Open Journal of
Clinical & Medical
Case Reports

Volume 4 (2018)
Issue 4

ISSN 2379-1039

Acquired haemophilia A, post partum

Bird R*; Jones E; Bojahr H

***Ruth Bird**

Anaesthetic Department, The Royal London Hospital, Barts Health NHS Trust, White chapel London, UK
Email: ruthhbird@doctors.org.uk

Abstract

Acquired hemophilia A is a rare bleeding disorder with a high mortality rate.

Diagnosis and treatment of this disorder can present a unique challenging for the team due to the acute, sudden onset of bleeding, requiring rapid haemostatic resuscitation.

This is often accompanied by a lack of a personal or familial abnormal bleeding history to aid a diagnosis.

Keywords

chronic pulmonary aspergillosis; malnutrition; immunosuppression; voriconazole

Case Report

Following spontaneous vaginal delivery of a term baby our 34 year old patients, had a 1st degree tear sutured with an estimated blood loss of just 50mls. She later went on to develop a post-partum haemorrhage of 1400mls requiring transfusion of 4 units of packed red cells.

Shortly after discharge she was readmitted with further bleeding from the sutured tear and an haemoglobin level of 56g/L. She was transfused 2 units and discharged home with no bleeding point identified on examination.

Three days later she was again admitted with bleeding, this time having a recorded loss of 800ml. Following initial resuscitation and stabilisation, she was transferred to the Royal London hospital for further management and specialist input following a factor VIII chromogenic assay result of 7.3%.

Examination under general anaesthesia revealed no surgically correctable reason for her ongoing bleeding. She was resuscitated with PRBC, FFP, and recombinant factor 7. A vaginal pack was placed and she was observed on the Obstetric high dependency unit.

Prior to this delivery, the patient had no history of abnormal bleeding, including a previous spontaneous vaginal delivery, wisdom teeth extraction and appendicectomy. There was also no known family history of abnormal bleeding or haematological diagnoses. Her only past medical history was of hypothyroidism for which she took thyroxine.

Following review by the haematologist she was diagnosed and treated for acquired haemophilia post partum and was commenced on prednisolone (continued for 6 weeks) and tranexamic acid.

During her subsequent inpatient stay there was no further evidence of significant bleeding and her haemoglobin remained stable at 109-110g/L. Platelets were within normal limits (416-422x10^9/L) and white cell counts were also normal. Following an initial abnormal APTT ratio of 1.9 when the patient was admitted, her clotting studies normalised. Bethesda Assay was done with a result of 0.9Bu (taken pre commencing on steroids). Testing for Lupus anticoagulant was negative. Factor VIII levels were monitored throughout the inpatient stay. A response to treatment was shown with levels increasing from 7.3% to 15.1% on discharge, then 38.2% 6 weeks after discharge.

Acquired Haemophilia

Acquired hemophilia (AH) is a rare autoimmune disorder characterized by bleeding that occurs in patients without a personal and family history of abnormal coagulation.

Autoimmune disorders occur when our immune system mistakenly attacks healthy cells or tissue. Auto-antibodies develop to endogenous coagulation factors.

Consequently, affected individuals develop complications associated with abnomal, uncontrolled bleeding into the muscles, skin and soft tissue, spontaneously, during surgery or following trauma.

AH can potentially cause severe, life-threatening bleeding complications in severe cases.

In approximately 50% of patients, there is an identifiable underlying clinical condition; in the other 50% no cause is known.

The incidence is around 1.5 per million per year in the UK and increases with age. [(4)] The most commonly found autoantibody is to factor VIII (acquired haemophilia A), although antibodies to any factor can be found.

Associated conditions include rheumatoid arthritis, asthma, penicillin allergy, malignancy, inflammatory bowel diseases, infection, diabetes, and respiratory or dermatological disease. Pregnancy-associated acquired haemophilia is extremely rare, with one UK study finding 1 in 350,000 births being affected, most commonly occurring post partum [4].

