Acquired haemophilia A as a cause of recurrent bleeding episodes in the elderly

Introduction

This article reports the case of a 73-year-old woman who presented with bilateral arm swelling and bruising. She had previously had many admissions for rectal and vaginal bleeding for which no cause had been identified. Investigations revealed that she was anaemic with a haemoglobin of 7.1 g/dl. Her activated partial thromboplastin time was prolonged at 45 seconds. Intrinsic pathway factor assay investigations revealed low factor VIII with no correction in activated partial thromboplastin time mixing studies, indicating strong inhibition of factor VIII. These findings were consistent with a diagnosis of acquired haemophilia A. The patient was given a 2-unit blood transfusion and commenced on prednisolone 40 mg once daily, fluconazole 50 mg once daily and co-trimoxazole 480 mg once daily. Two weeks after starting prednisolone, her activated partial thromboplastin time had decreased to 30 seconds and her haemoglobin remained stable at 12.0 g/dl. At this point her prednisolone dose was tapered down.

Discussion

The incidence of acquired haemophilia A in the UK is about 1.48 per million per year as demonstrated by Collins et al (2007). There are typically two peaks in incidence of acquired haemophilia A. The first peak is seen in young females aged 20–40 years and the second much larger peak is seen in the elderly where the incidence is estimated to be as high as 14.7 cases per million per year in patients over 85 years of age, as reported by Brunetti and Molinelli (2012). In the elderly, acquired haemophilia A can be associated with malignancy, drugs, autoimmune conditions and viral infections. However, Webert (2012) suggests that in 50% of patients a contributing factor cannot be identified.

Acquired haemophilia A is caused by the development of autoantibodies to factor VIII. Investigations typically show a prolonged activated partial thromboplastin time and a normal prothrombin time and platelet count. Intrinsic pathway factor assays show low factor VIII without significant correction in activated partial thromboplastin time mixing studies. As stated by Kessler and Asatiani (2007), the severity of acquired haemophilia A does not correlate with the strength of the inhibitor or factor VIII level, unlike congenital haemophilia where the severity is associated with the factor VIII level.

The two main goals of treatment are to control the bleeding and to eliminate the inhibitor. A bypassing agent such as recombinant activated factor VII or activated prothrombin complex concentrate are first-line treatment options to control bleeding in acquired haemophilia A. The use of a bypassing agent achieves significantly higher rates of bleeding control than the use of factor VII or desmopressin as shown by Baudo et al (2012).

There is no clear consensus on the optimum therapeutic strategy for inhibitor eradication. Some studies advocate corticosteroids alone. However, other studies

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Case Report

A 73-year-old woman was admitted with a 1-day history of extensive bilateral arm swelling and bruising. There were no reports from the patient's carers of any significant trauma sustained to her arms. She had a past medical history of advanced dementia and a previous stroke. She had previously been investigated for episodes of rectal and vaginal bleeding but a cause was not identified. She was not taking any antiplatelet medication or anticoagulants. She lived in a nursing home and was dependent for all activities of daily living. Examination of her arms showed that they were swollen, bruised, tender and hot to touch bilaterally. A cannula had been inserted on admission to the accident and emergency department and she experienced significant bleeding from the cannula site which required a pressure bandage to control the bleeding.

Her initial blood test results showed her to be anaemic with a haemoglobin of 7.1 g/dl. Her platelet count, prothrombin time and mean corpuscular volume were within normal limits. However, her activated partial thromboplastin time was prolonged at 45 seconds. The intrinsic pathway factor assay investigations showed normal factor IX, XI and XII levels. Her factor VIII level was low with no correction in activated partial thromboplastin time mixing studies which indicated strong inhibition of factor VIII. This picture is consistent with a diagnosis of acquired haemophilia A.

