HEPARIN-INDUCED THROMBOCYTOPENIA WITH ARTERIAL THROMBOSIS: AN UNUSUAL CASE

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ABSTRACT
A case of heparin-induced thrombocytopenia with thrombosis (HITT) is described. The patient, treated for several days with porcine Ca-heparin at a dosage of 10,000 IU/day, presented severe thrombocytopenia (Plt 36×10^9/L), intermittent right leg ischemia, and a positive heparin-induced platelet aggregation assay. We promptly discontinued heparin and started picotamide, an antiplatelet drug. Rapid clinical improvement was observed in a few days. We stress the unusual features of the reported case (HITT during prophylactic therapy with low doses of porcine heparin; intermittent thrombosis), and we suggest picotamide represents a rational therapy for HITT on the basis of clinical and pathogenetic considerations.

Key words: heparin, thrombocytopenia, thrombosis, picotamide

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tion within 15 minutes; 58.5% platelet aggregation was measured.

Heparin was promptly discontinued when thrombocytopenia was documented, and picotamide was started orally at a dose of 300 mg three times daily. After two days the patient complained of less frequent and less intense pain, and it completely disappeared the next day. At that time Doppler examination revealed a normal arterial flow. Platelet count was $67 \times 10^9/L$ after 3 days and $147 \times 10^9/L$ after 7 days of therapy.

**Discussion**

Our patient presented the clinical features of HIT complicated by arterial thrombosis, in agreement with diagnostic criteria reported in the literature: 1) thrombocytopenia with platelets less than $100 \times 10^9/L$ during heparin therapy; 2) normalization of platelet count after discontinuation of heparin therapy; 3) the presence of thrombotic complications; 4) exclusion of other causes of thrombocytopenia (bacteremia, disseminated intravascular coagulation, use of other medications).³

We could consider this case a type II HIT, the type in which thrombocytopenia is severe and can be complicated by thrombosis.¹ Moreover, type II HIT thrombocytopenia typically occurs after six or more days of heparin therapy (unless there has been a previous exposure to the drug), which is what probably happened in our patient since the thrombotic episode usually begins at the time thrombocytopenia is documented.²

HIT onset is rare in patients receiving low doses of subcutaneous porcine heparin, with an incidence of about 0.3% in prospective studies; moreover, only sporadic cases with severe thrombocytopenia (<$50 \times 10^9/L$) and/or thrombotic complications have been reported.⁴

The clinical manifestation of the thrombotic complication was also unusual in our patient. Heparin-associated thrombosis is fatal in 29% of cases and leads to limb amputation in 21% of affected patients.¹ However, our patient showed a benign clinical course due to the intermittent nature of the thrombosis.

Despite significant progress in understanding the mechanisms underlying HIT, the exact pathways leading to heparin-induced platelet activation are poorly understood. In vitro studies performed in patients with type II HIT showed that heparin can be a weak agonist inducing thromboxane-dependent platelet aggregation; however, in other cases it is a strong agonist inducing platelet aggregation irrespectively of thromboxane A2 (TxA2) synthesis. Furthermore, only TxA2-dependent platelet aggregation was prevented by cyclooxygenase inhibitors like aspirin.⁶ It should also be noted that not only heparin but also fibrinolytic drugs may have prothrombotic effects.² In our case the fluctuant course of the thrombosis could have been the consequence of unstable thrombi formation (being composed mainly of platelets) and vasospasm, both probably the result of increased TxA2 synthesis. On the basis of these observations we considered it proper to use picotamide since this antiplatelet drug inhibits TxA2 synthetase and blocks platelet receptors for TxA2.⁴

We suggest administering picotamide in selected patients with type II HIT, in whom thrombosis could be attributable to TxA2 activation. However, further studies are needed to support our observation.

**References**