Acute compartment syndrome: A rare first manifestation of severe haemophilia A in neonate

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SUMMARY

Congenital haemophilia A, though often associated with iatrogenic bleeding, rarely presents with acute compartment syndrome. In a resource-limited rural facility, such a case poses a significant challenge to the managing team in terms of both diagnosis and treatment. This case report describes a term male infant of aboriginal ethnicity, born in a rural district hospital, who developed acute compartment syndrome in the left hand following a venepuncture. Emergency fasciotomy was performed on the dorsum of the left hand, which led to profuse bleeding. A packing and compression bandage was applied to control the bleeding, accompanied by multiple blood product transfusions. Family history revealed that the infant's maternal uncle had suffered from a bleeding disorder and succumbed to complications of the illness in his 30s, raising suspicion of congenital haemophilia. Later, factor VIII assay confirmed a 0% level, and factor VIII replacement therapy was promptly initiated. Homeostasis was achieved following factor replacement, and the fasciotomy wound healed well after three weeks. This case highlights the importance of early recognition and multidisciplinary management in resource-limited settings, as well as the need for timely factor replacement therapy to prevent life-threatening complications in neonates with undiagnosed congenital haemophilia A.

INTRODUCTION

Congenital haemophilia A is an X-linked recessive bleeding disorder caused by a deficiency of clotting factor VIII (FVIII), resulting from mutations in the F8 gene located on the long arm of the X chromosome (Xq28).[1] It typically presents in early childhood with spontaneous bleeding into joints and soft tissues but may also manifest during the neonatal period, particularly following traumatic delivery or iatrogenic interventions.[2] One of the rare but serious complications of haemophilia A is acute compartment syndrome (ACS), a surgical emergency caused by increased pressure within a closed muscle compartment, leading to compromised circulation and tissue viability. In neonates, ACS is extremely uncommon and often unanticipated in the absence of a known bleeding disorder.

This case report describes a neonate with previously undiagnosed severe haemophilia A who presented with life-threatening ACS in the postnatal period. It highlights the challenges of early recognition and the need for timely, multidisciplinary management of this rare complication, particularly in a resource-limited rural healthcare setting.

CASE PRESENTATION

A term male neonate, born via spontaneous vertex delivery to a nonconsanguineous couple, was admitted to the Neonatal Intensive Care Unit (NICU) at 24 hours of life for a massive haematoma involving the left hand. He was the sixth child of a 36-year-old mother of aboriginal ethnicity with an uneventful antenatal course and no significant medical history. The infant had a birth weight of 3.3 kg and cried spontaneously at birth. The immediate postnatal period was unremarkable. He received intramuscular vitamin K and the first dose of hepatitis B vaccine prior to transfer to the postnatal ward. At 13 hours of life, he developed jaundice and was diagnosed with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency. A serum bilirubin sample was obtained via needle puncture from the dorsum of the left hand. Subsequently, the infant was nursed under phototherapy with his hands covered by mittens. The progressive swelling and discolouration of the left hand remained unnoticed until 10 hours later, when it was discovered during routine care, prompting an urgent referral to the NICU for further assessment and management.

Upon admission to the NICU, the infant's left hand was noted to be grossly swollen, bluish, and tense, with delayed capillary refill time and weak radial pulse volume – findings consistent with acute compartment syndrome (Figure 1). There was no evidence of bleeding or swelling at the site of the earlier intramuscular injection. The infant remained haemodynamically stable, and systemic examination was otherwise unremarkable. An emergency bedside fasciotomy was performed immediately as a limb-saving measure, even before blood parameter results were available. Unfortunately, the procedure was complicated by profuse bleeding from the incision site, necessitating two transfusions of fresh frozen plasma (FFP) and packed red blood cells, along with wound packing and compression. Empirical broad-spectrum antibiotic therapy was initiated, and intravenous tranexamic acid was administered in view of a presumptive diagnosis of haemophilia.

Subsequent investigations revealed a deranged coagulation profile (prothrombin time 15.8 seconds, INR 1.44, activated partial thromboplastin time >120 seconds) while haematological indices were within normal limits (total

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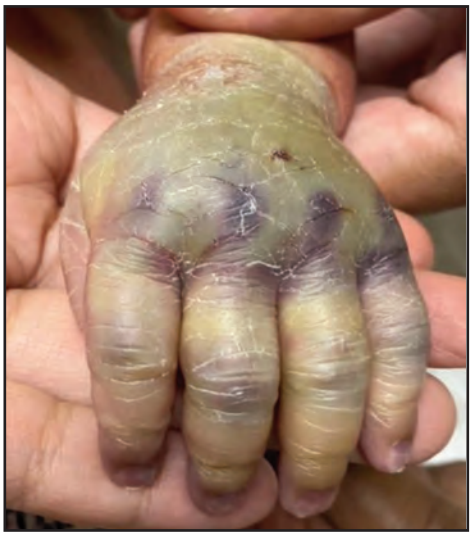

