Diagnosis and Management of Acquired Haemophilia - Full Clinical Guideline

Reference no.: CG-HAEM/2023/017

1. Introduction

Acquired haemophilia A (AHA) is a rare bleeding disorder that occurs when the body produces autoantibodies to factor VIII, a protein involved in blood clotting. The elimination from the blood of factor VIII caused by the autoantibodies is associated with an increased risk of bleeding, which may be spontaneous or in response to often minimal trauma or surgery.

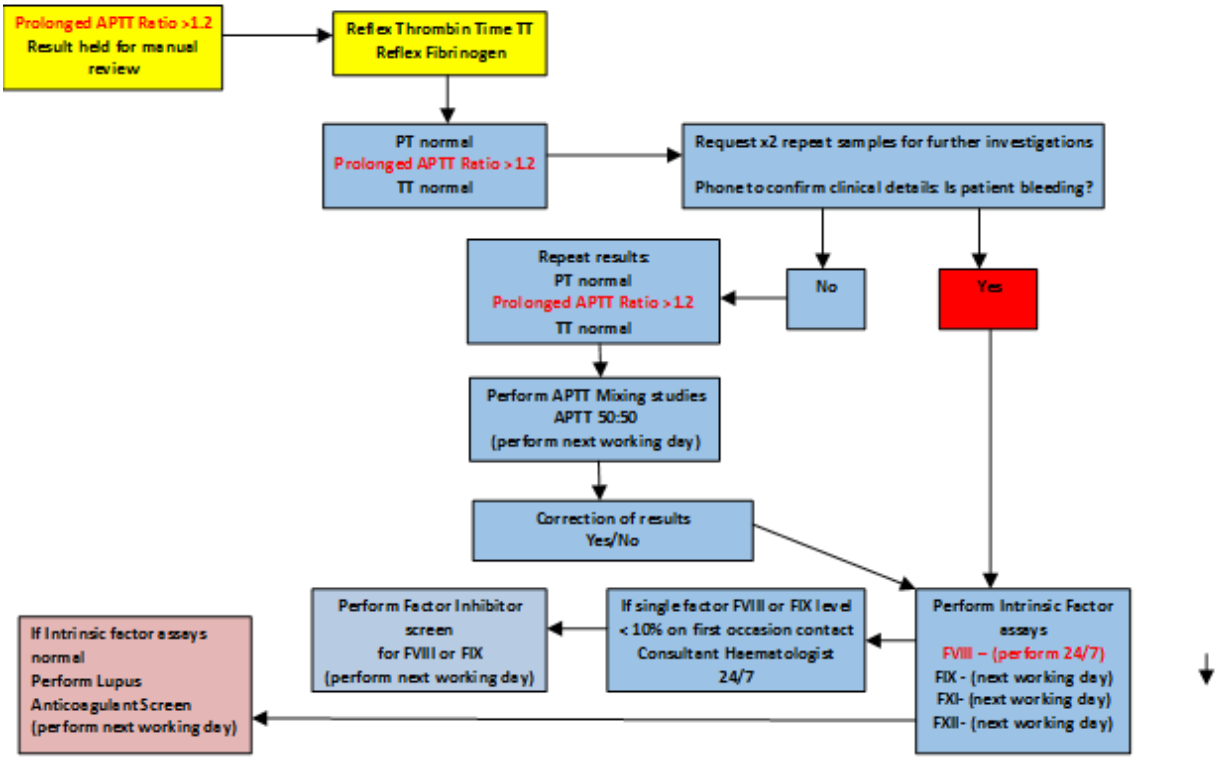
The pattern of bleeding in people with AHA differs from that seen in people with the more common congenital haemophilia. Bleeding most often occurs into skin and soft tissues, and people with AHA may present with, for example, compartment syndrome (where pressure within one of the body's compartments results in insufficient blood supply to tissue), haematuria (blood in urine), gastrointestinal bleeding and prolonged bleeding after giving birth. Bleeding may be life or limb-threatening; the reported mortality rate for AHA is between 3% and 22%. Therefore, people with AHA who present with bleeding are in need of urgent, specialist attention.

2. Aim and Purpose

To enable the prompt diagnosis and appropriate treatment of people with acquired haemophilia.

