DOI:10.1111/j.1365-2125.2006.02608.x

# Letter to the Editors

## Spontaneous retroperitoneal haematoma associated with clopidogrel therapy mimicking acute appendicitis

Darko Jurisic,[1] Marko Doko,[1] Elizabet Glavan, Dinko Vidovic,[1] Kristijan Matkovic[1] & Vlatka Pitlovic[1]
[1]Department of Surgery, University Hospital 'Sestre milosrdnice', Vinogradska 29, 10000 Zagreb, Croatia

Antiplatelet therapy plays a pivotal role in myocardial infarction and stroke prevention in patients with atherosclerosis. Regarding the bleeding site, there is only one published study report implicating clopidogrel as a risk factor for developing retroperitoneal haematoma, which presented as femoral neuropathy in the study [1].

The present case shows a rare clopidogrel side-effect, retroperitoneal haematoma, which manifested as an acute abdominal condition.

A male patient aged 49 years was hospitalized immediately upon arrival at the Department of Surgery due to a 3-day history of pain in the right lower quadrant, tenderness and nausea. His previous history included coronary artery bypass surgery performed 20 years ago and cerebral infarction 6 years ago, after which he started to receive clopidogrel (75 mg $day^{-1}$), and the follow-up period continued until the aforementioned event. The patient described the onset of abdominal pain as epigastric with nausea, but subsequently the pain moved into the right lower quadrant with progression into the right testicle. The patient had no history of trauma and denied any dysuria or gross haematuria as well as any changes in his dietary or bowel habits. His blood pressure was 110/65 mmHg with a heart rate of 70 beats $min^{-1}$. Abdominal examination revealed abdominal tenderness and guarding with signs of local peritoneal irritation in the right lower abdomen and a positive psoas test. On admission, axillar temperature was 36.8 °C and rectal 37.8 °C. Urogenital examination was unremarkable. Digital rectal examination demonstrated a nontender prostate of normal size. Preoperative abdominal ultrasound showed a nonhomogenic collection sized 5 × 5 cm in the projection of the appendix. No other abnormalities were found. Laboratory results showed elevated C-reactive protein of 150 mg $l^{-1}$ (normal < 10 mg $l^{-1}$) and an elevated leucocyte count of $14.4 \times 10^9$/l (normal range 3.6–$9.6 \times 10^9$/l). Haemoglobin concentration, haematocrit, and platelet counts were normal. Prothrombin time and activated partial thromboplastin time were within normal limits.

Diagnosis of acute appendicitis was established and appendectomy was performed through the right pararectal approach, yielding no evidence of appendicitis. By palpation, a retrocoecal and retroperitoneal mass was felt and intraoperative abdominal ultrasonography was performed. It revealed a clotted retroperitoneal haematoma. We removed the haematoma and placed a nonsuction latex drain in the pelvis. According to the patient's past history and intraoperative findings, we came to the conclusion that the haematoma was related to clopidogrel therapy. As the patient has a history of peptic disturbances, he had not been taking aspirin for the last few years, so we decided to replace clopidogrel with another platelet aggregation inhibitor, ticlopidin, even though there was no evidence from the studies that ticlopidin causes less bleeding complications than clopidogrel.

As there were no postoperative complications, the patient was discharged from the hospital after 7 days. At 1-month follow-up, the patient was feeling well. His clinical examination, laboratory findings and abdominal ultrasound findings were normal.

Clopidogrel inhibits platelet aggregation, prolongs bleeding time and delays clot retraction induced by adenosine diphosphate. Major adverse reactions of clopidogrel are white cell disorders and haemorrhagic reactions, which may occur due to thrombocytopaenia or platelet dysfunction. In the CAPRIE and CURE studies, the rate of bleeding disorders with clopidogrel was 9.27% (1.38% major) *vs.* 8.5% (3.7% major). The excess major bleeding episodes were gastrointestinal haemorrhages and bleeding at the sites of arterial punctures. Neither the CAPRIE, nor the CURE study mentioned the possibility of retroperitoneal bleeding [2, 3].

A Medline search of abstracts revealed various conditions associated with retroperitoneal haematoma

**Table 1**
Causes of retroperitoneal haematoma

| |
|---|
| Trauma |
| Benign and malignant renal tumours (renal cell carcinoma, malignant melanoma, angiomyolipoma, phaeochromocytoma, adenoma, myelolipoma) |
| Antithrombotic therapy |
| Inflammatory disorders (periarteritis nodosa, Wegener angeitis) |
| Severe portal hypertension |
| Vascular abnormalities (aneurysm) |
| Ureteral calculi |
| Iatrogenic (complication of coronary angioplasty) |
| Bleeding disorders (haemophilia) |
| Idiopathic |

(Table 1). In the absence of other pathology it was concluded that retroperitoneal haematoma in our patient was the result of clopidogrel therapy. Spontaneous retroperitoneal haematoma is in most cases related to warfarin or heparin therapy and has been well described. Clinical manifestations vary from leg paresis to abdominal pain or catastrophic shock [1]. Excluding abdominal compartment syndrome as an acute abdominal emergency after massive retroperitoneal bleeding caused by anticoagulant therapy, retroperitoneal haematoma presenting as an acute abdominal condition has not been reported so far.

Bleeding into the retroperitoneal space is a severe complication of antithrombotic therapy. The increase in number of patients treated with oral anticoagulants and antiplatelets will increase the number of rare side-effects, including bleeding into the retroperitoneal space. Because the incidence of the condition is still unknown, retroperitoneal haematoma should be considered in a differential diagnosis in patients receiving clopidogrel and patients receiving anticoagulant therapy.

This report reinforces the need for a careful evaluation of patients receiving antiplatelet therapy who have developed peritoneal irritation and leucocytosis.

## References


1 Gonzalez C, Penado S, Llata L, Valero C, Riancho JA. The clinical spectrum of retroperitoneal hematoma in anticoagulated patients. Medicine 2003; 82: 257–62.

2 CAPRIE Steering Committe. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1996; 348: 1329–39.

3 The CURE Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001; 345: 494–502.



**Received**
28 July 2005
**Accepted**
21 November 2005
**Published *OnlineEarly***
18 April 2006



**Correspondence**
**Dr Darko Jurisic MD,** Dobrise Cesarica 51, 10090 Zagreb, Croatia. Tel.: + 385 9873 5618; Fax: + 385 1376 9067; E-mail: djurisic@inet