Case reports

Spontaneous abdominal hematoma in a patient treated with clopidogrel therapy: a case report

Aytekin Guven, Gulizar Sokmen, Ertan Bulbuloglu*, Cemal Tuncer

*Department of Cardiology, *Department of General Surgery, Kahramanmaras Sutcu Imam University, School of Medicine, Kahramanmaras, Turkey*

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Clopidogrel is a new antiplatelet agent. To date, no case of a spontaneous abdominal hematoma during clopidogrel therapy has been reported. We report a case of a 70-year-old woman who developed a spontaneous abdominal hematoma following clopidogrel treatment. The patient has been suffering from a progressive swelling in the abdominal wall for 1-2 weeks and noticed a purple discoloration of the skin over the swelled abdominal region the week before hospitalization. There was a palpable mass in the right upper quadrant of the abdomen and ecchymoses surrounding the umbilicus. At abdominal ultrasonography, the mass was found to be consistent with the hematoma. The hematoma was drained under local anesthesia. The patient was discharged with no complication. She was advised to submit herself to regular physical examinations.

Although adverse reactions are generally rare, we suggest that physicians prescribing clopidogrel should be aware of the possibility of this adverse reaction.

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Address:

Prof. Aytekin Guven

Department of Cardiology
Kahramanmaras Sutcu Imam University
46050 Kahramanmaras
Turkey

Introduction

Clopidogrel is an oral thienopyridine antiplatelet agent that selectively and irreversibly inhibits the platelet adenosine diphosphate (ADP) receptor and the subsequent ADP-mediated activation of the glycoprotein IIb/IIIa complex, thereby inhibiting platelet aggregation. This action is noncompetitive and irreversible and results in a 40 to 60% inhibition of platelet aggregation[1]. Clopidogrel is now being used in the treatment of patients with cerebrovascular and peripheral vascular disease and to reduce risk for thrombosis in patients undergoing coronary artery stenting.

We present a case of a patient presenting with an abdominal hematoma that we hypothesize was an adverse effect induced by clopidogrel and review the literature of other similar reports.

Case report

A 70-year-old woman presenting with abdominal swelling and a purple discoloration of the abdominal skin was referred to our clinic. The patient referred that the swelling manifested approximately 2 weeks previously and that a purple discoloration of the skin developed over the swelled abdominal region 1 week prior to hospitalization. Her anamnesis included coronary artery bypass performed 2 years previously. She was on diltiazem (90 mg/day) for hypertension. Previously she has been prescribed ticlopidine as an antiplatelet agent due to her aspirin allergy and has been taking clopidogrel since 1 year. On physical examination, her arterial blood pressure was 120/80 mmHg and her pulse was 75/min and rhythmic. There was an incision scar in the sternal region of the thorax. Cardiovascular examination revealed normal physical findings. There was a palpable 5 × 10 cm mass in the right upper quadrant of the abdomen and 3 × 4 cm ecchymoses surrounding the umbilicus. At abdominal ultrasonography, the mass was found to be consistent with a hematoma. The diagnosis was confirmed at abdominal spiral computed tomography (Fig. 1). Laboratory analysis revealed that her blood glucose level and liver enzymes (lactate dehydrogenase 110 IU/l, gammaglutamyl transpeptidase 30 U/l, alanine aminotransferase 32 IU/l, aspartate aminotransferase 22 IU/l) were normal as were her hemoglobin level (12.7 g/dl), hematocrit (36.2%), and platelet count (202 × 10^9/l). The prothrombin time (12 s) and activated partial

Figure 1. *Smooth contoured, 12 × 8 cm mass consistent with hematoma localized in the abdominal wall.*

thromboplastin time (30 s) were within normal limits. The patient had no history of hemorrhagic diathesis, trauma or use of any drug that may cause bleeding. In view of this, it was concluded that the hematoma was the result of the clopidogrel therapy that was consequently stopped. The hematoma was drained out under local anesthesia (Fig. 2).

The patient was discharged with no complications. She was advised to submit herself to regular physical examinations. Ticlopidine (250 mg twice daily) was initiated in the first month of her follow-up as an antiaggregant therapy. At 8 months of follow-up, the patient's hematological profile was found to be normal.

