Case report

Heparin-induced thrombocytopenia and cardiopulmonary bypass: anticoagulation with unfractionated heparin and the GPIIb/IIIa inhibitor tirofiban and successful use of rFVIIa for post-protamine bleeding due to persistent platelet blockade

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Abstract

Heparin-induced thrombocytopenia was diagnosed in a 50-year-old man on day 5 after cardiac surgery (aorto-coronary bypass and mitral valve replacement). He required redo (para-prosthesis leak) on day 13. The cardiopulmonary bypass (CPB) was performed with unfractionated heparin (UFH) and the platelet glycoprotein (GP) IIb/IIIa inhibitor tirofiban. Post-protamine bleeding likely due to documented persistent platelet blockade by tirofiban was successfully treated with one dose of recombinant activated factor VII (rFVIIa, 60 μg/kg). No thrombotic complications were detected. The management of CPB with UFH and tirofiban is a convenient option and rFVIIa seems appropriate to handle bleeding issues.

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1. Introduction

Heparin-induced thrombocytopenia type II (HIT) is associated with poor outcome in the context of cardiac surgery [1]. Cardiopulmonary bypass (CPB) requires an efficient anticoagulation and unfractionated heparin (UFH) remains the gold standard. Successful use of a direct thrombin inhibitor such as lepirudin or argatroban during CPB has been reported several times [2] but the need for dedicated intraoperative laboratory monitoring and the lack of an antagonist make their management tricky and risky. Tirofiban, a platelet glycoprotein (GP) IIb/IIIa inhibitor, has been used during CPB for a little while, in association with UFH [3]. Tirofiban has a short half-life but its main elimination route is via the kidneys. By strongly inhibiting fibrinogen binding to GPIIb/IIIa onto the surface of activated platelets, tirofiban can block platelet aggregation (though not platelet activation) by HIT antibodies [2]. Recombinant activated factor VII (rFVIIa) is a powerful haemostatic agent increasingly used in cardiac surgery to stop refractory, life-threatening bleeding [4]. A case of HIT and CPB with porcine UFH and tirofiban is described hereafter, with the successful use of rFVIIa for post-protamine bleeding.

2. Case report

A 50-year-old man underwent four bypasses (LIMA and three saphenous grafts) plus a mechanical mitral valve replacement on the third day of a myocardial infarct. Since postoperative day 3 (POD 3), a continuous haemofiltration was required for anuric renal failure (creatininemia = 270 μmol/l). On POD 5, HIT was suspected in view of a persistent thrombocytopenia (35 G/l). UFH was stopped and danaparoid therapy was introduced through continuous intravenous infusion at the recommended dose. HIT was confirmed by positive ELISA and platelet aggregation tests. After a satisfactory evolution (increase in platelet count...
function as discussed below. The bleeding dramatically decreased to 50 ml/h within 30 min and PT shortened to 13.2 s. The chest could be readily closed and the patient left the operating room 2 h after protamine injection. Back in the intensive care unit, neither recurrent bleeding nor thrombosis was noticed.

3. Comment

To the best of our knowledge this is the first report of the use of rFVIIa on a patient under tirofiban during cardiac surgery. Tirofiban effect on platelet aggregation is major but reversible, with a short half-life as long as the renal function is not compromised. In this particular case, the patient had severe renal failure. The long lasting antiplatelet effect of tirofiban could not be handled by blood product transfusion, presumably since transfused platelets are inhibited by the high amount of plasma drug [5]. We used rFVIIa at the moderate dose that we are used to [6] and as already reported in cardiac surgery [7]. The haemostatic effect was noticed in as short a time as 30 min. We believe that rFVIIa overcame the antiplatelet effect of tirofiban by boosting thrombin generation as previously demonstrated [8]. Patients with inherited GPIIb/IIIa deficiency have been successfully managed with rFVIIa [9], and two tirofiban-treated patients have received it for major haemorrhage [10].

Thus, rFVIIa seems appropriate to manage bleeding consequences of tirofiban persistent effect, especially on patients with renal failure. Alternately, ultrafiltration or modified zero-balanced ultrafiltration can be used [2]. By contrast, a failure of rFVIIa could be anticipated if a direct thrombin inhibitor such as lepirudin was chosen, with dramatic accumulation in case of renal impairment. In spite of high thrombotic risk associated with HIT and potential thrombotic risk of rFVIIa, none of these adverse effects were observed. However, we suggest considering a dose of rFVIIa lower than 90 μg/kg in order to reduce this risk [6].

References