3. The diagnosis of AHA should be considered if acute or recent onset of bleeding is accompanied by an unexplained prolonged activated partial thromboplastin time (APTT). Acquired inhibitors for other clotting factors may be considered if acute or recent onset of bleeding is accompanied by unexplained prolonged screening tests [prothrombin time (PT), aPTT or thrombin time (TT)] that fail to correct with normal plasma.

Prolonged APTT Investigation for Acquired Factor Inhibitors



- The Laboratory should urgently inform clinicians of the potential significance of abnormal results.

- If a FVIII inhibitor is confirmed, blood should be sent urgently for a porcine FVIII inhibitor titre (send to Nottingham or Sheffield).

- Discuss management with Comprehensive Care Centre (Nottingham).

General Management.

1. Avoiding iatrogenic bleeding. Invasive procedures should only be undertaken if unavoidable and venepuncture should be kept to a minimum. If these procedures are necessary firm pressure should be applied for 20 minutes to the puncture site.

2. Bleeding can also result from the use of Blood Pressure cuffs and blood glucose monitoring. These should only be done if clinically necessary. Manual BP cuffs are preferable. Ward staff should be educated about these points.

3. IM injections are contraindicated.

4. The patient should be protected from the risk of falls.

Treatment of bleeds.

1. Not all bleeds need haemostatic treatment and many subcutaneous bleeds can be managed conservatively.

2. If indicated, bleeding should be treated without delay, initially using FEIBA or rFVIIa. If the initial bypassing agent is ineffective the other should be tried at an early stage.

3. Treat bleeds with a bypassing agent until the anti-pFVIII assay result is known. If the the ab titre is < 5.0 Bethesda units susoctcog alpha (porcine FVIII concentrate) may be used.

4. Tranexamic acid should be considered for all bleeds and especially those involving mucosal surfaces . Contraindicated in Haematuria.

Inhibitor eradication.

1. Patients with AHA should start immunosuppression as soon as the diagnosis is made. Immunosuppression should be initiated with prednisolone 1 mg/kg/day either alone or combined with cyclophosphamide 1–2 mg/d orally.

2. Rituximab can be considered as first-line therapy if standard immunosuppression is contraindicated, but may have limited efficacy if used as a single agent

3. If there is no response within 3–5 weeks, second-line therapies should be considered. The most common second-line treatment is with rituximab combined with other agents. Alternative options are calcineurin inhibitors (cyclosporin or tacrolimus), multiple immunosuppressive agents and immune tolerance protocols.

4. IVIG is not recommended as treatment for inhibitor eradication

5. Patients should be followed up at least monthly for the first 6 months because relapse is common.

6. Patients with a past history of acquired haemophilia should have a coagulation screen, or preferably a FVIII level measured before any invasive procedures.

7. When the FVIII level is normal, patient should be assessed for the risk of venous thrombosis and receive thromboprophylaxis if appropriate

Haemostatic agents.

Bypassing agents: FEIBA and rFVIIa. Both these can generate thrombin at the site of bleeding without the presence of FVIII. However, they have a risk of thrombosis in patients who are already at increased risk due to age and other comorbidities. Neither is measurable in routine laboratories.

Dosing:

FEIBA: 50 – 100 u/kg 12 hourly

rFVIII (Novoseven) – 90 micrograms/kg, may be repeated 2 hourly (for this reason FEIBA is usually preferred).

Recombinant Porcine FVIII concentrate (Susoctcog alfa). If there is no, or little, cross reactivity with the anti human FVIII inhibitor (< 5 – 6 Bethesda units) this may be preferable to a bypassing agent. It may be more effective, has less thrombotic risk and it is measurable using a standard 1 stage FVIII assay. If there is no cross reactivity with the patients' inhibitor, dose as per severe haemophila A without inhibitor i.e. 50 u/kg and then 25u/kg 12 hourly, adjusted according to levels. If there is more cross reactivity larger doses may be used.

4. References (including any links to NICE Guidance etc.)

Diagnosis and management of acquired coagulation inhibitors: a guideline from UKHCDO.

Br J Haematol, 162:758-773, 2013

5. Documentation Controls

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6. Appendices