A DITHYA Ananth*, all of 12, is a hero in many ways. For two consecutive years, he has completed the 5K run. What makes Ananth stand apart in his achievements is his condition: a rare affliction which puts him in the high-risk situation, should he suffer an injury, and, despite it, he has forged ahead.

It is just not the sheer grit and determination of Ananth that is commendable, but what is also endearing is the maturity and resolve he exhibits, for, he must be extremely cautious about normal physical activities that boys of his age do. However, he has learned to accept his condition, in fact, gathered all information about it, and even shares tips from his experience with others suffering silently trying to tackle a state like his.

He has been suffering from joint bleeds since the age of 1, and at 8, a minor fall led to hospitalisation and a blood transfusion. It took him a couple of months to recover; he encountered similar suffering after a few years while playing tennis.

Adithya suffers from a rare bleeding disorder called haemophilia, making him prone to severe bleeds even for minor injuries. In other words, his blood refuses to clot normally.

Though his condition is termed mild haemophilia, Adithya says: “When a bleed occurs, there is no difference between a mild or severe Haemophiliac.”
Plugging the Leak

So, what exactly is haemophilia and what happens when a person suffers from it? To understand haemophilia better, we must first know how the blood clots.

The immediate response of the body to a bleed (damage to the blood vessel due to an injury) is the noticeable process of forming a blood clot (called coagulation) which seals the damage. Within a few minutes, the clot closes the wound to prevent further loss of blood.

However, this automatic response is not so simple and straightforward, after all, and is a complicated biochemical process.

When injured, the wall of the blood vessel breaks, activating the platelets in the blood. The usually round-shaped cells begin to turn sharp and spine-like which attach themselves to the wall of the blood vessel and start to plug the damage. By now the blood vessel has already begun to constrict due to the injury.

From here starts the complex mechanism of clotting which involves 13 proteins, called the coagulation factors (F), numbered I to XIII.

- First, a glue-like substance called the von Willebrand factor is released by the wall of the blood vessel which helps the platelets bind together near the break.
- Then proteins collagen and thrombin contribute to chemicals which induce the platelets to stick together.
- As the platelets huddle, they further attract other platelets and proteins to quicken the process and enlarge to form a plug or clot — a gel-like substance — leading to haemostasis or the sealing of blood loss.
- During this process, specific clotting factors release which activates the generation of thrombin. Thrombin converts another clotting factor fibrinogen into strands of fibrin.

Fibrin threads radiate from the clumped platelet site forming a mesh which entraps platelets and other proteins to quicken the formation of the clot.

- Fibrin also helps to hold the clot by attaching to the wall of the ruptured blood vessel.
- Further, more chemical reactions are triggered which arrest the size of the growing clot when a sufficient clot seals the damage.

Let Down by the Genes

Haemophilia, one of the many bleeding disorders, is a condition wherein the bleeding is abnormal and profuse with poor clotting. Sometimes the bleeding is spontaneous — without a cause — bleeding can start anywhere in the joints without a trigger.

Haemophilia arises out of genetic mutation, and the defect expresses on the X-chromosome in a recessive pattern. Females are carriers of the error — where one of their X-chromosome carries the anomaly — while the disorder manifests in males on their one X chromosome. Hence haemophilia is rare, a
genetically inherited condition and is seen mostly in males.

Most often, females escape the affliction as they have two X chromosomes and the other X chromosome compensates the defective one. For haemophilia to show in females, both their X-chromosomes should be defective: an extremely rare condition which results out of the father being haemophilic and the mother being a carrier. However, even as a carrier, females can exhibit bleeding symptoms.

Haemophilia A occurs when F-VIII is less, and a similar deficiency of F-IX leads to Haemophilia B. The condition is considered mild for factor levels of 5-40%, moderate for 1-5% and severe for less than 1%.

Statistics say that 1 in every 5000 male births may be afflicted by type A, while type B is rarer seen in 1 in 20000 births.

However, these figures are significant for diagnosed conditions whereas several thousands go unrecorded, mainly due to lack of awareness about the defect. The situation turns alarming especially in developing countries as the people here lack knowledge and the appropriate medical attention.

Deadly Consequences
For a healthy person, minor cuts and bruises go unnoticed, whereas haemophilic injuries can soon turn life-threatening if medical attention is unavailable. Common falls, minor accidents and wounds can rupture muscles and joints. The result is that even a small injury will lead to excessive bleeding. A little bump on the head can trigger an internal bleed in the brain, and a slight crash can trigger bleeding in the internal organs, the consequences of which can become fatal in no time.

