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PATHCHAT

Dr Pamela Moodley – Haematologist

Acquired Haemophilia A: Are we missing the diagnosis?

Introduction

- Acquired Haemophilia A is a rare bleeding disorder caused by an autoantibody to factor VIII.
- The condition is often mistaken for other acquired bleeding disorders, such as disseminated intravascular coagulation (DIC).
- This may lead to delayed or suboptimal treatment.
- There is a poor correlation between measurable factor VIII or strength of the inhibitor and severity of bleeding.
- Patients remain at risk of life-threatening bleeding until the inhibitor has been eradicated.
- The aim of this overview is to increase awareness of the disorder among healthcare professionals.

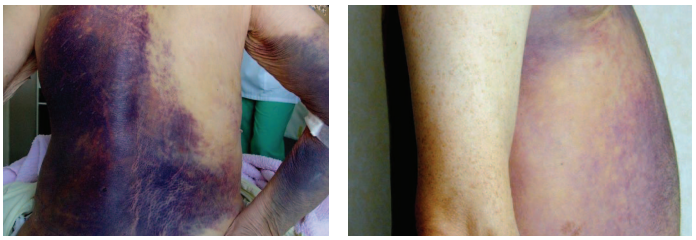
Comparison between classical and acquired Haemophilia A

Table 1

Classical Haemophilia A	Acquired Haemophilia A
Congenital – sex-linked inheritance	Acquired
Reduction in production of factor VIII	Autoantibody directed against factor VIII
Predominantly males Females are carriers	Both sexes
Usually presents at a young age	Presents at an adult age
Bleeding into joints (haemarthrosis) and muscles	Bleeding into skin and soft tissue

Clinical presentation

- Unusual or uncontrolled bleeding
- Purpura
- Soft tissue haemorrhage
- Prolonged bleeding following surgery
- Postpartum bleeding
- Compartment syndrome



Extensive ecchymoses
Adapted from Collins, P.et al., 2010.

Disease states associated with acquired Haemophilia A

- Collagen, vascular and other autoimmune diseases
- Asthma
- Skin disease
- Malignancy
- Pregnancy
- Drug interaction

Laboratory testing (Table 2)

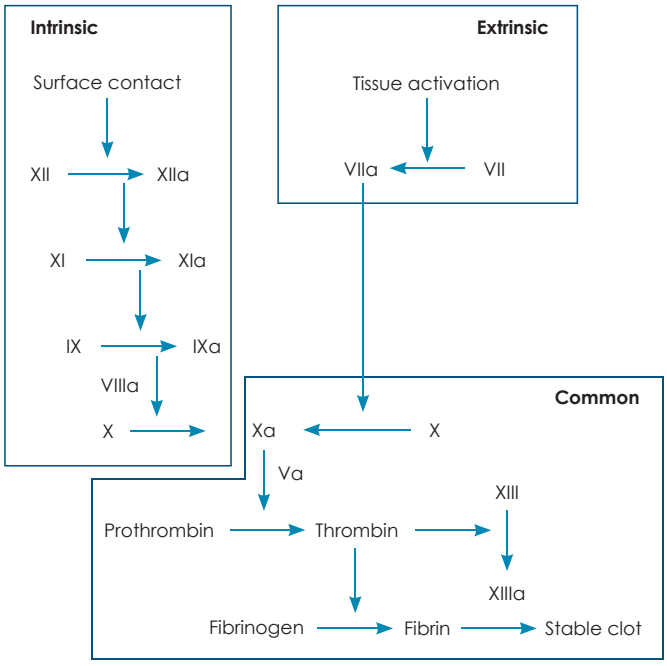
- A typical finding is an unexplained prolonged activated partial thromboplastin time (aPTT)
- With normal prothrombin time (PT)
- Normal platelet count and platelet function
- Presence of low factor VIII level
- Mixing studies are used to confirm the presence of a time-dependent inhibitor of factor VIII

Table 2

Parameter	Normal range	Acquired Haemophilia A
aPTT	25–40 s	Increased
PT	9.0–13 s	No change
Thrombin time	14.0–21.0 s	No change
Fibrinogen	2.00–4.00 g/dl	No change
FVIII	50–150% activity	Decreased
Anti-FVIII antibody	0	Present

