

Acquired Haemophilia Mimicking Dermatitis Artefacta

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Sir,

Haemophilia is a well-known X-chromosomal inherited bleeding disorder caused by deficiency of coagulation factors. In contrast, acquired haemophilia is an uncommon, rare but serious bleeding disorder with a significant risk of mortality caused by the spontaneous development of IgG autoantibodies against coagulation factor VIII. Both sexes are affected equally. It may be associated with various autoimmune disorders, malignancies, pregnancy or drugs, but in almost 50% of cases no underlying disorder is detected. Acquired haemophilia should be suspected in anyone presenting with haemorrhage for which no underlying cause is detected and in whom no history of bleeding is known. The pattern of bleeding differs from that of the congenital disorder, haemarthroses are infrequent, and soft tissue bleeding predominates. Haematuria and retroperitoneal haemorrhage are common.

CASE REPORT

In February 2006, a 28-year-old Turkish woman presented with multiple superficial and deep haematomas since 5 months. The haematomas were on her legs, arms and body. Otherwise she felt healthy; there was no loss of weight, weakness or night sweats. She denied any traumata or violence; she had no personal or family history of haematomas, intestinal or gynaecological bleeding episodes. There was no medication history. She had given birth to a healthy child 6 months previously.

On examination in our outpatient service, she showed some superficial haematomas from 5–8 cm on her upper legs and a 30 × 30 cm deep painful swollen haematoma on her left forearm (Fig. 1). Otherwise, clinical examination revealed nothing abnormal. International normalizing ratio and blood cells had been examined previously by her doctor and were reported to be normal.

The differential diagnosis of multiple haematomas in a young woman includes haemato-oncological disorders such as leukaemia or lymphomas, bleeding disorders and external or self-violence events.

The normal INR and normal blood cells and platelets reported by her doctor and the localization of the haematomas on her left forearm first suggested a traumatic cause including self-violence, painful bruising syndrome or domestic violence. The psychosomatic specialist could not find any psychiatric problems. Laboratory findings on admission showed normal values for haemoglobin, haematocrit, white blood cells, platelets and international normalizing ratio.

Testing revealed an isolated prolongation of the activated partial thromboplastin at 63 s (normal <40 s), not corrected by incubating the patient's plasma with equal volumes of normal plasma (mixing study). Additional serological testing was performed and revealed a reduced factor VIII level of 4% (normal 70–140%) and evidence of a factor VIII inhibitor of 1.4 BE (low titre <10 BE (Bethesda Unit), intermediate 10–20 BE, high titre 20 BE). Factor IX, XI and XII were within normal limits.

On the basis of the isolated prolongation of the activated partial thromboplastin, the low factor VIII levels and the presence of antibodies against factor VIII, the patient was diagnosed as having an acquired haemophilia. The patient was admitted to a regional haemophilia centre and was managed with recombinant activated factor VII concentrate for 5 days and prednisolone, initially 100 mg/day. She was asymptomatic without bleeding symptoms under 10 mg prednisolone maintaining therapy when seen by her haematologist after 8 weeks.

DISCUSSION

Acquired haemophilia A is a rare but severe autoimmune bleeding disorder due to autoantibodies against

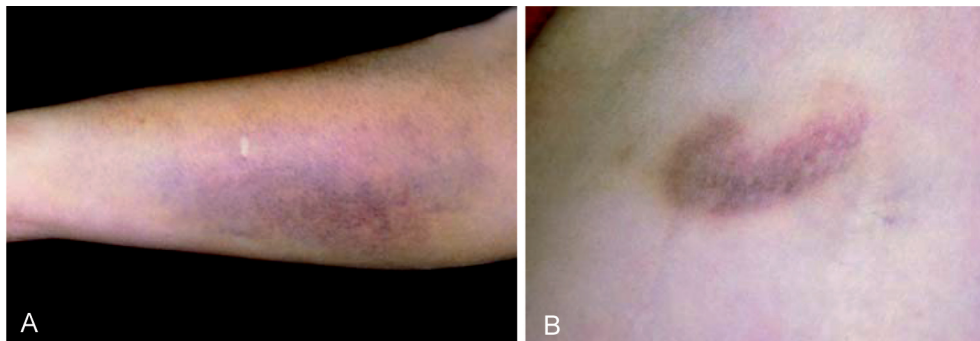


Fig. 1. (A) Deep painful swollen haematoma on the left forearm. (B) Close-up.

Table I. Conditions associated with acquired haemophilia. (Adapted from Franchini (1) and Green & Lechner (4))

Idiopathic (46.1%)
Autoimmune diseases (18%)
Rheumatoid arthritis, systemic lupus erythematosus, autoimmune haemolytic anaemia, myasthenia gravis, Goodpasture syndrome, multiple sclerosis, Sjögren's syndrome, temporal arteritis, Graves' disease, autoimmune hypothyroidism
Pregnancy/postpartum period (7.3%)
Malignancies (6.7%)
Solid: lung, prostate, colon, breast, pancreas, stomach, bile duct, head, neck, cervix, kidney, melanoma
Haematological malignancies: chronic lymphocytic leukaemia, Non-Hodgkin's lymphoma, multiple myeloma, M. Waldenström, myelofibrosis, myelodysplastic syndrome
Drug ingestion (5.6%)
Penicillin and its derivatives, sulfamides, phenytoin, chloramphenicol, methyl dopa, BCG vaccination, interferon alpha, fludarabine
Dermatological disorders (4.5%)
Psoriasis, pemphigus, epidermolysis bullosa acquisita
Various diseases (11.8%)
Respiratory diseases (asthma, chronic obstructive pulmonary disease)
Diabetes
Acute hepatitis B and C

factor VIII. It occurs in 0.2–1.0 cases per million persons per year (1, 2). Clinical symptoms usually include large, spontaneous haematomas and ecchymoses into the skin, muscles, soft tissue or mucous membranes (epistaxis, gastrointestinal, urological, gynaecological bleedings and retroperitoneal haematomas) of unknown origin. The mortality rate has been estimated to be in the range 7.9–22% with most haemorrhagic death occurring within the first weeks after presentation (1). There are two age peaks: the major peak at 68–80 years, with a small peak in young women between 20 and 30 years, mostly in association with pregnancy. Both sexes are affected equally (1).

Acquired haemophilia may be idiopathic or associated with several conditions: 7.3% occur in the postpartum period, usual in primiparas within the first month of delivery, as in our patient. 46.6% are associated with various underlying diseases (Table I).

However, in 46.1% of patients, no underlying disorder can be identified (3, 4).

Appropriate treatment depends on the titre of the inhibitor and should be carried out by an experienced haemophilia centre. Approximately one-third of patients may have spontaneous disappearance of the inhibitors, often observed in patients with low titre inhibitors (5, 6).

Treatment may require transfusion of human or porcine factor VIII concentrate, desmopressin, recombinant activated factor VII, prothrombin complex concentrate

or extracorporeal removal of the autoantibodies by plasmapheresis or immunoadsorption (3). Immunosuppression, including corticosteroids, cyclophosphamide, azathioprine or vincristine may be required. New therapeutic strategies, such as intravenous immunoglobulins, rapamycin, interferon α or rituximab, were reported to be effective in a few cases (2).

We present this case for the purpose of improving familiarity with this uncommon but potentially life-threatening haemorrhagic disorder, which should be considered and excluded before diagnosing dermatitis artefacta or external violence.

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