Discussion

Owing to the demonstrated benefits of antithrombotic agents in patients with cardiovascular diseases, the number of patients on this therapy is increasing. Moreover, since such conditions are more prevalent in the older population, and since life expectancy is also increasing, at least in developed countries, the average age of patients on antithrombotic drugs is also increasing. Bleeding is the main adverse effect of these agents, and the bleeding risk may also increase with advancing age[2].

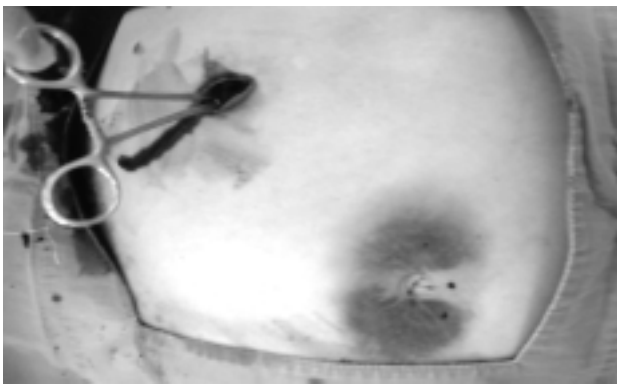

Figure 2. *Drainage of hematoma under local anesthesia and umbilical ecchymoses.*

Aspirin, ticlopidine and clopidogrel are the mostly used drugs for antiaggregant therapy. Aspirin has been the mainstay of antiplatelet therapy and prevents platelet aggregation by irreversibly inhibiting the formation of thromboxane A_2 which reinforces the effects of other physiologic platelet agonists, such as ADP and collagen[3]. Ticlopidine and clopidogrel, two antiplatelet drugs, are structurally related derivatives of thienopyridine. Clopidogrel is a new thienopyridine derivative with a similar mechanism of action, a more potent platelet antiaggregant effect, and a faster onset of action than ticlopidine. Its safety profile is at least as good as that of aspirin with the incidence of neutropenia not exceeding that observed in patients on the latter treatment[4,5]. Its most common adverse effects include gastrointestinal hemorrhage, diarrhea, rash, and pruritis[6]. It also has rare but serious side effects, such as neutropenia and thrombotic thrombocytopenic purpura[6]. Its side effects are summarized in table I.

Table I. Side effects of clopidogrel.

Gastrointestinal hemorrhage
Diarrhea, vomiting, dyspepsia
Rash
Pruritus
Neutropenia
Urticaria
Thrombotic thrombocytopenic purpura
Increased liver enzymes

Our patient could not take aspirin due to her aspirin allergy. She did not experience any side effect of ticlopidine while she was taking this drug. Various side effects of clopidogrel have been reported in the literature. However, we could not find a case report similar to ours, and we thought it fit to present this case.

Sare et al.[7] reported a perinephric hematoma developing after extracorporeal shockwave lithotripsy performed due to ureterolithiasis in a patient taking clopidogrel. Briguori et al.[8] reported thrombocytopenia and a purpura-like lesion in a patient to whom clopidogrel was administered after coronary bypass surgery. These lesions resolved within a few days of withdrawal of the drug. Bennett et al.[9] reported the clinical and laboratory findings in 11 patients in whom thrombotic thrombocytopenic purpura developed during or soon after treatment with clopidogrel. McCarthy and Kockler[10] reported a case of leucopenia in a patient receiving clopidogrel following intracoronary stent placement. In another study, clopidogrel was associated with a high incidence of upper gastrointestinal bleeding in high-risk patients[11].

Maher et al.[12] reported spontaneous varicose bleeding in the lower limbs of a patient taking clopidogrel in addition to aspirin plus enoxaparin. Another case report described life-threatening alveolar hemorrhage developing in a patient placed on clopidogrel following coronary artery stenting[13].

Although clopidogrel is a reliable antiplatelet agent, it should be taken into account that it may, even though rarely, cause significant bleeding. Patients on this drug should be accurately followed up.

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