Critical bleeding due to acquired haemophilia

Incidence and aetiology

Incidence

- Acquired haemophilia is rare, with two new cases per million population every year.

- Estimates of incidence vary; estimated as between 1 and 4 million of the population

- Testing of blood from asymptomatic donors has revealed autoantibodies in up to 15-17% of cases.

- Recent clinical evidence shows that the incidence of acquired haemophilia has either been underestimated or under-diagnosed in the past.

Aetiology

- Acquired haemophilia is the term used to describe the spontaneous development of inhibitors (autoantibodies) to factor VIII (most common) or IX. Why this occurs is unknown, as the formation of antibodies to other coagulation factors is extremely rare.

- About 50% of cases of acquired haemophilia are associated with an underlying disease state or with the administration of certain drugs.

- Associated diseases include autoimmune diseases (including systemic lupus erythematosus and rheumatoid arthritis, myasthenia gravis), dermatological diseases, lymphoproliferative malignancy, respiratory diseases, and ulcerative colitis.

- Patients with acquired haemophilia often present as life-threatening cases, with spontaneous bleeding episodes that are very difficult to control, even with infusions of large amounts of replacement clotting factors.

- The majority of cases occur in middle-aged or elderly individuals.

- Acquired haemophilia may occur in the post-partum period and there
have also been cases reported during the later stages of pregnancy.

Clinical and laboratory features

Clinical characteristics

- A sudden onset of bleeding in patients with no previous history of bleeding. Bleeds can be severe, frequent, and often present as an emergency.

- The pattern of bleeding is different to that observed in congenital haemophilia, in particular, spontaneous haemarthrosis is uncommon.

- Bleeding into the soft tissue, including purpura and muscle bleeds; gastrointestinal and intracerebral bleeds are also common.

- Bleeding is rarely intra-articular (spontaneous joint bleeding) as observed in congenital haemophilia.

- Other characteristic bleeds include haematuria, intra-abdominal and post-operative bleeds, and post-partum haemorrhage.

Laboratory characteristics

- Prothrombin and thrombin times and normal platelet count and function tests.

- Prolongation of the activated partial thromboplastin time (aPTT), which initially shows partial or full correction with normal plasma and further lengthening of aPTT after retest following further incubation.

- Reduced factor VIII level.

- Presence of antibodies to human and porcine factor VIII.

- Evidence of factor VIII inhibitor activity in a patient who has no history of a bleeding disorder.
Sequelae

Bleeding is the most common cause of death in patients with acquired haemophilia. Bleeds are more frequent and severe in acquired haemophilia patients than in patients with congenital haemophilia. Life-threatening haemorrhage is common, especially in the first few weeks of the haemorrhage.

**Mortality due to haemorrhage in patients with acquired haemophilia**

Mortalities due to haemorrhage of up to 15% have been reported in large studies. Mortalities due to haemorrhage of up to 45% have been reported in smaller studies. The reduction in mortality due to haemorrhage between the early and more recent studies may be the result of therapeutic advances in the treatment of acquired haemophilia.

**Management**

There are two strategies for the treatment of patients with acquired haemophilia: the treatment of the bleeding (haemostatic therapy) and immunosuppression to eliminate the inhibitor.

**Treatment of the bleeding**

- Treatment is almost the same regardless of whether factor VIII or factor IX inhibitors are present.

- Several different haemostatic agents may be used, depending on the patient and the circumstances, including associated conditions.

- Determination of the inhibitor titre may also help to establish the appropriate treatment for a patient, although this is less useful than with congenital haemophilia.
Types of therapy

Recombinant factor VIIa (NovoSeven®)

Porcine factor VIII

Human factor VIII

Prothrombin complex concentrates (PCCs)