Diagnosis

Diagnosis should be considered in patients with a recent onset of abnormal bleeding, when associated with an isolated prolongation of the activated partial thromboplastin time.

APTT is sensitive to FVIII, FIX, FXI and XII, whereas PT is sensitive to vitamin K dependant coagulation proteins synthesised by the liver.

Bleeding can occur anytime from immediately to several months after delivery. The majority of perinatal cases occur in the postpartum period with just 17% occurring antenatally [1].

Tests to rule out other causes of isolated prolonged APTT such as non-specific inhibitors (e.g, lupus or heparin therapy) are also performed.

APTT mixing tests are carried out by mixing patient's plasma with normal plasma. These are used to further confirm the diagnosis. A mixing study differentiates genetic factor deficiencies from factor inhibitors. A sample of blood is taken and mixed with blood from a control subject. In individuals with a factor deficiency the normal plasma restores the test value to normal; in individuals with a factor

inhibitor it does not.

Once a factor inhibitor is established, an assay will be done to measure the activity of coagulation factors and the titer of the inhibitor. In individuals with AHA, this will demonstrate factor VIII deficiency and can as certain the severity (titer count) as well.

Severity of the bleeding has been shown not to correlate with the antibody titre or factor VIII level.

Treatment, once stabilisation of any acute bleeding episodes has been achieved, focuses around immunosuppression either in the form of steroids or cytotoxic agents or both.

The goals of management of this condition, include controlling and preventing bleeding, eradication of the inhibitor, and treatment of the underlying disease (if applicable).

Bleeding may occur with little warning and be very severe. Prompt haemostatic control is vital in order to reduce morbidity and mortality. The International Recommendations state that anti-haemorrhagic treatment should be started in patients with severe bleeding in which a diagnosis of AH is confirmed, irrespective of inhibitor titer and factor VIII activity [5].

Two pharmacological approaches are available: the use of bypassing agents (concentrates of factors that bypass the acquired deficiency) or strategies to increase FV III levels.

The choice between these two options is based on the site and the severity of bleeding and the characteristics of each individual patient. Since hemostatic agents do not have a predictable effect, any treatment of bleeding should be supervised by a Haematology consultant.

Fibrin glue or anti fibrinolytic agents, and surgical packing may be useful in the control of local bleeding.

Bypassing agents are the recommended first-line therapy due to their rapid action and high level of effectiveness.

The bypassing agents presently available are recombinant activated factor VII (rFVIIa or NovoSeven® RT) or activated prothrombin complex concentrate (aPCC or FEIBA®). Neither of these therapies is effective in all individuals.

NovoSeven® RT is a genetically engineered (recombinant) version of factor VII and has been well-tolerated with a low side effect profile. Risk of thrombotic adverse effects (thrombosis) is below 1% for individuals with AH.

aPCC is a plasma-derived, anti-inhibitor complex that contains various activated clotting factors. These factors allow the drug to bypass certain steps in the formation of blood clots (including the steps that require factor VIII)

Factor VIII levels can be increased either directly (infusion of factor VIII concentrate) or indirectly (using DDAVP to induce release of factor VIII from endothelial cells)

however, they are usually considered inadequate unless either the inhibitor titre is very low (i.e. < 5 Bethesda units [BU]) and bypassing agents are not available.

Although in some cases inhibitor can disappear spontaneously as long as the inhibitor is present,

bleeding related morbidity and mortality is significant. Therefore therapy eradication therapy in adults is recommended to start immediately after the diagnosis of AH unless clearly contraindicated.

Corticosteroids alone or combined with cyclophosphamide are the first line therapy. No clear difference in long term survival is observed in these two modalities.

However, individuals respond differently to immunosuppressive drugs and what is effective in one individual may be ineffective in another. A variety of additional immunosuppressive agents have been used to treat acquired hemophilia including cyclosporine A, azathioprine, vincristine, mycophenolate mofetil, and 2-chlorodeoxyadenosine.

Criteria for the response to treatment have not been established; nevertheless, high inhibitor titer and low FVIII level seem to predict the response to therapy.

