Case Report

Heparin induced thrombocytopenia secondary to intraperitoneal heparin exposure

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Keywords: intraperitoneal dialysis; heparin induced thrombocytopenia

Background

Type II immune-mediated heparin-induced thrombocytopenia (HIT) is reported to occur in ~2% of individuals exposed to heparin for more than 4 days [1]. HIT has been well described in haemodialysis patients with a similar incidence to non-dialysis patients [2]. Patients treated with peritoneal dialysis are not routinely exposed to heparin during dialysis, and for this reason a switch from haemodialysis to peritoneal dialysis is often considered if HIT occurs in a hemodialysis patient. Previous studies have demonstrated that intraperitoneal heparin does not produce systemic anticoagulation and it has been suggested that a combination of large molecular weight and negative charge prevent systemic absorption of heparin across the peritoneal membrane [3]. However, it is unclear as to whether the reported lack of systemic absorption across the peritoneal membrane protects against the development of HIT. This is an important consideration because in many units it is standard practice to administer intraperitoneal heparin to prevent fibrin clot formation during episodes of peritonitis. In this case report we describe for the first time, to our knowledge, a case of type II HIT in a peritoneal dialysis patient who received intraperitoneal heparin.

Case

A 52-year-old man with end stage renal disease (ESRD) secondary to diabetic nephropathy started continuous ambulatory peritoneal dialysis (CAPD) in June 2000. His CAPD regimen included 2 l exchanges four times per day, alternating between 2.5 and 1.5% exchanges. The patient’s complete blood counts were normal, though his haemoglobin was maintained on IV venofer and eprex. Five weeks after starting CAPD, he presented to the peritoneal dialysis unit with cloudy dialysate effluent and was diagnosed as having CAPD peritonitis based on elevated peritoneal leukocytes. He was treated with oral ciprofloxacin and intraperitoneal vancomycin, though his peritoneal gram stain and cultures were ultimately negative. Consistent with our unit policy, he was also given intraperitoneal heparin for 7 days. This is given as 1000 U of unfractionated heparin daily via the intraperitoneal route. Bacterial cultures were negative and he received 14 days of antibiotic treatment. Prior to this exposure he had never received heparin (by any route). His blood count had been checked at a routine clinic visit 13 days prior to the diagnosis of peritonitis; the platelet count at that time was normal at 260\times10^9/l. Fourteen days after his last dose of heparin, he presented with epistaxis and petecceiae on his trunk and lower limbs. Platelet count was noted to be 25\times10^9/l. His platelet count spontaneously improved to normal over the next 7 days as is shown in Figure 1. HIT was confirmed by detection of antibodies against the heparin–PF4 complex using a serotonin release assay.

Discussion

The diagnosis of type II HIT is based on both clinical and laboratory findings. Manifestations of HIT include: thrombocytopenia following heparin administration (in the absence of another causative factor), normalization of platelet count once heparin is stopped, presence of thrombosis and a positive HIT assay. The typical clinical course is for the platelet count to drop at least 50% from baseline and usually fall below 150\times10^9/l. Thrombocytopenia typically occurs 7–10 days after the initiation of heparin; however, this may occur earlier if the patient was previously exposed to heparin. Arterial or venous
thrombosis occurs in up to 50% of all patients with HIT [4].

The evolution of type II HIT starts with heparin binding to platelet factor four (PF4), which is expressed on vascular endothelial cells. Via antigen presentation, T cell activation and T cell–B cell interaction, antibodies are ultimately produced to the heparin–PF4 complex. The resultant heparin–PF4-antibody (IgG or IgM) complex binds to the platelet FcgRIIA receptor (via the Fc portion of the immunoglobulin molecule). Binding of this complex to platelets leads to platelet activation and consumption of platelets via platelet aggregation. Platelet activation results in PF4 release from platelets, which acts as a positive feedback loop. The heparin–PF4-antibody complex also binds to glycosaminoglycans on the vascular endothelium, which may lead to direct endothelial damage. The combination of platelet activation and endothelial damage lead to thrombocytopaenia and a pro-thrombotic state [5]. The confirmatory test for diagnosing immune-mediated HIT is a serotonin release assay that quantifies platelet activation when donor platelets (labelled with radioactive serotonin) are combined with heparin and serum from the patient [4].

HIT most commonly occurs following intravenous infusion of heparin, but can also be seen during administration of low molecular weight heparin, heparin flushes, heparin in central lines and subcutaneous heparin. Previous studies in humans have shown that intraperitoneal heparin does not prolong the activated partial thromboplastin time (aPTT) [6]. Heparin’s large molecular weight (10 000–16 000 Da for unfractionated heparin) and negative charge have been assumed to limit its ability to cross the normal peritoneal membrane. However, animal studies using labelled heparin have shown that the drug does reach the systemic circulation, but not at a rate high enough to affect the aPTT [3]. The development of type II HIT in a peritoneal dialysis patient further supports animal studies that show heparin can be absorbed systemically. The route for systemic absorption remains unclear. We would speculate that in the case described, absorption was either via the peritoneal lymphatic system or across the peritoneal membrane that had an increased permeability due to peritonitis, or both.

This case highlights the fact that despite lack of a systemic anticoagulant effect, intraperitoneal heparin may induce HIT. Consequently, if intraperitoneal heparin has been administered, HIT should be considered in the differential of thrombocytopaenia in peritoneal dialysis patients. Moreover, haemodialysis patients who are switched to peritoneal dialysis because of HIT are still at risk for HIT if administered intraperitoneal heparin. Intraperitoneal heparin should be used judiciously in peritoneal dialysis patients.

Conflict of interest statement. None declared.

References


Received for publication: 14.2.05
Accepted in revised form: 9.6.05