Case Report

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Probable Etoricoxib-Induced Severe Thrombocytopenia: A Case Report

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Significance of the Study

- This report describes a case of etoricoxib-induced thrombocytopenia. It should draw the attention of medical practitioners to the possibility of such a complication.

Keywords
Thrombocytopenia · Etoricoxib · Petechial rash

Abstract
Objective: To describe a case of likely etoricoxib-induced severe thrombocytopenia. ***Clinical Presentation and Intervention:*** A 32-year-old woman was referred to our hospital for disseminated petechial rash after 7 days of therapy with etoricoxib. At admission, the patient's platelet count was 3,000/mm^3. At Naranjo's scale correlation between thrombocytopenia and drug was considered as "probable." With the diagnostic tests performed we did not find other causes of thrombocytopenia. Etoricoxib was discontinued. The patient was treated with intravenous immunoglobulin and corticosteroids with a complete resolution of the thrombocytopenia in a few days. ***Conclusion:*** The prevalence of thrombocytopenia induced by etoricoxib should be studied as it may not be very rare.

Introduction

Etoricoxib is a selective cyclo-oxygenase-2 (COX-2) inhibitor classified as a non-steroidal anti-inflammatory drug (NSAID). It is routinely used to treat osteoarthritis, rheumatoid arthritis, gout, back pain, etc. [1, 2]. Large-scale clinical gastro-intestinal outcome trials of selective COX-2 inhibitor have shown a significant risk reduction in the development of gastro-intestinal injuries compared with non-selective NSAIDs [3].

The most commonly reported side effects of etoricoxib are nausea, dizziness, headache, myocardial infarction, thrombotic cerebrovascular accident, hypertension and pretibial oedema and erythema [4, 5]. The product summary states that thrombocytopenia was reported in <1% of patients during clinical trials. Case reports of etoricoxib-induced thrombocytopenia have not been reported in the literature.

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Case Report

A 32-year-old woman was referred to our hospital with disseminated petechial rash and epistaxis. The patient had visited her general practitioner 7 days earlier, complaining of pain in the right ankle. She was prescribed etoricoxib 60 mg daily for 1 week. After 4 days of therapy the patient developed the first signs of petechial rash, and therefore she stopped etoricoxib. The following day, as the petechial rash did not improve, she visited the emergency department.

The patient's past medical history was negative. She had no known allergies and no history of drug use. On examination body temperature was 36.3 °C, she was eupnoeic with vital signs within normal limits (heart rate 65 beats/min, blood pressure of 120/75 mm Hg). Petechial rashes, purpura and ecchymosis over her upper and lower limbs were easily noticeable. No lymphadenopathy or hepatosplenomegaly was observed. The examination was otherwise benign. The electrocardiogram revealed sinus rhythm without alterations of ST segment. Chest X-ray was normal.

The admission laboratory values revealed a CRP level of 1.23 mg/dL, severe thrombocytopenia with platelet count of 3,000/mm^3, white blood cell count of 7,500/mm^3 and haemoglobin 13.9 g/dL. Renal, liver and coagulation studies were normal. Antinuclear antibodies and all subtypes were negative. Blood and urine cultures were negative for bacterial growth, and serological tests for hepatitis B and C, *Helicobacter pylori*, HIV, Cytomegalo and Herpes virus were also negative. Test for anti-platelet antibodies was negative. The abdominal ultrasound was normal (no splenomegaly).

After transfusion of 3 units of platelets, following the haematologist consultation, a bone marrow aspirate was performed. The examination showed an increased number of megakaryocytes and was negative for hypoplasia or neoplastic processes. After the results of these diagnostic tests and based on the patient's history the diagnosis of drug-induced immune thrombocytopenia (DITP) was considered and etoricoxib was suspected to be the causative agent. The patient was treated with intravenous methyl-prednisolone (1 mg/kg daily) for 6 days and with immunoglobulin 0.4 g/kg for 4 days. The platelet count increased to 38,240/mm^3 on day 6 and she was started on oral methyl-prednisolone 16 mg daily. On day 12 of hospitalization the platelet count increased to 168,345/mm^3.

At discharge (after 16 days of hospital stay) the platelet count was normal and her petechial rash had disappeared. She was discharged on tapering doses of methyl-prednisolone and at the follow-up (2 weeks after stopping steroid therapy) the blood count was normal.

Discussion

Thrombocytopenia may result from numerous diseases and it is a common side effect of many drugs. The underlying mechanism is an increased platelet destruction (immune-mediated) or a decrease in production [6].

The laboratory test used most frequently for the diagnosis of DITP measures circulating antiplatelet IgG antibodies. Drug-dependent antiplatelet antibody assays, where available, are not well standardized [7]. Ultimately the diagnosis of drug-induced thrombocytopenia is by exclusion [8]. The primary treatment for DITP is to discontinue the suspected drug [7]. Patients at risk of life-threatening bleeding may benefit from intravenous immunoglobulin therapy, plasmapheresis and platelet transfusion. Although the use of corticosteroids in the treatment of DITP is common, it is not supported by clinical evidence.

Compared with non-selective NSAIDs, etoricoxib has a significantly lower incidence of gastrointestinal adverse events and is generally well tolerated by patients. Most adverse events experienced are self-limited and benign [9].

Etoricoxib was the only drug used by the patient before the onset of symptoms and there were no laboratory or instrumental findings that could suggest another cause of thrombocytopenia. The causality assessment was carried out using the Naranjo Adverse Drug Reaction Probability Scale. A score of 6 was obtained, and therefore the correlation between symptoms and drug was considered as "probable." The correlation could not be determined with certainty because our patient was not rechallenged with etoricoxib (given the severity of thrombocytopenia experienced by the patient).

The patient developed severe thrombocytopenia with occurrence of potentially life-threatening bleeding. Before bone marrow aspiration she was transfused with platelets. After the examination we started therapy with intravenous immunoglobulin. We also started therapy with corticosteroids because of the difficult initial differentiation between DITP and idiopathic thrombocytopenic purpura [10]. With this therapy we observed a complete resolution of petechial rash and a progressive rise of platelet count up to normalization in 12 days.

Conclusion

The diagnosis of drug-induced thrombocytopenia is often difficult and time consuming. Etoricoxib can cause severe thrombocytopenia with a potential risk of life-threatening bleeding. Given the severity of the adverse reaction we found in this patient, further studies are needed to better assess the incidence of such events.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report.

Disclosure Statement

The authors report no conflicts of interest in this work. The authors did not receive funding from any organization.

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