Factor XII Deficiency in a Patient with Severe Burns: A Case Study

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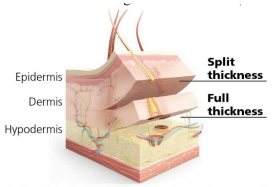


Split-thickness grafts harvest the epidermis and part of the dermis, rather than both layers.

1. Introduction

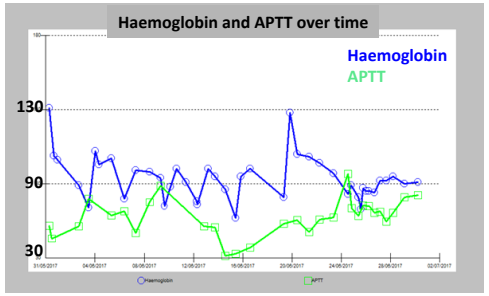
Factor XII deficiency has an estimated incidence of 1-3%. For many years, it was believed to be unique amongst the factor deficiencies in the sense that it was thought to have no clinical significance. We present an interesting case of a patient with Factor XII deficiency who presented with a 13% burn to her forearm, face and abdomen due to smoking in bed. She was taken to the operating theatre eight times for repeated debridement and application of split thickness skin grafts. Due to significant post-operative bleeding, her haemoglobin dropped to 57. She required regular blood transfusions, in total receiving 22 units of packed red blood cells.

Recent studies involving murine models have shown that mice with Factor XII deficiency have impaired formation of thrombi in arterial injury models. Burns surgery involves extensive and repeated debridement of dermal skin, which is rich in capillaries, venules and arterioles. We propose that our patient may have been unable to achieve adequate haemostasis of the small vessels sheared during debridement, such that her Factor XII deficiency may have been responsible for her delayed but significant post-operative oozing.

2. Case Study

Ms ST was a 55 yo F admitted to the Severe Burns Unit, RNSH in 2017 with 13% TBSA burns on the right side of her body following a smoking accident in bed. Her past medical history included a left middle cerebral artery stroke, which caused her to have long-standing right sided hemiplegia, expressive dysphagia and double incontinence. She also had Type 2 diabetes (insulin dependent), hypercholesterolaemia, GORD and depression.

During the pre-operative workup, she was found to have an elevated aPTT, fluctuating between 50-90 (normal range 24-36). Her aPTT corrected with mixing studies, in keeping with a factor deficiency. Her level of factor XII was 0.001 unit/ml (1% of normal). During her admission, she underwent three initial surgical debridements with no issues, even whilst on aspirin.

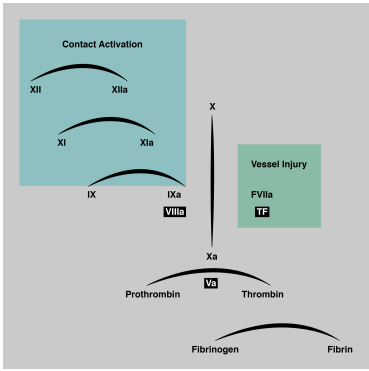


However, after her fourth operation, Ms ST suffered heavy bleeding from her freshly debrided elbow and shoulder burns. The bleeding was stopped with a combination of sutures and Kaltostat. Her haemoglobin was 84 pre-operatively and she was transfused 3 units intra-operatively. However, after this bleed, her haemoglobin had dropped to 65. Two days later, she started bleeding heavily from her donor site. Bleeding was stopped with pressure dressings and sutures but her haemoglobin again fell from 90 to 66. The next day, her enoxaparin was ceased. She was transfused 1 unit of platelets and 1g of transexamic acid. We consulted the haematology team who noted that Factor XII deficiency is not associated with a bleeding diathesis, but can cause clotting. Their impression was that Ms ST's significant bleeding was due to a combination of hypocalcemia and acidosis and that it was compounded by her aspirin and enoxaparin. After the platelet transfusion and the transexamic acid, Ms ST started bleeding from her debrided axilla. The bleeding was so severe it was thought to be arterial in nature and could only been stopped by tying off the bleeding points with sutures. Her haemoglobin after this event was 57.

Soon after this, Ms ST deteriorated due to sepsis and was admitted to the Intensive Care Unit. In ICU, her INR was found to be elevated at 1.6, which the ICU doctors thought might have been secondary to a vitamin K deficiency. She then went into anuric renal failure and passed away several days later. Her burns had not healed and she was in multiorgan failure. Throughout her admission, she had been transfused with a total of 21 units of packed red blood cells, four units of fresh frozen plasma and 1 unit of platelets.

3. What is Factor XII deficiency?

- Factor XII is a zymogen that sequentially activates factor XI and factor IX; it is part of the extrinsic clotting cascade
- Factor XI deficiency is a rare disease with an incidence of 1.5-3%, although those with a severe deficiency amount to < 1%
- It is often discovered as an unexpected prolongation in the activated partial prothrombin time (aPTT), as happened with our patient
- Human and mouse models have shown that Factor XII deficiency is not associated with abnormal hemostasis. This is most likely due to a redundancy in the extrinsic cascade, that is, factor XII is not the only mechanism via which factor XI is activated.



- It was previously thought that patients with Factor XII had a high rate of premature venous thromboembolic events (8-10%)
- However, recent studies have debunked this theory

1. A 1994 study on 350 Dutch patients with idiopathic DVT showed no increase in patients with factor XII deficiency over controls.
2. The 2006 SMILE study (Study of Myocardial Infarction-Leiden) showed an inverse relation between factor XII levels and risk of myocardial infarction
3. Renné et al.'s 2005 study in mouse models showed that mice with factor XII deficiency did not experience higher rates of spontaneous bleeding, but did have a severe defect in the formation and stabilisation of occlusive thrombi in settings of arterial injury

KEY TAKEAWAYS

- **Recent studies are challenging the notion that thrombosis is haemostasis in the wrong place**
- **If the results from murine models are translatable, patients with factor XII deficiency may have normal haemostasis combined in an inability to produce effective thrombi in settings of arterial injury**
- **This could explain the significant post-operative ooze from our patient's surgical and donor sites**

4. References

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