Fig. 1: Haematoma formed at the previous venepuncture site, resulting in compartment syndrome of the left hand

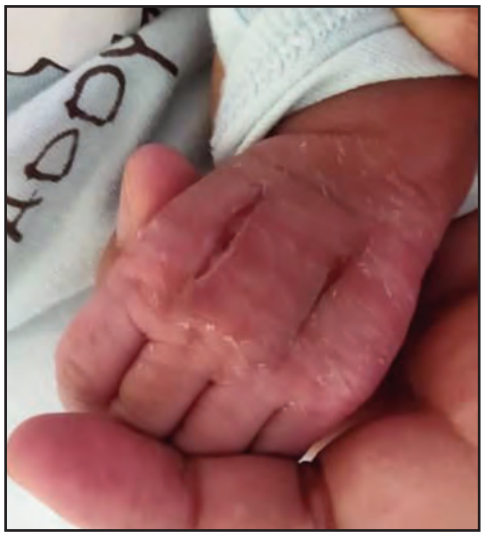

Fig. 2: Condition of left hand prior to discharge

white cell count 19.36 x 10^9/L, haemoglobin 20.3 g/dL and platelet count 202 x 10^9/L). A more detailed family history revealed that a maternal uncle had experienced frequent hospital visits for unexplained bruising and died in his 30s due to complications of the disease, raising suspicion of congenital haemophilia. An urgent coagulation factor assay subsequently confirmed the diagnosis of severe haemophilia A, with a factor VIII (FVIII) activity level of 0% and a factor IX (FIX) activity level of 49.6%.

High-dose intravenous FVIII replacement therapy (ALPHANATE®) was initiated. Despite a four-hour delay in starting treatment due to logistical delays in obtaining the factor concentrate (sourced from a tertiary facility located four hours away), the infant's haemostatic status improved significantly (prothrombin time 14.5 seconds, INR 1.32, activated partial thromboplastin time 62 seconds). FVIII activity increased to 22%, allowing gradual dose tapering guided by serial assays. The fasciotomy wound healed completely, with minimal scarring (Figure 2). The range of movement of the fingers and wrist joint were full, with immediate capillary refill time.

The infant was discharged on day 28 of life with a plan for weekly prophylactic intravenous ALPHANATE® therapy. Unfortunately, he developed a high-titre FVIII inhibitor after one month of therapy (FVIII inhibitor level 27.6 BU/mL), leading to discontinuation of FVIII replacement and a heightened risk of severe or life-threatening bleeding. As the infant resides approximately one hour from the nearest healthcare facility, a comprehensive multidisciplinary care plan was established. This included family and primary healthcare education, prepositioning of bypassing agent (recombinant factor VII) in the local pharmacy, and coordinated care planning involving emergency, medical, surgical, and dental teams in anticipation of potential catastrophic bleeding events.

DISCUSSION

Haemophilia A is an X-linked recessive disorder caused by a deficiency of factor VIII (FVIII), leading to impaired haemostasis.[1] While it most often presents between one and two years of age with joint bleeds, neonatal presentations such as intracranial haemorrhage after birth or iatrogenic bleeding are well described.[2] In rare instances, extensive intramuscular bleeding may precipitate ACS.[3]

ACS is defined as a critical elevation of interstitial pressure that leads to compromised microvascular blood flow and reduced tissue perfusion within a confined anatomical compartment.[3] It is recognised as a surgical emergency, as delayed diagnosis and intervention may result in irreversible tissue ischaemia and severe complications such as muscle necrosis, rhabdomyolysis, infection, limb amputation, or even death. The exact incidence is unknown; however, it is estimated to be approximately 3.1 per 100,000 adults. In the neonatal population, the incidence is not well established, with only a few cases reported. The most common causes include intrauterine compression, oligohydramnios, malpresentation at birth, birth trauma, arterial thrombosis and other perinatal factors such as sepsis and acquired coagulopathy.[4] Although rare, haemophilia has also been documented as an underlying cause in neonates.[5] Given this context, it is important to consider bleeding diatheses - most notably haemophilia A.

ACS is a clinical diagnosis. It warrants a prompt diagnosis as patient outcomes are dependent on immediate recognition and decompression. In situations where signs are equivocal, Doppler ultrasound or direct intracompartmental pressure measurements may be employed to confirm the diagnosis.[3] In our patient, the diagnosis of ACS was established on the basis of classical skin changes. With no immediate family history of bleeding disorders, no clinical evidence of active haemorrhage, and a progression of swelling over the preceding ten hours, an urgent fasciotomy was performed prior to confirmation of an underlying bleeding disorder.

Prompt decompression is critical in restoring function and preventing muscle necrosis, contractures, and long-term sequelae.

