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An unusual cause of bleeding in an elderly patient

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Case presentation

An 84-year-old woman of Afro-Caribbean origin presented to the emergency department following a collapse at her home. She gave a one-month history of decreased appetite and unintentional weight loss, and her family had noted a general decline in her mobility and well-being. She had a past medical history of Alzheimer's disease and arthritis. She was not taking any regular medication or non-steroidal anti-inflammatory drugs (NSAIDs). On examination, she was pale and cachectic, and complaining of pain in the left hip and groin. She was tachycardic and had significant postural hypotension, but there was no evidence of bruising or any gastrointestinal (GI) bleeding. Initial investigations revealed a haemoglobin of 34 g/l (115–165) and mean corpuscular volume (MCV) of 74 fl (80–96), with a ferritin of 9 ng/ml (13–150), but normal B12, thyroid function and red cell folate. Prothrombin time (PT) and thrombin time (TT) were normal, but activated partial thromboplastin time (APTT) was prolonged at 92.8 s (30–40), with a ratio (APTR) of 3.3 (0.8–1.2).

What is the differential diagnosis and probable diagnosis?

Gastrointestinal blood loss is the most common cause of iron-deficiency anaemia in postmenopausal women and adult men, and is usually secondary to peptic ulcer disease resulting from NSAID use or GI malignancy. Angiodysplasia and malabsorption syndromes, most commonly coeliac disease, are the other important causes. When investigated, the coeliac serology of this patient was normal, and an inpatient oesophagogastroduodenoscopy (OGD) did not identify a source of bleeding.

The differential diagnoses for an isolated prolonged APTT include:[1]

- deficiencies of factors V, IX, X, XI and XII
- severe von Willebrand's disease
- lupus anticoagulant
- use of unfractionated heparin.

The patient was negative for lupus anticoagulant and had not been receiving heparin before admission. Disseminated intravascular coagulation (DIC) would have been considered in this patient if both the APTT and PT had been prolonged.

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What was the initial management?

The patient was resuscitated, given five units of blood and then treated with an iron supplement. She underwent a computerised tomography (CT) scan of abdomen and pelvis to investigate her left hip and groin pain. The scan revealed a normal small bowel and colon but a large iliopsoas haematoma, measuring 6 cm × 5.2 cm (Fig. 1). The iliopsoas haematoma was felt to be secondary to trauma sustained from her collapse at home and bleeding in to the psoas muscle was the probable cause of the drop in her haemoglobin level. Further clotting studies were performed; the APTT on a 50:50 mixture of the patient's plasma and normal plasma was prolonged at 60.4 s. Factor VIII levels were reduced at 24 IU/dl (50–150). The specific inhibitor quantification (Bethesda) assay confirmed the presence of an inhibitor (475 BU/ml) to factor VIII and the patient was subsequently found to have acquired haemophilia A.

Case progression

Once the diagnosis of acquired haemophilia A had been made, discussion took place between the patient, her family and the medical team regarding the possible management options (including intensive clotting factor replacement and immunosuppressive therapy). It was agreed that it would not be in the patient's best

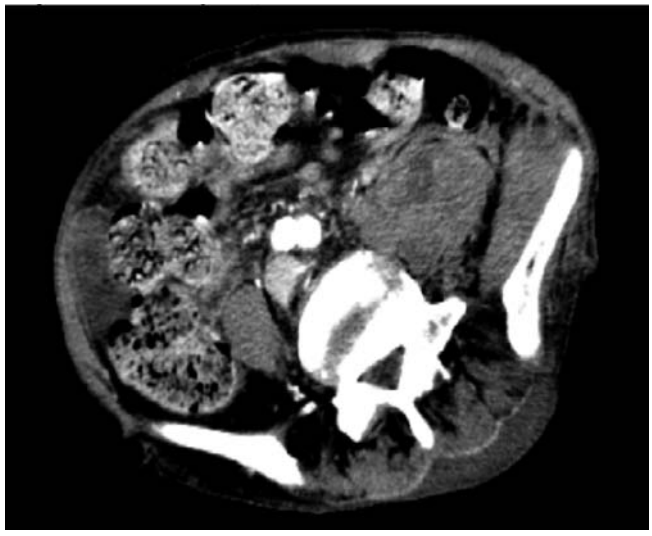

Fig 1. Axial slice of a CT abdomen and pelvis post-intravenous contrast showing an abnormally enlarged left psoas muscle with heterogenous attenuation compared with the normal right psoas muscle.

interest to treat her in view of the intensity of therapy and the need for close laboratory monitoring. The decision was made to manage her condition conservatively; keeping her comfortable and performing blood transfusions as appropriate. One week following the diagnosis, she developed a right-sided facial-swelling haematoma. Input from the ear, nose and throat team was sought; however, invasive strategies could not be used because of the significant risk of bleeding. She was reviewed by the palliative care team and prescribed low-dose opiates and benzodiazepines to keep her as comfortable as possible. She sadly passed away the following day.

