Heparin resistance refractory to Antithrombin III and Fresh Frozen Plasma

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Introduction:
We report heparin resistance (HR) in a patient presenting for aortic valve replacement and coronary artery bypass grafting (CABG).

Case report:
A 60 y/o male with a history of CAD, PCI and hyperlipidemia presents for a 3-vessel CABG and aortic valve replacement. Standard monitoring and induction techniques were utilized and the pre-bypass course was unremarkable. After administration of 27,000 IU of heparin (300 IU/kg), the ACT was 200 seconds (s) (baseline 150 s). An additional 50,000 IU of heparin were given over the next 10 minutes but the ACT remained at 200 s. The patient was given 1,208 IU of Antithrombin III (AT III) and 2 units of fresh frozen plasma (FFP). The highest ACT was 370 s after a total heparin dose of 167,000 IU. At this point, it was decided to perform a 2-vessel Off-Pump CABG. The remainder of the procedure was uneventful. The last ACT was 125 s and no protamine was given. The next day he was transferred to the floor and discharged home without complications. AT III activity measured 48 hours later was 68%.

Discussion:
Our case report demonstrates an important and clinically significant experience of HR. Heparin potentiates AT III activity and the formation of inactive AT III-Thrombin complex. The incidence of HR, defined as failure to achieve an ACT value above 480 s following a 500 IU/kg bolus dose of intravenous heparin (1), is in the range of 4 to 22% in patients undergoing CPB (2). Common causes of HR include: AT III deficiency due to preoperative heparin treatment, a platelet count ≥ 300,000/mL, and albumin concentration ≤ 3.5 g/dL (3). Another mechanism of action of heparin is inhibition of factor Xa activity. A decrease in clotting factors caused by hemodilution from pump priming may also lead to possible HR (4). Despite the general belief that pretreatment with heparin decreases AT III activity leading to HR, some reports showed no effect of preoperative AT III levels on the ACT response to a heparin loading dose (5-7). Our patient did not receive heparin before surgery. We did not check AT III levels preoperatively. Postoperative AT III activity was normal (68%).

Reports have showed an association between thrombocytosis and HR (3). Platelet Factor 4 released by activated platelets during CPB is a strong heparin inhibitor (4) and can explain HR in the absence of AT III. Our patient had a platelet count < 300,000 K/mm3 preoperatively.

Chan (3) reported HR in the presence of plasma albumin concentrations < 35 g/L. The patients plasma albumin postoperatively was 2.2 g/dL which can explain low heparin sensitivity. We experienced HR despite 167,000 IU for a 90 kg of body weight (> 1800 IU/kg). We were unable to identify any clinical data to explain HR except low plasma albumin levels and concluded that while the majority of HR cases are due to acquired AT III deficiency from pretreatment with IV heparin, other etiologies need to be identified.

References:
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