Acquired haemophilia: an important but often unrecognised cause of bleeding in elderly people

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Elderly patients with severe bleeding need their clotting screen checked as early treatment of acquired haemophilia improves outcome

Acquired haemophilia is a rare condition caused by the spontaneous acquisition of antibodies to clotting factor VIII. Although the reported incidence is 1 in 1 000 000,¹ the diagnosis may be missed and the condition may in fact be more common. We present two cases and discuss the reasons for the different outcomes.

Case 1

A 79 year old man presented with epigastric pain and melaena. He had a history of melaena from a bleeding duodenal ulcer, diagnosed on barium meal examination 20 years previously, and a hiatus hernia, diagnosed on endoscopy two years previously. On admission his blood haemoglobin concentration was 96 g/l and he required transfusion. Endoscopy showed superficial ulceration in a deformed duodenal cap, hiatus hernia, and mild oesophagitis.

Despite treatment with ranitidine he had two further episodes of serious gastrointestinal bleeding. During a third episode his haemoglobin concentration fell to 51 g/l and he developed a widespread ecchymotic rash. A clotting screen showed a prolonged activated partial thromboplastin time of 72.9 (normal range 26-36) and a normal prothrombin time, thrombin time, and plasma fibrinogen concentration. The activated partial thromboplastin time remained high with normal plasma, and assay of specific clotting factors showed a factor VIII concentration of 30 IU/l (normal range 500-1500 IU/l) and normal concentrations of other intrinsic factors. These results indicate the presence of a factor VIII inhibitor; the titre was not measured. Rheumatoid factor was positive (titre of 128) and plasma protein electrophoresis gave normal results.

He developed persistent melaena, haematuria, retroperitoneal haemorrhage (confirmed on computed tomography), intestinal obstruction due to an irreducible inguinal hernia, and renal failure. Over the next week he required 10 units of blood to maintain his haemoglobin concentration above 90 g/l. His bowel obstruction was treated conservatively and medical measures were used to correct the metabolic consequences of renal failure. At the request of the patient active treatment was withdrawn, and he died peacefully. In retrospect, early control of bleeding by treating the clotting inhibitor may have led to a better outcome.

Case 2

An 82 year old woman presented to the accident and emergency department with extensive bruising after minor trauma. Her blood haemoglobin concentration was 96 g/l, with a mean corpuscular volume of 74 fl; a clotting screen showed a prolonged activated partial thromboplastin time of 74 s and a normal prothrombin time. The activated partial thromboplastin time fell only partially, to 46.7 s, with normal plasma. The factor VIII concentration was 50 IU/l with a concentration of progressive inhibitor of 2 Bethesda units/ml. (A Bethesda unit is the amount of antibody that neutralises 50% of factor VIII in pooled normal plasma in two hours at 37°C; normally no antibody is

detectable.) Concentrations of rheumatoid factor and the results of an autoimmune profile and of plasma protein electrophoresis were all normal.

Extensive bleeding into the superficial tissues of the limbs led to a fall in haemoglobin concentration to 72 g/l. She was treated with prednisolone 1 mg/kg daily and oral cyclophosphamide 100 mg daily. One week later the haemoglobin concentration was 80 g/l and inhibitor concentration had fallen to 1 Bethesda unit/ml, so the dose of prednisolone was reduced slowly to zero. One month later the inhibitor was undetectable and the factor VIII concentration had risen to normal. She continued taking cyclophosphamide for six months.

She subsequently suffered from increasingly painful osteoarthritis of the hip, for which she took non-steroidal anti-inflammatory drugs. She underwent hip replacement surgery, with no untoward bleeding, and remained well and free of bleeding two years later.

Discussion

Spontaneous acquisition of factor VIII antibodies can occur in isolation, particularly in elderly women, or in association with autoimmune disease, malignancy, pregnancy, or drugs (particularly penicillin).² The antibodies seem to be heterogeneous, are usually IgG, and have varying activity against animal factor VIII. Porcine factor VIII is a useful treatment in patients whose antibody has no activity against it.³

Acquired haemophilia should be suspected in anyone presenting with haemorrhage for which no cause can be found and in whom there is no history of bleeding. The pattern of bleeding differs from that of the congenital disorder in that haemarthroses are infrequent and soft tissue bleeding predominates. Haematuria and retroperitoneal haemorrhage are common. Suspicion of an abnormal bleeding tendency should be investigated urgently with a clotting screen. An increased activated partial thromboplastin time that cannot be corrected by the addition of normal plasma indicates a clotting inhibitor, and this needs to be further investigated by a haematologist. Prothrombin time is normal. Normal results in a clotting screen rule out the abnormality.

Treatment relies on control of haemorrhage, which may often be life threatening, and eradicating the antibody. Various forms of immunosuppression have been tried, but corticosteroids and oral cyclophosphamide are most commonly used.² Success has also been reported using plasmapheresis, intravenous immunoglobulin, and protein A immunoabsorption. Spontaneous disappearance of the antibody has been described, particularly in pregnancy.

Since the antibody can be fairly easily suppressed, resulting in a good clinical outcome, it is important to consider acquired haemophilia in elderly patients presenting with haemorrhage.

1 Green D, Lechner K. A survey of 215 non-haemophilic patients with inhibitors to factor VIII. *Thromb Haemost* 1981;45:200-3.

2 Anonymous. Acquired haemophilia [editorial]. *Lancet* 1981;i:255.

3 Morrison AE, Ludlam CA. The use of porcine factor VIII in the treatment of patients with acquired haemophilia: the United Kingdom experience. *Am J Med* 1991;91:235-65.

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