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SEVERE HAEMOPHILIA A: CASE REPORT

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ABSTRACT:
Background: Haemophilia A is the most common inherited coagulation disorder (~1 in 5,000 male births) caused by factor VIII (FVIII) deficiency. Severe disease (FVIII <1%) presents in infancy with spontaneous or trauma-related bleeding. While prophylactic FVIII therapy has improved outcomes in high-income countries, many patients in low- and middle-income settings receive only on-demand treatment.
Case summary: A male child presented at around one year of age with persistent bleeding after head trauma. Laboratory evaluation showed prolonged APTT, and a correction study confirmed FVIII deficiency. Factor assay demonstrated FVIII activity <1%, establishing severe Haemophilia A. Over the next eighteen years, recurrent bleeding episodes were managed exclusively with on-demand plasma transfusions without FVIII prophylaxis.
Outcome: The patient survived repeated bleeding episodes but probable cumulative joint damage remains a concern. No inhibitor screening was documented. Severe Haemophilia A may present without family history. On-demand plasma therapy does not prevent arthropathy, both prophylaxis and inhibitor surveillance are essential.

KEYWORDS: Haemophilia A; Factor VIII deficiency; on-demand therapy; prophylaxis gap; coagulation correction study; Inhibitor Surveillance.

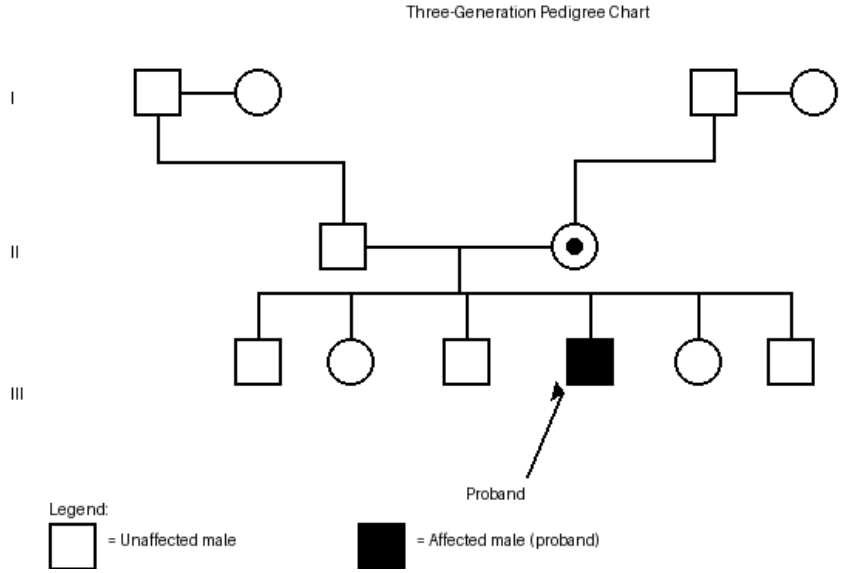
INTRODUCTION

Background: Haemophilia A is an X-linked recessive bleeding disorder caused by deficiency of coagulation factor VIII (FVIII) and occurs approximately 1 in 5,000 male births worldwide.[1] Disease severity is determined by residual FVIII activity: mild (>5–40%), moderate (1–5%), and severe (<1%). Severe haemophilia A, accounting for nearly half of cases, presents in infancy with spontaneous haemarthroses, muscle haematomas and occasionally life-threatening intracranial haemorrhage.[2] Current management in high-income countries is based on early prophylactic FVIII replacement therapy initiated before recurrent joint bleeding. Clinical trials have demonstrated that prophylaxis markedly reduces bleeding episodes and prevents haemophilic arthropathy compared with episodic treatment.[3] However, many low- and middle-income countries, including India, continue to face a substantial treatment gap due to limited availability and high cost of factor concentrates.[4] As a result, many patients receive only reactive, on-demand therapy during bleeding episodes. This case report describes the long-term clinical course of a patient with severe haemophilia A managed exclusively with on-demand therapy for nearly two decades in a resource-limited setting.
Case Presentation: A male child presented at approximately one year of age with persistent bleeding following minor head trauma sustained during play. The bleeding did not respond to local pressure and medical evaluation was sought. On examination the child was conscious and haemodynamically stable. Active bleeding from a scalp laceration and mild gum bleeding were noted. There was no pallor, jaundice, lymphadenopathy or organomegaly. Immunisation status was appropriate for age and there was no previous history of abnormal bleeding. Family history of bleeding disorders was absent.
Initial coagulation screening demonstrated markedly prolonged activated partial thromboplastin time (APTT) with normal prothrombin time and platelet count. A coagulation mixing study corrected the prolonged APTT when mixed with normal plasma but not when mixed with factor VIII-deficient plasma, indicating factor VIII deficiency consistent with haemophilia A.
During childhood and adolescence the patient experienced several episodes of bleeding including scalp haematomas, gum bleeding and joint swelling following minor trauma. Each episode was managed with transfusion of plasma components and supportive treatment. No prophylactic therapy was initiated during the available period of follow-up.

