BMJ Case Reports

Rare disease

Acquired-transient factor X deficiency in a teenager with extensive burns

Andreia Mascarenhas,[1] Marilene Eusébio,[2] Orquídea Freitas,[3] Teresa Almeida[3]

[1]Department of General Pediatrics, Hospital Dona Estefânia, Rua Jacinta Marta, Lisboa, Portugal;
[2]Department of General Pediatrics, Centro Hospitalar do Barlavento Algarvio Sítio do Poço Seco, Portimão, Portugal;
[3]Hematology Unit, Hospital Dona Estefânia, Rua Jacinta Marta, Lisboa, Portugal

Correspondence to Dr Andreia Mascarenhas, amascarenhas22@yahoo.com

Summary

Acquired factor X deficiency is an extremely rare situation. It has shown to be associated with systemic amyloidosis, respiratory mycoplasma infection, factor X inhibitors, antiphospholipid antibodies, vitamin K deficiency/liver disease as well as the use of certain medications (meropenem, valproic acid). The pathogenesis and transient nature of this deficit remain poorly understood. The authors describe the case of a teenager hospitalised for extensive burns that developed active bleeding after removal of central venous catheter. He was diagnosed with transient factor X deficiency. Normalisation of coagulation status and factor X levels occurred spontaneously 10 days after the bleeding episode.

BACKGROUND

Congenital deficiency of factor X is a rare autosomal recessive bleeding disorder with an incidence of 1:1 000 000 in the general population.[1 2] An acquired factor X deficit in children with a normal homeostasis is an even rarer situation, and most cases are associated with systemic amyloidosis.[3] The acquired form also appears sporadically in patients with respiratory mycoplasma infection, vitamin K deficiency/liver disease and during the use of certain medications (valproic acid, topical thrombin).[4–6] In paediatric burn victims, three cases of transient factor X deficiency are described: one due to the presence of an inhibitor,[7] another associated with anti-cardiolipin antibody[8] and the third apparently related to meropenem use.[9] The pathogenesis and transient nature of this deficiency remain poorly understood. The authors present a case of a teenager with extensive burns who later developed bleeding due to lack of factor X.

CASE PRESENTATION

We report the case of a 16-year-old adolescent, admitted to the Pediatric Intensive Care Unit (PICU) due to a high-voltage electrical burn (railroad tracks), with 80% of total body surface area (TBSA) (head, face, feet and the distal left leg spared). His family and personal history were negative, especially with regards to a history of bleeding disorder. After initial stabilisation with intravenous fluids, topical therapy with silver sulfadiazine was initiated. Given the extent of burns, deep sedation and mechanical ventilation were initiated and maintained for 6 days without complications. On the second day of hospitalisation (D2) he underwent surgical debridement without the need of transfusion therapy, and alternate-day silver sulfadiazine dressings were maintained. Due to maintenance of hypotension after expansion with saline, inotropic support was started (dopamine and epinephrine). On D3, due to development of high fever and elevation of C reactive protein (370 mg/l), antibiotic therapy with flucloxacillin (2 g, 6/6 h, for 21 days) and gentamicin (14 days) was instituted. Blood cultures were negative. The coagulation results at this stage showed no alterations – thrombin time (PT) 12.1 s, international normalised ratio (INR) 1.1 and partial thromboplastin time (APTT) 33 s. Haemodynamic stability was achieved progressively, and inotropes were suspended on D8. On D9, venous thromboembolism prophylaxis with enoxaparin and acetylsalicylic acid was initiated. His remaining stay in the PICU progressed favourably and uneventfully from a clinical standpoint. In terms of laboratory results, on D18, a good outcome was confirmed, with haemoglobin 9.3 mg/dl, leucocytes 18 470/µl with 76.9% neutrophils, C reactive protein of 4.4 mg/dl, PT 13.1 s, APTT 30.5 s, INR 1.1, fibrinogen 227.2 mg/dl (154–488), D-dimer 178 (<250) and absence of fibrin degradation products.

After 22 days of hospitalisation in the PICU, given the good clinical outcome and after stopping antibiotics, he was transferred to the Pediatric Surgery ward. On D23, after removal of a central venous catheter, abundant bleeding was noted, controlled by local compression. Thromboembolism prophylaxis was immediately discontinued. Concomitantly, a transient (48-h duration) maculopapular, non-pruriginous rash was noted, which after Immunoallergology consult was interpreted as an irritant dermatitis and treated with hydroxyzine.

INVESTIGATIONS

At this time, the laboratory evaluation revealed no alterations significant for bacterial infection (leucocytes 11 000/µl; neutrophils 59.2%; 484 000 platelets/ml; C reactive protein 35.4 mg/l), but significant coagulation changes were demonstrated (PT 28.1 s, INR 2.40, APTT 38.8 s).

Clinically, there were no signs of disseminated intravascular coagulation.

A summary examination of the urine showed microscopic haematuria (erythrocyturia 3+). The liver function

tests were normal. Factor X measurement showed greatly decreased values (10% – normal value between 60% and 150%). A plasma-mixing test was performed with normalisation of plasma coagulation tests, ruling out the presence of an inhibitor.

