Immunization by bovine thrombin used with fibrin glue during cardiovascular operations. Development of thrombin and factor V inhibitors.

Authors: Berruyer M, Amiral J, Ffrench P, Belleville J, Bastien O, Clerc J, Kassir A, Estanove S, Dechavanne M

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Abstract:

Brief case histories of three patients aged 58, 38, and 44 years are reported. All underwent cardiovascular operations. Subsequently hemostasis test abnormalities developed between the seventh and eighth postoperative days after exposure to bovine thrombin used with fibrin glue. These were characterized by an increased activated partial thromboplastin time (64 to 147 seconds), prothrombin time (19 to 24 seconds), bovine thrombin time (> 120 seconds) and a markedly reduced factor V level (< 10% in two patients and 16% in the third patient). A patient plasma dilution of 1 in 200 with a normal plasma pool was necessary to correct bovine thrombin time. No fast-acting or progressive inhibitor against factor V could be detected by coagulation tests, and fresh frozen plasma perfusion had no effect. Plasmapheresis was performed preventatively to avoid bleeding, and factor V levels stabilized at around 50% after two to four exchanges. Immunologic studies showed that the inhibitors were directed not only against bovine factors but also against human ones. Therefore factor V decrease could have been the result of rapid clearance from the circulation of complexes formed with a nonneutralizing inhibitor that is not detected by clotting tests. These antibodies were purified by standard methods and immunoaffinity. Fast immunization could be explained by a prior sensitization to bovine thrombin exposure during previous operations. It is suggested that bovine thrombin used with fibrin glue contains small amounts of factor V and may be responsible for these abnormalities. This is in agreement with

previous literature reports. However, these described neutralizing factor V inhibitors, which were easily detected.