Family History and Pedigree

A three-generation pedigree chart prepared at GMAH (Figure 1) documents no affected males and no confirmed or suspected carrier females on either the maternal or paternal side. The patient therefore represents a sporadic case, consistent with the approximately 30% of Haemophilia A cases attributable to de novo FVIII gene mutations.7 The absence of any family history precluded antenatal diagnosis or cascade testing.

Figure 1. Three-generation pedigree chart



The chart demonstrates sporadic case of severe Haemophilia A with no family history on either side. Generation I: paternal grandparents (left pair) and maternal grandparents (right pair), all phenotypically unaffected. Generation II: father (unaffected male, □) and mother (obligate carrier female, ◉ — filled central dot). Generation III: proband (■, affected male, indicated by arrow) with unaffected male and female siblings. No prior family history of a bleeding disorder was identified on review of the three-generation pedigree. Pedigree symbols follow ACMG/NSGC 2008 standardised nomenclature.

Pedigree Symbol Legend
□ Unaffected male ■ Affected male (proband) ─ Mating pair
○ Unaffected female ◉ Obligate carrier female (dot denotes carrier status) ↗ Arrow = proband
Roman numerals I–III denote generations. Vertical lines denote biological offspring.

Investigations

Routine coagulation screening showed markedly prolonged APTT. A correction coagulation mixing study demonstrated normalisation with normal plasma, adsorbed plasma and Factor IX-deficient plasma, but persistent prolongation with FVIII-deficient plasma and aged serum, localising the defect to factor VIII. Correction with FIX-deficient plasma excluded haemophilia B.

Table 1. Coagulation Correction Study Results

Test	Result	Interpretation
APTT — Control	33 seconds	Normal reference
APTT — Patient	65 seconds ↑	Markedly prolonged
+ Normal plasma	33.5 sec	Corrected ✓
+ Adsorbed plasma	35.0 sec	Corrected ✓
+ Aged serum	55.0 sec	Not corrected ✗
+ FVIII-deficient plasma	62.0 sec	Not corrected ✗ — diagnostic
+ FIX-deficient plasma	34.5 sec	Corrected ✓ — FIX intact
Final Diagnosis		Factor VIII Deficiency — Haemophilia A

Quantitative FVIII assay was subsequently performed and the result confirmed FVIII level <1%, establishing severe Haemophilia A.

Differential Diagnosis

At presentation, a male infant with isolated prolonged APTT, normal prothrombin time and normal platelet count raised several differential diagnoses.

Haemophilia A was confirmed by the correction study. Haemophilia B was excluded by correction of APTT with F-IX-deficient plasma. Von Willebrand disease type 3 was considered but was less likely given the correction pattern and clinical context. Factor IX deficiency was also excluded based on the laboratory findings. Platelet function disorders, such as Glanzmann thrombasthenia and Bernard-Soulier syndrome, were unlikely because these conditions typically present with normal APTT and prolonged bleeding time.

Treatment

Blood and component transfusion: Each bleeding episode was treated with fresh frozen plasma (FFP) and occasionally packed red blood cells. No FVIII concentrate therapy was documented. As FFP contains only small amounts of FVIII (~1 IU/mL), haemostatic correction was limited compared with FVIII concentrates.[9]

Antifibrinolytic therapy: Tranexamic acid was used as adjunct treatment for mucosal bleeding.[2]

Analgesia: Paracetamol was prescribed for pain relief, while NSAIDs were appropriately avoided.