OUTCOME AND FOLLOW-UP

By D32, both coagulation studies (PT 11.8 s, INR 1.3, APTT 31.5 s) and the measurement of factor X were normal. The patient suffered no further episodes of bleeding disorder.

DISCUSSION

Patients with major burns develop a tendency towards hypercoagulability, and prophylactic anticoagulant therapy was used earlier. In these patients, bleeding disorders may be associated with severe infection or disseminated intravascular coagulation. Acquired factor X deficiency is extremely rare with few cases reported in the literature. This factor plays a central role in the coagulation cascade, justifying the concomitant changes in APTT and PT (INR). Symptoms related to the factor X deficiency depend on its serum concentration – values between 1% and 10% are associated with minor bleeding, especially during surgical procedures, or, as was the case with our patient, on removal of a central intravenous catheter. Severe bleeding is described when values fall below 1%.[9] In the present case, despite the absence of fever, significant inflammatory markers or positive blood cultures, an initial diagnosis of infection, was entertained. After factor X deficiency was confirmed, the most frequent causes were systematically excluded. Systemic amyloidosis was highly unlikely given the presence of a previously healthy child. A respiratory mycoplasma infection was rejected given the absence of respiratory symptoms. Vitamin K deficiency or liver diseases, other possible causes, were also rejected because they usually present with associated deficits of other coagulation factors. In addition, liver function tests were normal. The presence of acquired inhibitors of coagulation factors in children with normal haemostasis is rare. There are two cases reported in paediatric burn victims where the factor X deficiency results from the presence of inhibitors.[7 8] The plasma-mixing test, with resultant normalisation of PT and APTT, contradicted this hypothesis.

In our case, the hypothesis of haemorrhage secondary to anticoagulant therapy was also placed, and this therapy was immediately suspended. However, antithromboembolic prophylaxis cannot explain the observed bleeding disorder because the low molecular weight heparins (HBPM) do not interfere with the PT and APTT.[10]

Previous studies report problems in correcting bleeding disorders caused by the factor X deficiency, requiring fresh frozen plasma and prothrombin complex. In our patient, the minor bleeding and a benign outcome observed were mainly due to the fact that the factor X deficit was moderate (10%), as most cases described in the literature have values less than 1%.

Jennes *et al* describe a case of transient factor X deficiency in a 12-month-old child with extensive burns, apparently associated with meropenem use. Other medications have also been implicated, such as valproic acid and topical thrombin.[5 6] In the described case, the antibiotic had been suspended on the eve of the bleeding episode and therefore could not exclude cause–effect relationship.

In conclusion, our case study is due to a transient deficiency of factor X, possibly associated with flucloxacillin. In fact, in the previously described three cases, the bleeding disorder also did not develop in the time-span immediately after burn, in which more complications are to be expected, but between 15 and 19 days of hospitalisation. Further studies of factor X levels in burn patients will have to be conducted to better understand this relationship.

Learning points

- Acquired factor X deficiency is extremely rare.
- In paediatric burn victims, three cases of transient factor X deficiency are described: one due to the presence of an inhibitor, another associated with anticardiolipin antibody and the third apparently related to meropenem use.
- We report a transient deficiency of factor X in a teenager with extensive burns possibly associated with flucloxacillin.
- The pathogenesis and transient nature of this deficiency remain poorly understood.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Uprichard J,** Perry DJ. Factor X deficiency. *Blood Reviews* 2002;**16**:97–100.
2. **Steen CJ,** Schwartz RA. Factor X, Emedicine, 2008.
3. **Choufani EB,** Sanchorawala V, Ernst T, *et al*. Acquired factor X deficiency in patients with amyloid light-chain amyloidosis: incidence, bleeding manifestations, and response to high-dose chemotherapy. *Blood* 2001;**97**:1885–87.
4. **Peuscher FW,** van Aken WG, van Mourik JA, *et al*. Acquired, transient factor X (Stuart factor) deficiency in patient with mycoplasma pneumonial infection. *Scand J Haematol* 1979;**23**:257–64.
5. **Gallais V,** Bredoux H, le Roux G, *et al*. Acquired and transient factor X deficiency associated with sodium valproate treatment. *Eur J Haematol* 1996;**57**:330.
6. **Israels SJ,** Leaker MT. Acquired inhibitors to factor V and X after exposure to topical thrombin: Interference with monitoring of low molecular weight heparin and warfarin. *J Pediatrics* 1997;**131**:480–83.
7. **Matsunga AT,** Shafer FE. An acquired inhibitor to factor X in a pediatric patient with extensive burns. *J Pediatr Hematol Oncol* 1996;**18**:223–26.
8. **Haberal M,** Basaran O, Sakallioğlu AE, *et al*. Acquired-transient factor X deficiency associated with anticardiolipin antibodies in a child with extensive burns. *J Burn Care Res* 2006;**27**:113–16.
9. **Jennes S,** Saidane G, Fauville JP, *et al*. Transient selective factor X deficiency in a severely burned child. *Burns* 2008;**34**:1037–40.
10. **Hirsh J,** Warkentin TE, Shaughnessy SG, *et al*. Heparin and low-molecular-weight heparin mechanism of action, pharmacokinetics, dosing, monitoring, efficacy, and safety. *Chest* 2001;**119**:64S–94S.