Discussion

Acquired haemophilia is a rare disorder that is the result of the development of autoantibodies against factor VIII. It has an annual incidence of approximately 1.5 per million per year[2] and occurs in a bimodal age distribution, with the first peak occurring in females aged 20–30 years because of the association with pregnancy and the postpartum period.[3] The second bigger peak occurs in older people because of the association with malignancy and drugs.[3]

Acquired haemophilia can be associated with the underlying conditions detailed in Table 1.[1,3]

In congenital haemophilia, patients tend to develop haemoarthroses. By contrast, patients with acquired haemophilia bleed into the skin, muscles, soft tissues or mucous membranes.[2] Both forms of haemophilia are associated with bleeding into the iliopsoas muscle. Bleeding can vary from mild to potentially life threatening.

The principles of management of acquired haemophilia are to first control the bleeding, then eradicate the factor inhibitor and finally treat the underlying cause.[2,3] The current first-line treatment for controlling haemostasis is the use of bypassing agents, such as recombinant actor VIIa (rFVIIa) (NovoSeven®) or factor VIII inhibitor bypassing fraction (FEIBA).[2] Techniques can also be used to increase the level of circulating factor VIII, such as administering human factor VIII.[2] This can be used in patients with low titres of the inhibitor, because it is possible for the factor to overcome levels of the inhibitor.[1,2] Desmopressin infusion (DDAVP) can also be considered in the management of minor bleeding episodes.[2]

Immunosuppressive therapy can be used to eradicate the factor inhibitor. One treatment option is corticosteroids alone or in combination with cyclophosphamide.[2,4] Green and Lechner demonstrated that corticosteroids alone eradicated the factor in 22 of 45 patients. They also showed the beneficial effects of cyclophosphamide.[4] Rituximab is another treatment that is becoming popular.[2] Wermke and colleagues demonstrated the success of treating with a single low dose of rituximab.[5] Other management options include cyclosporin A and intravenous immunoglobulin.[2]

Common causes of death in patients with acquired haemophilia include sepsis resulting from immunosuppression, infection from blood-borne viruses with human factor VIII replacement, and tachyphylaxis with DDAVP.[3]

Patients with acquired autoantibodies can present with a bleed or can be found to be anaemic, as in this patient's case. The clinician should always analyse the clotting screen; the diagnosis is dependent first on the recognition of an abnormal APTT, a parameter that can be overlooked in the presence of a normal PT. Although acquired haemophilia A is a potentially life-threatening disorder, early diagnosis and intervention can lead to successful responses to treatment and to remission.[1]

Table 1. Underlying causes of acquired haemophilia.

Underlying condition	Percentage of patients with acquired haemophilia and an underlying condition
No underlying condition	46.1
Autoimmune (eg rheumatoid arthritis and lupus erythematosus)	18.0
Pregnancy, postpartum period	7.3
Malignancy (particularly head and neck, chronic lymphocytic leukaemia and non-Hodgkin's lymphoma)	6.7
Drugs (particularly penicillin)	5.6
Dermatological (eg psoriasis and pemphigus)	4.5

Key learning points

- Acquired haemophilia is a rare condition, but should be considered in a patient of any age who presents with bleeding or anaemia.
- The condition is commonly idiopathic, but can also be because of autoimmune conditions, malignancy, pregnancy, drugs and dermatological conditions.
- An isolated prolonged APTT will be the only abnormal parameter of the clotting screen.
- Following detection of a prolonged APTT, a mixing study, specific clotting factor assays and thereafter a Bethesda assay need to be sent for analysis to confirm low levels of the factor and the presence of a factor inhibitor.
- Acquired haemophilia can be treated by stopping the bleeding and eradicating the inhibitor. Treatment is aggressive and complex, and is also associated with significant morbidity.

References

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