The role of fasciotomy in the management of ACS in patients with haemophilia remains a subject of debate, as the primary treatment focus is on achieving haemostasis. Current recommendations suggest that the initial step in suspected ACS among haemophilia patients is the prompt replacement of the deficient clotting factor, which may help alleviate rising compartment pressure.[3] However, the risk of irreversible tissue ischaemia remains high due to the narrow therapeutic window between symptom onset and permanent damage. Therefore, clinicians must carefully balance the risk of bleeding complications against the potential limb morbidity.

Blood product transfusion, particularly fresh frozen plasma or cryoprecipitate, and early administration of clotting factor replacement prior to fasciotomy may reduce the risk of significant intraoperative bleeding. However, in settings where clotting factor concentrates or blood products are unavailable, timely surgical intervention should not be delayed, as the risk of irreversible tissue ischaemia outweighs the risk of haemorrhage. The use of antifibrinolytics agents such as tranexamic acid may be considered as adjunct therapy. Antibiotic prophylaxis is also recommended, as persistent bleeding and open wounds pose a substantial risk of infection.[6] In this case, both tranexamic acid and prophylactic antibiotics were administered.

While fasciotomy can result in good functional recovery, the presence of an open wound necessitates high-dose and prolonged factor replacement therapy. Guidelines recommend maintaining the FVIII levels between 80-100% during the first 48 hours, and 30-60% between days 3 and 5 postoperatively.[6] These target levels were not achieved in our patient, with serial FVIII assays ranging between 2% and 22% despite high-dose therapy. Nevertheless, factor replacement was gradually titrated as haemostasis improved. With intensive and prolonged replacement therapy, the risk of inhibitor development is a major concern, as observed in this case. Inhibitors are reported to occur in approximately 30-35% of previously untreated children with severe haemophilia A, and are associated with increased morbidity, including joint deformities, life-threatening bleeds, and impaired quality of life for both patients and caregivers.[7] In the presence of FVIII inhibitor, the FVIII replacement therapy has to be discontinued to prevent further development of inhibitor. As the patient is still non-ambulating, the risk of active bleeding is still low, and no replacement therapy is mandated. However, in the case of future active bleeding, the usage of a bypass agent such as recombinant factor VII (rFVII) is recommended to bypass the common coagulation pathway that utilises factor VIII.[6] rFVII needs to be readily available in the nearby health facility to facilitate prompt treatment and eventually prevent catastrophic bleeds and further complications.

Optimal management of children with severe haemophilia with inhibitors requires a multidisciplinary approach, aiming to minimise bleeding complications and support long-term health and function.[8] Although this case was managed in a rural healthcare setting with limited resources, the multidisciplinary coordination between the surgeon, haematologist, emergency physician, pharmacist, public health team, and rehabilitation services ensured the patient received timely and appropriate care. Caregiver education is equally important to ensure adherence to therapy and long-term monitoring.

CONCLUSION

Severe congenital haemophilia A can present with life-threatening complications during the neonatal period, including the rare occurrence of ACS. In the case of unexplained ACS in neonate, haemophilia should be strongly suspected. Early recognition of ACS is critical, as delayed diagnosis may result in irreversible tissue damage and the need for surgical intervention. Prompt administration of clotting factor replacement remains the cornerstone of ACS management, with fasciotomy required in cases where haemostasis is not rapidly achieved. This case underscores the importance of high clinical suspicion, timely multidisciplinary intervention, and caregiver education, particularly in resource-limited settings. Specialised medications like the clotting factors also should be made more accessible especially to rural healthcare facilities.

REFERENCES

1. Tantawy AAG. Molecular genetics of hemophilia A: clinical perspectives. Egypt J Med Hum Genet 2010; 11(2): 105-14.
2. Dyson H. Neonatal haemophilia – a guide to recognition and management. Infant 2006; 2(4): 156-9.
3. Donaldson J, Goddard N. Compartment syndrome in patients with haemophilia. J Orthop 2015; 12(4): 237-41.
4. Shen AH, Tevlin R, Kwan MD, Ho OH, Fox PM. Neonatal compartment syndrome and compound presentation at birth. J Hand Surg Glob Online 2020; 2(3): 166-70.
5. Lassandro G, Amoruso A, Palladino V, Palmieri VV, Giordano P. The risk of venipuncture in newborn with severe hemophilia: Case report of a large elbow hemorrhage and literature review of compartment syndrome. Hematol Rep 2021; 13(2): 8967.
6. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia 2020; 26 Suppl 6: 1-158.
7. Wight J, Paisley S. The epidemiology of inhibitors in haemophilia A: a systematic review. Haemophilia 2003; 9(4): 418-35.
8. Bertamino M, Riccardi F, Banov L, Svahn J, Molinari AC. Hemophilia care in the pediatric age. J Clin Med 2017; 6(5): 54.