The dangers of internal bleeds are often around the joints. Prolonged internal bleeding in muscles and joints leads to a deterioration in the functioning of the joint. When the bleeds are spontaneous, osteoarthritis and muscular degeneration set in; chronic pains and debility hamper the quality of life. Depending on whether the person is mild, moderate or severely haemophilic, the degree of deterioration increases. The condition is diagnosed with blood tests and evaluation of medical and family history.

World Federation of Haemophilia (WFH)

- Frank Schnabel is the founder-father of WFH, who started it in 1963.
- A haemophilic himself, he was aware of the fatality of the situation which could arise out of ignorance of the condition.
- It was his vision to provide better care for the numerous haemophiliacs around the world. Through his organisation, he conducted workshops, brought the families of the haemophiliacs together and sensitised the developing nations about this rare disorder.
- His relentless efforts earned him and the organisation recognition from WHO, and since 1969, WHO is actively participating and promoting WFH activities.
- Now WFH has chapters all over the globe who are keenly taking part in their drives to bring awareness about the condition, treatment options and care for haemophiliacs.
- The World Haemophilia Day is observed on April 17th — Schnabel’s birthday — to honour his efforts.

Falling Short
Sadly, haemophilia has no known cure presently, neither is there a preventive medication for it. It can only be managed. The primary method of treatment is by intravenously injecting synthetic recombinant coagulation factors, and one may require regular replacement therapy: multiple infusions per week are needed to maintain healthy joints, which is a significant challenge in children. The most important and feared situation
is, however, the development of inhibitors in the receiver’s blood which neutralise the effect of the infusions.

Sometimes the person may require a blood transfusion which comes with risk factors and susceptibility to life-threatening infections.

According to a report in the Indian Journal of Medical Research, India harbours the second highest number of global patients with haemophilia A. According to their estimate, though only around 11586 haemophilia cases are registered, the undiagnosed numbers may well cross 50000.

Moreover, a low public health priority for rare genetic disorders that prevails makes India fall short on drug manufacturing companies to produce Anti-Haemophilic Factor Concentrate VIII or IX forcing it to be an import. These factors make replacement therapy an economically challenging option for many.

Managing Mantras
Preventive care goes a long way in managing this condition. Choosing safer physical activities and refraining from intense daily activities, seeking immediate medical help in case of an injury and learning a few basic first aid methods help to no small extent. Training the person or their caregivers in the RICE (Rest, Ice, Compression and Elevation) first aid technique can help as parallel approaches until medical assistance arrives.

Haemophiliacs should endeavour to keep themselves fit by choosing appropriate and safe methods of exercising under medical guidance. Being part of a support group is invaluable in getting required medical attention in case of accidents, the necessary psychological support, and staying up-to-date on the available facilities.

Promise of Gene Therapy
The hope to combat this life-threatening condition lies in gene therapy, which is an ongoing and active research area.

Australian researchers from the Royal Prince Alfred Hospital in Sydney spent 20 years working on clinical trials on a small group of participants suffering from Haemophilia B. In December 2017, their study produced successful results when all the patients showed a substantial increase in the levels of F-IX. Their study was published in The New England Journal of Medicine.

The single injection of gene therapy resulted in no bleeding episodes. In fact, 8 out of 10 people did not need clotting factor replacement therapy since then. The lead researcher Professor John Raski said: “Before the study started, all 10 participants had very low factor levels, below 2%. After treatment, their factor levels were sustained at a mean of approximately 30%. Only one participant needed to use factor replacement therapy for bleeds after treatment but used 91% less factor than before. There were no serious side effects.”

Raski opines that this small clinical trial opens avenues for research on a large scale. As a primary indication of ground-breaking success in haemophilia treatment involving experimental gene therapy, his team is now targeting Haemophilia A in 2018.

The Indian Journal of Haematology and Blood Transfusion in a recent publication reports that gene therapy research on haemophilia by premier medical research institutes like CMC Vellore, AIIMS New Delhi and NIIH Mumbai are promising. In fact, CMC Vellore has spearheaded an investigation by advancing the study of gene mutations in haemophilia and produced directionality to develop factor VIII concentrates with supernormal activity.

The ministry of AYUSH (Ayurveda, Yoga, Unani, Siddha and Homoeopathy) expresses that these alternate systems of medicine may hold potential in the treatment of Haemophilia. Presently they can provide care in pain management and other outcomes of haemophilia.

While it may take a little while for reliable results to emerge, we look forward in hope to a promising future for combating haemophilia.

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