Relapse of AH can occur in individuals who achieve remission once immunosuppressive therapy is stopped or if the dose is reduced. However, because of associated side effects, long-term immunosuppressive therapy is not recommended. Individuals with AH are encouraged to avoid activities that have a significant risk of trauma until after inhibitor eradication.

Relevance to Anaesthesia

Inherited bleeding (haemostatic) and clotting (thrombotic) disorders are rare but sometimes encountered by anaesthetists during emergency or elective surgeries. The perioperative management of these uncommon conditions can be challenging. Multi disciplinary involvement comprising haematologists, surgeon, and anaesthetists, is vital. Prompt liaison with laboratory services to ensure that appropriate factor concentrates are available and in sufficient quantity is an essential step in controlling haemorrhage. Early communication with theatre coordinators ensuring staff with cell salvage capability is useful.

Peri-operatively avoidance of mucosal trauma, I. M. injections, maintenance of normothermia, and pressure point care must be considered. Ultrasound should be used to aid vascular access.

A careful risk assessment should be undertaken prior to administering central neuraxial or regional blocks, and in most cases will be best avoided.

There have been recorded cases of epidural haematoma following epidural insertion prior to patients acquiring the disease. Senior assessment and serial monitoring should be observed in these cases [2].

A high index of suspicion is essential for the accurate and prompt diagnosis of acquired haemophilia A, when the patient is bleeding and has an isolated abnormality in APTT.

The diagnosis of AHA can be difficult as there is usually no history of personal or family bleeding disorders and the disease is rare. The European Acquired Haemophilia Registry (EACH2) reports a delay of an average of three days between the onset of bleeding and diagnosis.

Major bleeding has been reported in 87% of patients with acquired haemophilia with an associated mortality of 22%.

However, the subgroup of patients in whom there is an association with pregnancy may have a

more favorable outcome with one review of 51 cases demonstrating 97% survival at 2 years and almost 100% remission (absence of the inhibitor and normalisation of factor VIII activity) by 30 months [3].

References

1. Tengborn, L., Baudo, F., Huth-Kühne, A., Knoebl, P., Lévesque, H., Marco, P., Pellegrini, F., Nemes, L., Collins, P. and on behalf of the EACH2 registry contributors (2012), Pregnancy-associated acquired haemophilia A: results from the European Acquired Haemophilia (EACH2) registry. BJOG: An International Journal of Obstetrics & Gynaecology, 119: 1529–1537.

2. Green D. The management of factor VIII inhibitors in non-hemophilic patients. Progress in Clinical Biological Research 1984; 150: 337–52.

3. Angela Huth-Kühne et al, International Recommendations On The Diagnosis And Treatment Of Patients With Acquired Hemophilia A. Haematologica April 2009 94: 566-575.

4. Acquired hemophilia A in the United Kingdom: a 2-year national surveillance study by the United Kingdom Haemophilia Centre Doctors' Organisation Peter W. Collins, Sybil Hirsch, Trevor P. Baglin, Gerard Dolan, John Hanley, Michael Makris, David M. Keeling, Ri Liesner, Simon A. Brown, Charles R. M. Hay, UK Haemophilia Centre Doctors' Organisation Blood Mar 2007, 109 (5) 1870-1877.

5. Angela Huth-Kühne et al, International Recommendations On The Diagnosis And Treatment Of Patients With Acquired Hemophilia A. Haematologica April 2009 94: 566-575.

Manuscript Information: Received: October 11, 2017; Accepted: February 25, 2018; Published: February 28, 2018

Authors Information: Bird R*; Jones E; Bojahr H

Anaesthetic Department, Fourth Floor, North Tower, The Royal London Hospital, Barts Health NHS Trust, White chapel London, UK

Citation: Bird R, Jones E, Bojahr H. Acquired haemophilia A, post partum. Open J Clin Med Case Rep. 2018; 1383.

Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at **www.jclinmedcasereports.com**
For reprints and other information, contact editorial office at **info@jclinmedcasereports.com**