Outcome and Follow-up

At each documented discharge, the patient's condition was recorded as 'improved' with stabilisation of haemodynamic parameters. The pattern of recurrent admissions across approximately ten years — involving at minimum three documented inpatient episodes for scalp haematoma, gum bleeding, and head trauma — reflects the inherent inadequacy of on-demand-only management in severe Haemophilia A (Table 2).

Table 2. Summary of Documented Hospital Admissions

Period	Presenting Features	Management
Dec 2006	Head injury; gum bleed; fever; vomiting. First presentation.	Blood/component transfusion; Haemophilia A confirmed; discharged improved. No prophylaxis prescribed.
Jan–May 2007	Known Haemophilia A; scalp haematoma; gum bleed; HR 106/min, RR 26/min.	Component transfusion; liver and spleen soft; discharged improved. No prophylaxis.
Jun 2016	Head trauma; scalp haematoma with fluctuation; referred from Paediatric Surgery. HR 105/min, BP 90/60 mmHg.	Hb 10.5 g/dL; component transfusion; discharged improved.

No formal joint assessment was documented, but recurrent haemarthroses suggest possible arthropathy. No FVIII inhibitor testing (Bethesda assay) was recorded despite multiple transfusions. Ongoing engagement with a haemophilia support organisation offers an opportunity for structured care and monitoring.

DISCUSSION

This case provides longitudinal documentation of severe Haemophilia A managed exclusively with on-demand blood component therapy over nearly two decades—a pattern representative of the majority experience in resource-constrained settings globally.

Diagnostic considerations: Diagnosis was established only after traumatic presentation at approximately 1 year, as the absence of family history precluded neonatal screening. The correction study performed was appropriate for available infrastructure and accurately identified FVIII deficiency. This approach retains value in settings where specific factor assays are unavailable.(5)

The prophylaxis gap: Current guidelines recommend primary prophylaxis initiated before the second joint bleed or by age 3 years.(1) Randomised trials demonstrate prophylaxis reduces joint damage probability from 74% to 7% by age 6 years compared with on-demand treatment.(2)

The failure to initiate prophylaxis in this case reflects systemic barriers—including limited FVIII concentrate availability and out-of-pocket costs—rather than individual clinical decisions.

Treatment limitations: Fresh frozen plasma provides suboptimal and short-lived haemostatic correction. The volumes required to achieve therapeutic FVIII levels often exceed safe fluid administration limits in children.(6) Cryoprecipitate offers an intermediate option where concentrate is unavailable but was not documented in this case.

Inhibitor surveillance: Cumulative FVIII exposure creates meaningful inhibitor risk. The complete absence of documented inhibitor testing must be addressed urgently, as inhibitors render standard replacement ineffective and necessitate costly bypassing agents or immune tolerance induction.(7)

Future priorities: Recommended management includes enrolment at a recognised haemophilia treatment centre for secondary or tertiary prophylaxis initiation; urgent inhibitor titre measurement before any elective concentrate use; comprehensive musculoskeletal assessment; structured physiotherapy; genetic counselling for female relatives; and psychosocial support addressing educational and occupational consequences of chronic undertreated disease.

Learning Points

1. Severe haemophilia A may present in infancy with traumatic bleeding even without family history; ~30% arise from de novo mutations.
2. Mixing (correction) studies are useful low-resource tests to identify coagulation factor deficiencies when specific assays are unavailable.

3. On-demand FFP therapy provides limited haemostatic correction and does not prevent haemarthrosis or arthropathy.
4. FVIII prophylaxis, even when started late, reduces bleeding and joint damage.
5. Regular FVIII inhibitor screening is essential; absence of testing represents a significant care gap.

Patient's/Guardian's Perspective

The family maintained medical documents spanning approximately eighteen years — receipts, discharge , coagulation reports, and society membership records — demonstrating a sustained commitment to accessing and preserving health information in the face of significant systemic barriers. The family sought specialist consultations, enrolled the patient with the Haemophilia Society at the time of diagnosis, and re-engaged with organised haemophilia support into adulthood. The socioeconomic burden of repeated hospitalisation, travel costs from a rural district , blood bank fees, and the patient's interrupted schooling represents a profound and undocumented dimension of this case that aggregate clinical outcomes data do not capture.

Declarations

Patient consent: Written informed consent was obtained from the patient's guardian for publication of this anonymised case report.

Competing interests: None declared.
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