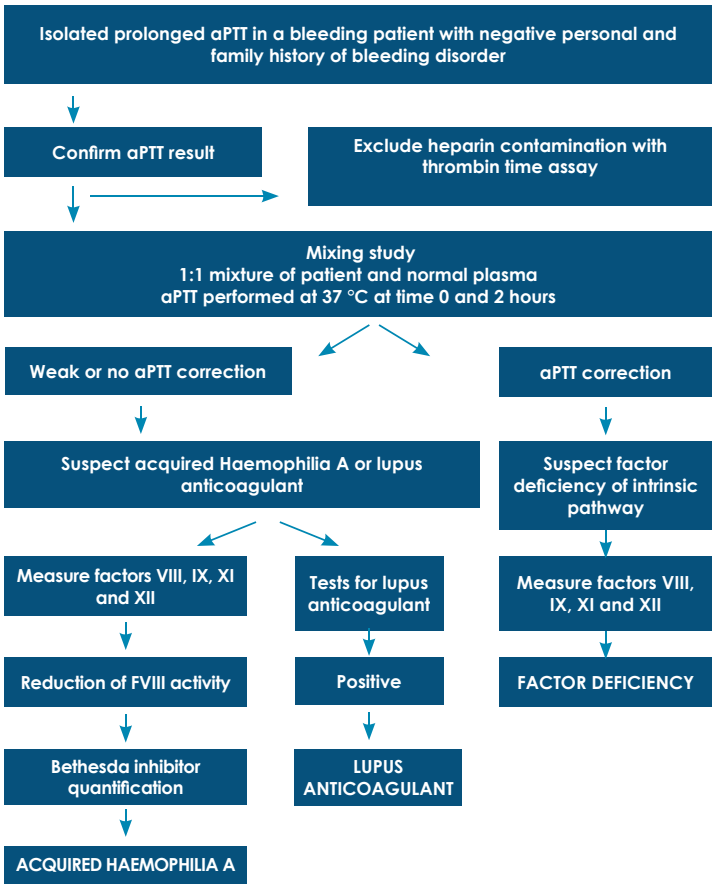
Values may not represent those seen when confounding drugs or illnesses are present. Normal ranges are based on Ampath reference ranges-site specific.

Figure 1: Simplified coagulation pathway



- An abnormality in the extrinsic pathway results in a prolonged prothrombin time (PT).
- An abnormality in the intrinsic pathway results in a prolonged activated partial thromboplastin time (aPTT). The factors involved are factors XII, XI, IX and VIII. It is important to establish if the prolonged aPTT is due to a factor deficiency or autoantibody.
- An abnormality in the common pathway results in prolongation of PT and aPTT.

Figure 2: Diagnostic guideline for clinicians



Treatment

- Treatment is a two-pronged approach.
- It involves stopping the bleeding and eradicating inhibitors.

Treatment of bleeding

- First-line treatment with bypassing agents:
  - Recombinant activate factor VII-NovoSeven
  - Activated prothrombin complex concentrates-FEIBA (contains factor VII, IX and X)
- Alternative treatment (if bypassing therapy is unavailable):
  - Human or recombinant FVIII concentrates
  - Desmopressin

Inhibitor eradication

- The inhibitors can be eliminated in a number of ways.
- First line would be immunosuppressive medication, which dampens down (suppresses) the body's immune system:
  - Prednisone alone or with cyclophosphamide.
- Second line:
  - Immunomodulatory drugs, which prevent the body producing antibodies to clotting factors.
  - Occasionally, a technique called plasmapheresis is used, which involves passing the patient's blood through a machine to try to filter out the antibody.

Follow-up

- Relapse can happen with dose reduction and stoppage.
- Recommended follow-up is one year after treatment.
- Monitor using aPTT levels.

Important

- FVIII levels and Bethesda titres in acquired haemophilia are poor predictors of bleeding risk.
- Fatal bleeds can occur at any time until the inhibitor has been eradicated.
- Consult with haematologist to ensure accurate diagnosis.

References

1. Giangrande, P. 2012. *Acquired Hemophilia. Treatment of Haemophilia*. No.38.
2. Collins, P et al. 2010. Consensus recommendations for the diagnosis and treatment of acquired Haemophilia A. *BMC research notes*.
3. Huth-Kühne, A et al. 2009. International recommendations on the diagnosis and treatment of patients with acquired Haemophilia A. *Haematologica*.
4. Rest available on request.