Petechiae are the first to appear when there is a drastic fall in platelet count. The common sites are ankles and feet. Wet purpura and blood blisters in oral mucosa are indicators of risk of life threatening haemorrhage.⁵

Immune or idiopathic thrombocytopenic purpura (ITP) is an acquired disorder characterized by thrombocytopenia. It may be primary or secondary. Primary ITP is seen in both adults and children. Secondary ITP occurs in lymphoproliferative disorders, systemic lupus erythematosus and antiphospholipid antibody syndrome. It is also seen in association with infections like hepatitis B and C, HIV, and *Helicobacter pylori*. The administration of certain drugs can also cause thrombocytopenia.⁶

Drug induced thrombocytopenia (DITP) includes thrombocytopenia induced by drugs, beverages, foods and herbal products. There are several mechanisms leading to DITP. Heparin induced thrombocytopenia is one of the commonest forms, where there is thrombosis rather than bleeding.⁷ Drugs like quinine cause immune thrombocytopenia, where drug dependent antibodies are formed that react directly with the sensitizing drug to form an immune complex; which in turn reacts with the platelets causing its destruction.⁸ Certain drugs like penicillin trigger a humoral immune response only when they are linked to a macromolecule such as a protein, which act as a hapten.⁹ Tirofiban and eptifibatid are GPIIb/IIIa inhibitors that can cause thrombocytopenia by formation of antibodies that recognize GPIIb/IIIa in a complex with the particular ligand-mimetic.¹⁰ Medications like L-dopa, penicillamine and sulfamethoxazole trigger the production of platelet-specific autoantibodies, leading to a clinical picture similar to autoimmune thrombocytopenia.¹¹ Chemotherapy agents cause a decrease in platelet production by generalized myelosuppression,¹² while drugs like bleomycin can cause non-immune platelet destruction.¹³ Thiazide diuretics can cause thrombocytopenia either by selective suppression of megakaryocyte production or by an immune mediated mechanism.¹⁴

DITP should be suspected in cases of unexpected severe thrombocytopenia as well as recurrent thrombocytopenia with prompt recovery. Several drugs causing thrombocytopenia have been listed and reviewed systematically, and the data along with criteria for individual patient evaluation are

available at www.ouhsc.edu/platelets. Our patient met 3 out of the 4 criteria, suggestive of probable DITP.

Flow cytometry is a highly sensitive technique used for the detection of platelet-reactive antibodies induced by several drugs. Other tests include the platelet immunofluorescence test, enzyme-linked immunospecific assay and immunoprecipitation-Western blotting. Laboratory tests should be done to check for infectious causes of ITP i.e. hepatitis B and C, HIV and *H. pylori*. Coombs' test is done to rule out Evans' syndrome. The conditions like SLE and multiple myeloma should also be considered. Bone marrow examination can be reserved for those who do not respond to therapy, or those who have features not corresponding to ITP.

The complete withdrawal of the drug is the first step in treatment of drug induced ITP. The recovery of thrombocytopenia occurs within 1 to 2 days of discontinuation of the drug. Platelet transfusions are indicated in cases of severe thrombocytopenia (wet purpura) due to high risk of bleeding. The role of corticosteroids is controversial.¹⁵ Intravenous Ig and plasma exchange have been tried in cases of persistent thrombocytopenia and bleeding with no proven benefit.^{16,17}

Etoricoxib is a non-steroidal anti-inflammatory drug (NSAID), belonging to the category of selective COX-2 inhibitors. COX-2 is involved in the production of irritant substances in the body in response to disease and injury; and by blocking its action, etoricoxib reduces the symptoms of pain and inflammation. It is commonly used in conditions like arthritis, back pain, ankylosing spondylitis and gout. The incidence of myocardial infarction and thrombotic cerebrovascular accident have been reported to be higher with etoricoxib.¹⁻³ Other common adverse effects include gastric irritation, hypertension and pretibial oedema and erythema.^{3,4} Thrombocytopenia following etoricoxib intake is a rare side effect.

CONCLUSION

Etoricoxib, a COX-2 inhibitor, is used as a pain killer in conditions like arthritis etc. Its gastrointestinal tolerance is better compared to other NSAIDs. Hypertension, pretibial oedema, myocardial infarction and thrombotic stroke are some of the noted events with etoricoxib. However, thrombocytopenia is an uncommon complication, and cases of severe DITP with wet purpura following etoricoxib intake have not been reported previously. This report also

highlights the need to monitor the platelet counts of patients on long term therapy with etoricoxib for arthritis and gout.

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Authors Contribution:

RGM - Concept and design of case report, reviewed the literature, manuscript preparation and critical revision of manuscript; VK - Treating physician.

Source of Support: Nil. Conflict of Interest: None.