CASE REPORT

Acquired haemophilia A initially diagnosed as angioedema

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SUMMARY

Acquired haemophilia (AH) is a bleeding diathesis caused by inhibitors to factor VIII. Patients developing AH may present with catastrophic bleeding episodes despite having no prior history of bleeding disorder. The authors report a patient with AH who presented with tongue swelling and was diagnosed with angioedema on presentation. However, the patient started bleeding spontaneously after presentation and was diagnosed with AH and the workup revealed haematoma of the tongue, which was the cause of tongue swelling. As previously reported in the literature, AH in this patient might have been precipitated secondary to exposure to an ear infection or exposure to the penicillin group of antibiotics. Laboratory examination was confirmatory for AH, which was appropriately treated with recombinant activated factor VIIa and immunosuppressive therapy with good outcomes. Understanding the pathophysiology of AH and appropriate management is important to prevent life-threatening bleeding.

BACKGROUND

Acquired haemophilia (AH) is a rare, idiopathic, autoimmune bleeding diathesis caused by inhibitors to factor VIII (FVIII). Patients who develop AH may present with catastrophic bleeding episodes despite having no prior history of bleeding disorder. The authors report a patient with AH who presented with tongue swelling and was diagnosed with angioedema on presentation. However, the patient started bleeding spontaneously after presentation and was diagnosed with AH and the workup revealed haematoma of the tongue as the cause of tongue swelling.

CASE PRESENTATION

A 51-year-old Caucasian woman presented to the emergency department with tongue swelling and progressive difficulty breathing for a day prior to presentation. She was diagnosed with angioedema clinically and was admitted to the intensive care unit. She was treated with diphenhydramine and intravenous hydrocortisone as well as intramuscular epinephrine; however, failed to respond and had to be intubated to maintain airway patency. On the day of admission, she was noted to be bleeding profusely from the intravenous line site. She had no family history of bleeding diatheses and no personal history of postsurgical or postdental extraction bleeding. The patient was on amoxicillin for otitis media a few days prior to her current

admission. She had no known drug allergy and had tolerated the penicillin group of antibiotics in the past.

On physical examination, the patient was intubated and had a swollen tongue protruding from her oral cavity. There was diffuse ecchymosis noted on the patient's upper extremities. There was no evidence of other bleeding diathesis noted on physical examination.

INVESTIGATIONS

At presentation, activated partial thromboplastin time (APTT) was prolonged at 68 s, which did not correct on mixing study with 2 h incubation. Further studies revealed low FVIII activity (less than 4%), FVIII inhibitor titre of 15 Bethesda unit (normal <1) and elevated factor IX level. Dilute viper venom test was negative and ANA (antinuclear antibody), anticardiolipin antibodies, prothrombin time (PT) and international normalised ratio (INR) were within normal limits. A CT scan showed a tongue-base haematoma leading to airway obstruction. A diagnosis of acquired haemophilia was made.

TREATMENT

The patient was initially started on recombinant-activated factor VIIa (rFVIIa) in an attempt to control active bleeding. Immunosuppressive therapy was then initiated with a high-dose steroid, cyclophosphamide and weekly rituximab for 4 weeks with improvement in FVIII inhibitor and level of FVIII increased to 75%.

DISCUSSION

AH/acquired FVIII inhibitor is a rare autoimmune disease of FVIII inactivation due to polyclonal IgG4 antibodies that bind to A2 or C2 domain of FVIII.¹ It affects elderly and postpartum women (20–40 years) with the incidence of approximately 1.5–1.3/million/year.² Although uncommon, these autoantibodies are associated with a high rate of morbidity and mortality as severe bleeds occur in up to 90% of affected patients and the mortality rate is high, ranging from 8% to 22%.^{2–3} About 50% of AH cases occur without underlying disease while the remaining cases may be associated with postpartum period, autoimmune diseases, underlying haematological or solid organ malignancy, infections, or use of medications.^{1–2} Unlike congenital haemophilia, this condition results in gastrointestinal bleeding, retroperitoneal and other soft tissue haematomas.^{1–3} An isolated prolonged APTT, which does not correct with mixing studies and subsequent

To cite: Demissie A, Shahani L, Khan A, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200246

identification of a reduced FVIII level with evidence of FVIII inhibitor activity that can be quantified with a Bethesda assay, is required to establish the diagnosis.^{1 3} The therapeutic priorities are to control active bleeding and to eliminate the inhibitor.^{3 4} Activated prothrombin complex concentrate (aPCC) or recombinant activated factor VIIa (NovoSeven) controls bleeding episodes.^{3 4} Immunosuppressive therapy to eradicate the autoantibody should begin immediately upon diagnosis to reduce the morbidity and mortality associated with the protracted presence of FVIII inhibitor activity.^{3 4} A literature review shows that the most effective first-line treatment for eradication of FVIII autoantibodies is a combination of steroids and cyclophosphamide.^{1 4} However, use of rituximab and immune tolerance regimens are being reported to be effective.^{3 4}

The authors report a patient presenting with tongue haematoma secondary to AH which was initially misdiagnosed as angioedema. As previously reported in the literature, AH in this patient might have been precipitated secondary to exposure to an ear infection or exposure to the penicillin group of antibiotics.³ Laboratory examination was confirmatory for AH, which was appropriately treated with rFVIIa and immunosuppressive therapy with good outcomes. Understanding the pathophysiology of AH and its appropriate management is important to prevent life-threatening bleeding and is also important to reduce morbidity and mortality in these patients.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Learning points

- ▶ Acquired haemophilia A (AH)/acquired factor VIII (FVIII) inhibitor is a rare autoimmune disease of FVIII inactivation due to polyclonal IgG4 antibodies that bind to A2 or C2 domain of FVIII.
- ▶ About 50% of AH cases occur without underlying disease, while the remaining cases may be associated with postpartum period, autoimmune diseases, underlying haematologic or solid organ malignancy, infections or use of medications.
- ▶ An isolated prolonged APTT, which does not correct with mixing studies and subsequent identification of a reduced FVIII level with evidence of FVIII inhibitor activity that can be quantified with a Bethesda assay, is required to establish the diagnosis.
- ▶ The therapeutic priorities are to control active bleeding and to eliminate the inhibitor using immunosuppressive therapy.

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