There Will be Bleed

The Rare Blood Disorder - Haemophilia

Haemophilia is a rare inherited blood disorder in which the blood fails to clot properly. This is due to a defect in the body's clotting system, which is a complex process that involves multiple clotting proteins. If you are lacking in one or more of these clotting proteins, you can develop haemophilia.

A person with haemophilia will take a longer time for his bleeding to stop after an injury. Haemophilia mainly affects males. The prevalence of haemophilia in Singapore is estimated to be around 10-12 cases per 100,000 males, based on a national study published in 2015.

TYPES OF HAEMOPHILIA

There are two main types of inherited haemophilia: Haemophilia A and Haemophilia B. The former is 5 times more common than the latter. Haemophilia A has a deficiency in clotting factor VIII (F8), while haemophilia B has a deficiency in factor IX (F9). Both have varying degrees of severity depending on the level of functioning clotting factor.

Haemophilia has been called a "royal disease". This is because the haemophilia gene was passed from Queen Victoria, who became Queen of England in 1837, to the royal families of Russia, Spain and Germany.

Haemophilia A and B are X-linked inherited disorders. X-linked inheritance refers to the fact that the genetic abnormality for haemophilia is transferred on the sex-linked X-chromosome. Males have the XY sex chromosomes, while females carry the XX set of sex chromosomes.

F8 and F9 genes are both located at the X-chromosome. Hence, abnormality in these genes is passed down from a mother to her son. A female can be a carrier of abnormal F8 and F9 genes, but will not have any bleeding complication. This is because the other X-chromosome is normal. For an illustration of this, please see figure 1.

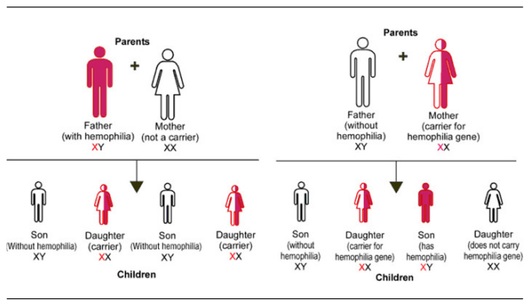

Figure 1: Illustration of how haemophilia is passed down (extracted from Haemophilia Volume 27, Issue 3, May 2021 – Wiley Online Library)

SYMPTOMS

The symptoms are dependent on the severity of the haemophilia. Most cases fall into the category of mild haemophilia, where the residual clotting protein is enough to prevent spontaneous bleeding and most minor bleedings are stopped easily, albeit taking longer than the average person.

A severe case of haemophilia can present with spontaneous bruises, and bleeding into the muscles, joints, stomach and even brain, which can be life-threatening. A severe haemophiliac could present to the emergency department with severe headache, reduced consciousness level, double vision, and one-sided weakness if he suffered a bleed in the brain. More often, they present with a painful swollen joint, especially at the knee and hip joints. Some may present with blood in the urine or stool, and recurrent nosebleeds. In milder forms of haemophilia, the condition is only discovered after prolonged bleeding following a tooth extraction, or excessive bleeding from a surgery. Figure 2 illustrates the various symptoms that may present in a haemophiliac.

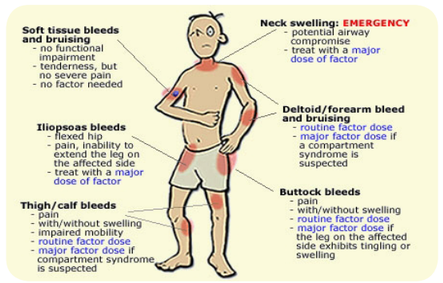

Figure 2: Symptoms of haemophilia (extracted from SingHealth)

TREATMENTS

There are various forms of treatments that can be used to make the patient better. They include:

Antifibrinolytic therapy

Antifibrinolytics are medicines that promote blood clotting by slowing down the breakdown of blood clots - a process called fibrinolysis. They are used as a treatment for haemophilia, in surgical procedures to prevent excessive blood loss and for heavy menstrual bleeding.

Clotting factor replacement

Haemophiliacs who present with serious bleeding, such as bleeding into a large joint, gastrointestinal bleed, or bleeding in the brain would need urgent clotting factor replacement. These are readily available in most major hospitals.

Prevention of major bleeding episodes is the cornerstone of care in severe haemophilia, especially those who already have a history of major bleed. This is done by administering low doses of clotting factor, such as factor VIII (for haemophilia A) and factor IX (for haemophilia B), 2 to 3 times a week to maintain a minimal amount of clotting factor required to prevent spontaneous bleeding. Severe haemophiliacs with no appropriate clotting factor replacement will eventually suffer from recurrent bleeding into the joint and irreversible damage to the affected joint.

On the other hand, the milder form of haemophilia only requires clotting factor replacement prior to a surgical procedure to reduce the risk of excessive bleeding during and immediately after the operation.

Many haemophiliacs with the severe form of the disease have learnt to self-administer the clotting factor intravenously, which is still quite a challenge for most patients. More recently, Emicizumab - a newer form of therapy which is administered subcutaneously - could soon replace the intravenous factor VIII as the main prophylaxis. Besides the ease of administration, it is also effective for haemophilia A patients who have developed antibodies against the factor VIII.

GENE THERAPY

Haemophilia is a genetic disorder that results in deficiency in clotting factors. Correction of the underlying genetic abnormality can potentially reverse the deficiency. Gene therapy for haemophilia involves using a modified virus (which does not cause disease) to introduce a copy of the gene that encodes for the clotting factor that is missing in patients. Following treatment with the virus, patients should begin to produce their own clotting factor normally. This treatment is still at an early phase of development. Perhaps in another 5-10 years' time, we may see this as the new standard of care for haemophilia.

LONG-TERM COMPLICATIONS

The major long-term complications of haemophilia are chronic haemarthrosis (recurrent bleeds into a joint) causing permanent damage to the affected joint (haemophilic arthropathy), and other sequelae of bleeding like bleeding into the brain, which can be quite devastating as it can leave one with permanent neurological deficit like hemiplegia. Other long-term complications can be related to infection transmitted by plasma-derived factor concentrates, especially those who received regular plasma-derived replacement clotting factor during the 1970s-1990s. The incidence rate has greatly reduced nowadays with improvement in the process of plasma-derived blood products.

EARLY DIAGNOSIS AND APPROPRIATE MEASURES

Haemophilia is a rare inherited blood disorder which mainly affects males. A haemophiliac has problems in forming clots and suffers bleeding complications due to specific clotting factor deficiencies. Early diagnosis and taking appropriate measures to prevent life-threatening bleeding would reduce the risk of long-term complications. Do consult a haematologist early if you notice unexplained bruises, prolonged gum bleeding, recurrent nosebleeds, etc. PRIME

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