# Rare Late Presentation of Severe Congenital Hemophilia A in a Ugandan Soldier - Case Report

Barnabas Atwiine[1] and Gladstone Airewele[2]

[1]Mbarara University of Science and Technology
[2]Texas Children's Cancer Center and Hematology Centers

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**Abstract**

Patients with severe hemophilia are usually diagnosed in infancy due to early onset of abnormal bleeding symptoms that characterize the disease. Affected individuals require coagulation factor routinely or prior to surgical procedures to prevent bleeding and are usually excluded from activities with a high risk of trauma. A 25-year old active-duty soldier was diagnosed with severe congenital hemophilia A after presenting with initial episode of prolonged bleeding. His case demonstrates a rare late presentation of a disease that typically presents in infancy and highlights the need for improving knowledge about bleeding disorders among health workers and the community.

## Introduction

Hemophilia A is an X-linked congenital deficiency of coagulation factor VIII and is characterized by spontaneous or prolonged bleeding after trauma. Individuals with the most severe form, hemophilia A, typically develop symptoms during infancy and get diagnosed by a demonstration of serum coagulation factor VIII levels that are <1% of the normal. These individuals require lifelong plasma-derived or recombinant coagulation factor concentrate routinely or prior to surgical procedures to prevent bleeding and are usually excluded from contact sports or other activities or professions with a high risk of trauma and resultant bleeding. It is very unusual for the severe form of hemophilia A to present in an adult, who reports no prior abnormal bleeding symptoms.

## Case

A 25-year-old soldier currently serving in the Uganda People's Defense Force (UPDF) was referred for consultation to the hematology clinic due to abnormal bleeding. One month earlier, he bled excessively after an elective circumcision uneventfully performed by freehand. Bleeding started 12 hours after surgery and lasted for two weeks. To manage the bleeding, he was admitted to hospital, his wound explored, and an incisional hematoma evacuated. During hospitalization, he received intravenous tranexamic acid and vitamin K, plus intravenous antibiotics. His vital signs remained normal throughout.

In the hematology clinic, the patient reported no history of painful joint swelling, abnormal bruising, or bleeding and he had completed rigorous military training without any problems. Additionally, none of his family members including his mother, seven full siblings with 4 brothers, several maternal cousins, and three maternal uncles had experienced abnormal bleeding, bruising, or joint deformity.

He was of normal stature, weighed 69.8kg; a height of 183.6 cm and a normal body mass index (BMI) of $20.7m^2$. He had no joint swellings, tenderness or deformity and no skin or mucous membrane bruising. His circumcision wound was dry and clean.

Laboratory evaluation included haemoglobin of 14.8 g/dL; platelet count 257,000/μL; activated partial thromboplastin time (aPTT) 58 seconds (reference range 27–43 seconds); prothrombin time (PT) 13.9 seconds (reference range 11.5–15.5 seconds); and INR 1.25. Given his elevated aPTT, a mixing study with normal plasma was done which demonstrated correction of aPTT into the normal range (30 seconds). Subsequent factor VIII activity assay was < 1% and factor IX assay 104%. Similar results were obtained on repeat testing after one week in another laboratory. He was enrolled in the hemophilia clinic, from where he will receive on-demand treatment with factor VIII if he bleeds. He is back in the military barracks and his superiors have been apprised of his diagnosis and its implications.

**Discussion**

Although hemophilia is thought to occur in about 1 in 3500–5000 male births without major geographic or ethnic differences,[1,2] the actual number of affected patients reported from low-income countries (LIC) is significantly lower than expected. For example, Uganda with a current population of 45 million and 1.7 million births yearly reported a total of only 221 individuals living with hemophilia in 2018.[3] This wide disparity between the expected number and the actual number of individuals living with haemophilia in Uganda is most likely due to a high number of undiagnosed patients combined with premature death due to bleeding. Data from the World Federation of Hemophilia (WFH) show a consistent relationship between the economic status of individual countries and the prevalence of hemophilia.[4] As a group, countries with a gross national product lower than $2000 report only about one third of the expected total number of individuals with hemophilia.[4]

While almost all patients with severe hemophilia (defined as <1 percent factor VIII or IX activity) in high-income countries (HIC), are diagnosed during the first few months of life,[5,6] diagnosis is often delayed in LIC due to a dearth of hematologists, basic knowledge about bleeding disorders, and hematology laboratory infrastructure. Our patient bled for two weeks after circumcision, was hospitalized to evacuate a hematoma, and was not diagnosed with hemophilia until he presented to the hematology clinic.

We diagnosed our patient with congenital severe hemophilia A with milder than expected clinical phenotype. Milder-than-expected severity of hemophilia as we found likely results from differences in the specific causal hemophilia mutation, as well as innate differences in the genetic factors that control each individual's anticoagulant and fibrinolytic systems.[7,8] Similar to our patient, Shapiro et al. diagnosed severe congenital hemophilia in a 33-year-old enlisted US Marine with 10 years of active service when he presented with bleeding after routine shoulder surgery.[9]

Though the absence of a family history of bleeding in our patient suggests sporadic haemophilia due to a spontaneous mutation, we were unable to perform genetic testing of the patient and his mother, or to obtain a reliable history of the patient's grandparents, plus their siblings and the descendants of those siblings. Considering these factors plus the possibility that familial severe hemophilia A may be similarly mild in our patient's asymptomatic brothers, we advised them to be screened with an aPTT test.

An alternative explanation for bleeding with isolated prolonged aPTT and low factor VIII activity such as acquired hemophilia A from the development of autoantibodies against endogenous factor VIII was considered. However, this was ruled out based on the patient's excellent general health, relatively young age, and full correction of his aPTT when mixed 1:1 with normal plasma.

This case highlights the need to improve general knowledge about bleeding disorders among health workers and the community, and upgrade the quality of hematology laboratory infrastructure in LIC. This patient bled for 2 weeks before he was diagnosed with severe hemophilia. One way to accomplish these objectives is by building collaborative relationships between medical organizations in LIC and their counterparts in HIC. As an example, the hematology clinic where this patient was diagnosed is the only one in Western Uganda – a region with a population of 10 million. It would not exist but for collaboration between Makerere University in Uganda and Baylor College of Medicine in Texas, United States to train haematologists in sub-Saharan Africa (SSA). This Global Hematology-Oncology Pediatric Excellence (Global HOPE) initiative from the Texas Children's Cancer and Hematology Centers, in partnership with Makerere University College

of Health Sciences, the affiliated Mulago National Referral Hospital, and Uganda Ministry of Health has graduated three sets of fellows from its 2-year training program and currently enrolls 10 trainees from five SSA countries.[10] More opportunities for training like this one will facilitate the comprehensive care of individuals with hemophilia and secondarily stimulate the growth of organizations that support individuals with hemophilia plus improve awareness in the general population of LIC.

**Declaration of Conflicting Interests**

The Authors Declare No Competing Interests

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