■ CASE REPORT

Heparin-induced thrombocytopenia

A COMPLICATION OF THROMBOPROPHYLAXIS

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Heparin is a drug widely used for thromboprophylaxis or treatment in many clinical situations. However, it can cause serious adverse effects, including thrombocytopenia, which is a potentially life-threatening condition. Unfortunately, heparin-induced thrombocytopenia is generally under-recognised and under-diagnosed. A case of heparin-induced thrombocytopenia occurring in a post-operative orthopaedic patient in association with prophylactic low-molecular-weight heparin is described.

The use of heparin for thromboprophylaxis is common practice. However, while it has many positive effects, heparin can also cause complications such as the life-threatening thrombocytopenia. The prompt clinical and laboratory recognition of thrombocytopenia is essential so that the drug can be stopped immediately and treatment with an appropriate alternative commenced. Unfortunately, heparin-induced thrombocytopenia can be under-recognised and under-diagnosed. Its delayed recognition can be a significant problem for some patients.

The occurrence of thrombocytopenia associated with the use of prophylactic low-molecular-weight heparin (LMWH) and complicated by a non-ST elevation myocardial infarction, in a post-operative orthopaedic patient is reported.

Case report

A dynamic hip screw operation was performed on a 76-year-old woman as treatment for a fractured neck of femur. There was no past medical history of note. Routine blood tests on the day of admission, including full blood count, clotting screen, urea and electrolytes, were within normal limits. Treatment with prophylactic LMWH started on the day before surgery. On the 11th post-operative day she complained of chest pain. An ECG revealed anterolateral ischaemia. Repeat routine blood tests revealed a platelet count of $37 \times 10^9/l$ (normal, 150 to $400 \times 10^9/l$). Furthermore, the level of troponin-T was raised, confirming myocardial infarction. She was placed on a full dose of LMWH for a non-ST elevation myocardial infarction. The platelet count a day

later was $35 \times 10^9/l$. The LMWH was continued and a haematology consultation was obtained. Heparin-induced thrombocytopenia was suspected and the LMWH was changed to danaparoid. Heparin-induced thrombocytopenia was subsequently confirmed by serology. Following the change to danaparoid she made a good recovery and was discharged.

Discussion

Heparin-induced thrombocytopenia is an antibody-mediated adverse effect of heparin, whose frequency is much lower with the use of LMWH than with unfractionated heparin. It is clinically important because of its strong association with venous and arterial thrombosis. Patients treated with heparin who develop heparin-induced thrombocytopenia have a substantially increased risk of thrombosis, in both relative (odds ratio for thrombosis, 20 to 40) and absolute (thrombosis risk, 30% to 75%) terms, depending on the patient population affected.¹⁻⁵

The frequency of thrombocytopenia in patients exposed to heparin is variable. The risk in post-operative patients receiving LMWH is 0.1% to 1%. Heparin-induced thrombocytopenia is a clinicopathological diagnosis based upon clinical and serological grounds. Thus, a diagnosis is made when heparin-induced thrombocytopenia antibody formation is accompanied by an otherwise unexplained drop in platelet count ($\geq 50\%$, or to fewer than $150 \times 10^9/l$). The presence of antibodies can be confirmed by various methods. The thrombocytopenia typically occurs seven to 14 days after starting heparin therapy. Hence, a recent consensus conference recom-

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mended platelet monitoring every two to three days from day four to day 14, or until the heparin is stopped.⁶

The pathophysiology of heparin-induced thrombocytopenia is immune-mediated. Its antibodies are provoked not by heparin alone, but by the complex of heparin and platelet-factor-4. These antibodies bind to the heparin-platelet-factor-4 complex on the platelet surface and this interaction triggers activation and aggregation of the platelets. The activated platelets release procoagulants, leading to a hypercoagulable state. The activated platelet aggregates are removed prematurely from the circulation, leading to thrombocytopenia. This is rarely severe, with platelet counts typically above $20 \times 10^9/l$ so that spontaneous bleeding is unusual.

Therefore, heparin-induced thrombocytopenia is a prothrombotic condition. However, it is also transient, with platelet counts reverting to normal within days or weeks, and the heparin-induced thrombocytopenia antibodies disappearing within weeks or a few months. Optimal anti-thrombotic management over the relatively brief risk period which follows this unusual adverse event will pay dividends.

The major complication associated with heparin-induced thrombocytopenia is thrombosis, both venous and arterial. The major manifestations of this are deep-vein thrombosis and pulmonary embolism. Arterial thrombosis, although less common, can lead to a variety of clinical manifestations, including stroke, myocardial infarction (as occurred in our patient), limb ischaemia from peripheral arterial occlusion, or organ infarction.

The top priority in a patient with heparin-induced thrombocytopenia should be the immediate cessation of exposure to heparin. However, this in itself is not sufficient, as these patients remain at risk from thrombosis. The non-heparin agents, lepirudin, argatroban, bivalirudin and danaparoid, in therapeutic doses are recommended for use in heparin-induced thrombocytopenia, whether complicated by thrombosis or not. Warfarin alone should not be used to treat heparin-induced thrombocytopenia because of the

risk of causing venous gangrene and/or skin necrosis. Warfarin is safe to use when given to a patient who is adequately and safely anticoagulated with one of the non-heparin agents referred to, which will reduce the generation of thrombin. It may be prudent to delay the use of warfarin until the platelet count is more than $100 \times 10^9/l$, and preferably more than $150 \times 10^9/l$. The anticoagulation must be continued until the platelet count returns to normal.

Heparin-induced thrombocytopenia is a life- and limb-threatening complication, so all those prescribing heparin should be aware of the risks involved. It is important to remember that it can occur even when using prophylactic LMWH, as occurred in our patient. However, thromboprophylaxis with LMWH is important and the risk of heparin-induced thrombocytopenia should not be regarded as a reason for not using it. Platelet monitoring for early detection of heparin-induced thrombocytopenia is a laudable concept, but unfortunately is not common clinical practice. A dramatic drop in the platelet count should arouse suspicion and the diagnosis can be confirmed by the presence of heparin-induced thrombocytopenia antibodies.

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