The patient was given a 2-unit blood transfusion. Although acquired haemophilia A can be associated with malignancy, in view of this patient's multiple comorbidities and functional status, actively investigating for a source of malignancy was not felt to be appropriate. She was commenced on prednisolone 40 mg once daily. She was also commenced on fluconazole 50 mg once daily for fungal prophylaxis and co-trimoxazole for pneumocystis pneumonia prophylaxis as a result of the long-term steroid use. Two weeks after starting the prednisolone, her activated partial thromboplastin time had decreased to within normal limits at 30 seconds. Her haemoglobin also remained stable at 12.0 g/dl. Her prednisolone was then tapered down and eventually stopped. Once the prednisolone had stopped, the fluconazole and co-trimoxazole were discontinued.

The patient remained relatively well for the next few months without any major bleeding episodes. However, she was re-admitted 5 months after her last admission with a further episode of rectal bleeding. She was reviewed by the haematologists again who felt that in view of her general frailty and poor prognosis, it would not be in her best interests to continue actively investigating and treating her rectal bleeding, and that she should be palliated in the community if there was any further deterioration in her condition.

such as Collins et al (2012) have reported that patients given cyclophosphamide in addition to corticosteroids had a higher likelihood of achieving stable remission compared to steroids alone. Rituximab is often considered if patients do not respond to corticosteroids and/or cyclophosphamide.

Acquired haemophilia A has a mortality rate of 8–22%, and relapse rates can be 10–20% within the first 6 months after stopping immunosuppression. Patients with advanced age or malignancy, and patients not attaining complete remission, are associated with higher rates of mortality as shown by Bitting et al (2009). BJHM

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LEARNING POINTS

- Acquired haemophilia A should be considered in elderly patients who present with recurrent bleeding episodes.
- Prompt diagnosis and treatment is essential to avoid the life-threatening complications of acquired haemophilia A.
- Intrinsic pathway factor assays show low factor VIII without significant correction in activated partial thromboplastin time mixing studies.
- The two main goals of treatment are to control the bleeding and to eliminate the inhibitor.

Iatrogenic calcinosis cutis following a neonatal extravasation injury

Extravasation injuries usually heal spontaneously with conservative management. As such, the potential sequelae are often underestimated. Extravasation damage can lead to adverse scars, necrosis, tissue loss, contractures and deformity (Lake and Beecroft, 2010).

A 4-day-old neonate on intravenous calcium gluconate infusion suffered an extravasation injury to his right dorsum of hand (*Figure 1*). He was referred to the on-call plastic surgery team. Radiographs showed calcinosis cutis (*Figure 2*). This was managed conservatively and there was good return of skin quality at 20 weeks post injury.

Calcinosis cutis is an uncommon condition but can be easy to diagnose following extravasation injury and typically resolves spontaneously with conservative management (Puvabanditsin et al, 2005; Sonohata et al, 2008). However, its presentation can mimic serious soft tissue and bone infections leading to misdiagnosis and unnecessary interventions. Concomitantly, there needs to be a high level of suspicion for other differential diagnoses such as osteomyelitis. This case highlights the importance of increased awareness of the condition, early referral and diagnosis. BJHM

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Figure 1. Day 3 post extravasation injury to dorsum of right hand from calcium gluconate.

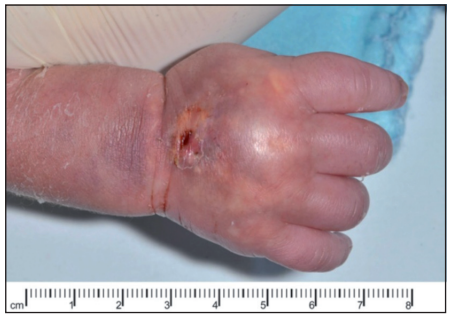
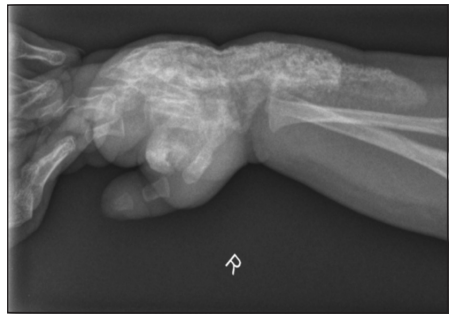


Figure 2. X-ray post calcium gluconate extravasation injury showing extensive calcification over the right dorsal region of the hand and wrist.



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