Reminder of important clinical lesson

Failure of fresh frozen plasma infusion and vitamin K to correct elevated international normalised ratio

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An 83-year-old, otherwise well, Caucasian gentleman was admitted with an incarcerated inguinal hernia. Routine preoperative tests revealed a raised international normalised ratio of 7.4, prothrombin time of 72.1 s and activated partial thromboplastin time of 73.1 s with normal liver and renal function tests. Despite fresh frozen plasma 15 ml/kg, and vitamin K, his repeat clotting remained deranged. The patient went on to have his hernia repair, and intraoperative bleeding remained normal despite the deranged clotting. The presence of endogenous clotting inhibitors can cause deranged coagulation studies but not impair bleeding. As in this case, the patient underwent surgery with no abnormal bleeding.

BACKGROUND

The National Institute for Health and Clinical Excellence guidelines for preoperative tests do not routinely require clotting studies unless the patient is on oral anticoagulation therapy. Abnormal activated partial thromboplastin time (aPTT), prothrombin time (PT) and/or international normalised ratio (INR) are usually corrected by the administration of fresh frozen plasma or vitamin K, which replaces the lacking clotting factors. In rare cases, haemostatic disorders are due to the presence of endogenous clotting inhibitors in the host's bloodstream, which are not correctable. In these cases, despite deranged clotting values, the host clotting response remains normal.

CASE PRESENTATION

An 83-year-old Caucasian gentleman presented with an incarcerated right inguinal hernia. He had a medical history of benign prostate hypertrophy treated with tamsulosin.

On examination, the patient appeared systematically well. A small, tender irreducible lump was found in the right inguinal region.

INVESTIGATIONS

A CT scan revealed a loop of small bowel within the hernia sac, but no bowel obstruction. The patient was booked and prepped for theatre.

His preoperative bloods were essentially normal with the exception of his deranged clotting: platelet count of $115 \times 10^9/l$, PT of 72.1 s, aPTT of 73.1 s, INR of 7.4 and fibrinogen 2.05 g/dl. A second sample confirmed the deranged clotting. A 50:50 mixing study demonstrated no deficiency of contact activation (intrinsic) or tissue factor (extrinsic) pathways.

TREATMENT

Fresh frozen plasma, which is a source of clotting factors and fibrinogen; and vitamin K, which binds to factors II, VII, IX and X to calcium and membranes¹ was administered to the patient to correct the abnormality with no effect.

OUTCOME AND FOLLOW-UP

The patient proceeded to theatre and surgery was completed uneventfully and haemostasis was adequately maintained throughout. The patient made a good recovery and was fit for discharge the next day.

Further investigation as an outpatient, including a measure of the Taipan Snake Venom Time,² revealed the cause of this patient's deranged clotting to be due to the presence of lupus anticoagulant.

DISCUSSION

Clotting disorders may not be due to the lack of clotting factors, but due to the presence of acquired inhibitors of coagulation in the patient's plasma.^{1 3 4} In these much rarer situations, the patient may display evidence of bleeding or may be completely asymptomatic, as in this case.

Patients with a normal fibrinogen level suggests the failure of coagulation is due to a non-specific inhibitor present in the patient's plasma,⁵ the most common of which is lupus anticoagulant.⁶ Alternatively, a direct thrombin inhibitor was present, or much less likely; multiple inhibitors are present disrupting clotting via both the contact activation and tissue factor pathways. The latter is highly unusual; in the majority of cases inhibitors act on the contact activation pathway and thus cause an increase in the aPTT alone. The most common coagulation inhibitor, for example, is

antiFactor VIII and interestingly there have been reports of the spontaneous haemophilia A in patients with adenocarcinoma of the prostate,^{7 8} although not to our knowledge in those with benign prostatic hyperplasia.

Rarely, however, inhibitors may act on the tissue factor pathway, such as a Factor VII inhibitor. Finding the reason for abnormal clotting is extremely important, as specific factor inhibitors are far more likely to result in increased bleeding risk than non-specific inhibitors.⁶ Indeed, the ultimate cause in this case, lupus anticoagulant is an in-vitro phenomenon in which the antiphospholipid antibody slows clot formation, thereby lengthening the clotting time. This is probably due to impairment of the assembly of the components of prothrombinase on phospholipid due to interference by the antibody.⁹

Lupus anticoagulant remains the most common non-specific inhibitor, found in ~5% of the general population, and can delay emergency surgery while a cause for clotting abnormalities is detected.

Learning points

- ▶ Patients with endogenous clotting factor inhibitors demonstrate normal haemostasis.
- ▶ The detection of a prolonged aPTT and/or PT can delay emergency surgery while investigating for an underlying cause.

Competing interests None.

Patient consent Obtained.

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