

## Aortic valve replacement and ventricular septal defect repair in factor XII deficiency: An anesthetic challenge

Sir,

Factor XII deficiency is a rare genetic disorder with an incidence of one in 1 million.<sup>[1]</sup> It shows an autosomal recessive pattern of inheritance. Patients are clinically asymptomatic, hence remain undiagnosed.<sup>[1]</sup> There is no additional risk of bleeding but a definite risk of thrombosis.

The present case scenario describes anesthetic management of a patient posted for aortic valve replacement and ventricular septal defect repair who presented with isolated high partial thromboplastin time (APTT) of >140 s. Other coagulation parameters were normal, except low levels of factor XII, (0.2 U/ml, normal 0.5–1.5 U/ml). A thromboelastograph was run that was largely inconclusive, except an increased reaction time ( $R > 30$  min).

Before surgery, a baseline activated clotting time (ACT) was obtained, which was 680 s. So authors considered that it is prudent to infuse 350 ml of fresh frozen plasma (FFP) prophylactically before surgery to compensate for deficient factor XII. Repeat ACT was 150 s. Following this routine, cardiac induction was done and routine heparinization regime was followed. Before institution of cardiopulmonary bypass (CPB) 300 IU/kg intravenous of heparin was given and ACT was targeted to >480 s throughout CPB. Total cross-clamp time was 72 min and CPB time was 102 min. Heparin was reversed with protamine at a dose of 1.3 mg per mg dose of heparin. ACT at the end of protamine was 142 s.

The patient was shifted to intensive care unit. There was no transfusion of blood or blood products during or after the surgery. Total drain output was 600 ml at the end of 18 h. Thromboprophylaxis was started thereafter in the form of oral aspirin 100 mg/day.

Factor XII deficiency has additional implications for surgeries with CPB. It becomes challenging to monitor optimum heparinization as underlying prolonged APTT, or ACT is not a true indicator of coagulation status.<sup>[2,3]</sup> Literature regarding management of cases with factor XII deficiency is rather inconclusive. Different strategies have been employed such as monitoring prolongation of ACT from baseline high value,<sup>[2]</sup> patient-modified heparin

dose–response curve,<sup>[4]</sup> factor Xa levels,<sup>[5]</sup> correcting sample with plasma for modified ACT, or infusion of FFP for normalization of factor XII.<sup>[6]</sup> However, the authors were more in favor of FFP infusion as it was simple, easy, avoided drawing multiple samples, and cost-effective. It did not lead to increased risk of infection associated with transfusion of blood products. Other techniques mentioned although feasible were time-consuming and expensive.

Based on a previous study, it is known that a minimum of 10% of total blood sample of plasma is required with activator calcium gluconate to optimally compensate for factor deficiency.<sup>[6]</sup> Hence 350 ml was infused for the patient who was 50 kg.

Factor XII is a serine protease that initiates the intrinsic arm of the coagulation pathway on contact activation with kaolin or celite.<sup>[7]</sup> It is worth mentioning that the TEG tracing obtained was from a kaolin-activated sample that acts as factor XII activator, hence the intrinsic pathway could not be activated. Tissue factor activated sample could not be obtained as the equipment shortly became unavailable.

Factor XII also impairs conversion of plasminogen to plasmin, which is implicated in increased risk of thrombosis.<sup>[8]</sup> There have been reports of increased risk of coronary artery diseases associated with this condition. Hence antifibrinolytics should best be avoided.

Standardization of heparin monitoring strategy in factor XII deficiency cases is warranted in future. Also, the concerned anesthetists should be mindful of the potential thrombotic risk associated with the same.

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### Conflicts of interest

There are no conflicts of interest.

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