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Acquired haemophilia in an elderly woman

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Abstract

Acquired haemophilia is a rare autoimmune condition with an annual incidence of one per million. It is more common in the elderly and is associated with the presence of anti-factor VIII IgG antibodies. Most cases are idiopathic but there are also known associations with malignancy, other autoimmune diseases and drug interactions. As aging itself is not a cause of changes in range of coagulation tests (prothrombin time, activated partial thrombin time or thrombin time), platelet count or fibrinogen levels, an abnormality in these should prompt the physician to search for a cause of the change. The case of an elderly lady who presented with severe soft tissue bleeding secondary to factor VIII inhibitor deficiency is presented in this report.

Keywords

Acquired haemophilia; factor 8 inhibitors; clotting factors.

Case report

An 88-year-old woman was admitted with a history of generally feeling unwell and bruising in both forearms which started a week ago after a routine venepuncture at the GP surgery. Her past medical history included ischaemic heart disease and hypertension. She was otherwise quite well and was fairly independent. Her physical examination was entirely normal except for extensive haematoma in both forearms from her elbow to the tips of her fingers. Her haemoglobin concentration was 92 g/L with a mean corpuscular volume of 95.9 fL. She also had mild renal impairment (urea, 8.9 mmol/L; creatinine, 117 μmol/L). Coagulation screening revealed a very prolonged activated partial thrombin time (APTT) of 60.9 s with a normal prothrombin time (PT; 15.9 s). A 50:50 mix of the patient's plasma with normal plasma showed only partial correction of the APTT consistent with the presence of an inhibitor of coagulation rather than deficiency of an intrinsic clotting factor, when full correction of the APTT would be expected. Coagulation mixing studies are done to investigate bleeding tendencies. A 50:50 mixture of normal and patient plasma is tested at several timed intervals to see if the abnormal patient's plasma is corrected by addition of normal plasma, and if the correction is maintained for a 2-h period when incubated at 37°C. If the patient's plasma corrects and stays corrected, then it is consistent with a factor deficiency; if the patient's plasma does not correct or corrects less than 70% then it is consistent with a Lupus-like inhibitor; and if the patient's plasma corrects but returns to abnormal

coagulation after 2 h, then it is consistent with a factor inhibitor[1]. Her factor VIII level was 2.3% and her factor VIII inhibitor level was 25 Bethesda units (measure of the level of inhibitor to coagulation factor VIII; equal to the amount of inhibitor in patient plasma that will inactivate 50% of factor VIII in an equal volume of normal plasma after a 2-h incubation period. http://medical-dictionary.thefreedictionary.com/Bethesda+unit).

The diagnosis was acquired haemophilia caused by the formation of factor VIII inhibitors in her serum. She was started on prednisolone (1 mg/kg body weight) and was also treated with factor VIII inhibitor bypassing activity (FEIBA), which resulted in partial correction of her APTT. She had further relapses in the hospital and needed blood transfusions and immunoglobulin infusions. A search for malignancy was negative with a normal computed tomography (CT) scan of her thorax, abdomen and pelvis. CT of the head was normal except for age-related atrophy. She continued to have minor relapses and minor bleeding episodes and needed symptomatic treatment for a while.

Discussion

Classic haemophilia is caused by an inherited deficiency of factor VIII or factor IX and tends to present at an early age with bleeding into the joints. Acquired haemophilia, on the other hand, is a very rare condition (incidence of one per million per year) tends to occur in adults or older persons and tends to present with bleeding into soft tissues rather than joints. This is due to the production of auto antibodies against factor VIII, which inactivates factor VIII and causes a bleeding tendency. Most often the cause is idiopathic in 50% of patients with no underlying cause (as in this patient) or it can be associated with other autoimmune diseases, malignancy, pregnancy or drugs.[2] It tends to occur with equal incidence in both sexes.

A patient with factor VIII inhibitor usually presents with bleeding into the skin or soft tissues. They may also present with haematuria, gastrointestinal bleeding, postpartum bleeding, internal haemorrhage or an intracranial bleed. Typical laboratory findings in acquired haemophilia include an isolated prolongation of APTT and a low level of factor VIII. The PT, thrombin time, platelet count and function are normal. A 50:50 mix of patient's plasma with normal plasma does not result in correction of APTT if an inhibitor is present. Antibodies are invariably directed towards factor VIII and not factor IX.

Management includes control of haemorrhage, replacing lost blood and inactivating the antibody. Most patients with this condition are elderly and frail with multiple comorbidities. Recent medications should be reviewed as drugs (including sulphonamides and penicillin) could be a cause of inhibitor production. Other agents specifically used for bleeding episodes are FEIBA (factor VIII inhibitor bypassing activity containing activated factors VII, IX or X) or recombinant activated factor VII[3]. Immunosuppression remains the mainstay if tolerated. This helps in inhibitor eradication and should be initiated immediately if there is no contraindication. The most common regimen used for inhibitor eradication is prednisolone monotherapy (1 mg/kg/day).[4] The recent data from the European Acquired Haemophilia (EACH2) Registry[5] shows that a combination of oral prednisolone and cyclophosphamide (1–2 mg/kg/day) achieved a higher rate of complete remissions then just a single agent. Rituximab, an anti- CD20 monoclonal antibody, has also proved valuable in the management of acquired haemophilia and could be tried as initial therapy if antibody titres are high[6]. Immunoglobulin infusions may also be helpful.

Teaching points

Being a rare condition and potentially fatal, a high index of suspicion is needed in elderly patients presenting with a bleeding disorder especially with other comorbidities. Liaison with haematologists is of vital importance in managing such patients in a general medical ward.

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