CASE REPORT

Atypical presentation of Haemophilia A. A case report of a 12-year old boy in Abeokuta, Nigeria

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Abstract
Haemophilia A typically manifests with soft tissue or joint bleeds. Rarely, bleeds may occur at intracranial, iliopsoas, oropharyngeal or penoscrotal sites. These uncommon bleeding sites necessitate a high index of suspicion for prompt diagnosis, to prevent potential life-threatening outcomes. We report a 12-year-old known patient with severe haemophilia A who at different times, had spontaneous jaw bleeding extending to the anterior neck and spontaneous penile shaft haematoma. Bleeding resolved following administration of factor VIII concentrates and anti-fibrinolytic agents. He was subsequently discharged to our clinic for follow-up and has been symptom-free.

Keywords: Atypical bleeds, Haemophilia, Penile haematoma, case report

Introduction:

Haemophilia is a rare genetic bleeding disorder characterized by the deficiency of any of coagulation factors VIII (FVIII), IX (FIX), and XI (FXI), known as Haemophilia A, B and C respectively.[1] It is inherited as an X-linked recessive disorder and almost exclusively a disease of males; nearly one-third of cases may however arise from spontaneous mutation.[1,2] Manifestation of the disorder in females is rare. In such cases, both X chromosomes are either affected, or the individual possesses only one X chromosome as seen in Turner syndrome. In addition, females with skewed lyonization may be symptomatic for the disease. Skewed lyonization is a situation in which a significant number of normal X chromosomes are converted into bar body, making more numbers of abnormal X chromosomes carrying the disease active.[1] The main pathophysiologic mechanism of the disease is reduced, or lack of synthesis of coagulation factors, which if not managed appropriately may lead to mortality or life-long disabilities.[1-3]

Eighty-five per cent of the 1.125 million global estimated patients with haemophilia are deficient in FVIII while 10-15% are deficient in FIX.[2] There is no racial predilection as the disease occurs in all ethnic groups.[1,2] More than two-thirds of patients with haemophilia, as estimated by the World Federation of Haemophilia (WFH) are undiagnosed and untreated, with the majority of these undiagnosed patients hailing from low-income countries.[2] Despite its enormous morbidity, the disease receives negligible attention from health workers and policy makers in these countries. The poor attention could have resulted from competing priorities from infectious diseases such as malaria, tuberculosis, and respiratory tract infections among others.[2,4] In addition, inadequate healthcare infrastructure and non-availability of factor concentrates are among the challenges limiting the care of patients with haemophilia in resource-poor countries.[4] A major solution to these challenges is the creation of an active organization by patients living with haemophilia, which performs advocacy and also establishes internal and external

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collaborations with stakeholders to foster optimal care in this population.[4]

The severity of haemophilia is classified based on patients' baseline clotting factor levels into severe (<1% of normal), moderate (1-5% of normal) and mild (>5% to < 40% of normal).[1] The severity of clotting factor deficiency correlates well with the severity of bleeding in patients. Nearly 418,000 (43%) of those with the disorder have the severe form.[1,2]

Bleeding is the main characteristic feature of haemophilia and can occur at various sites of the body.[1,4] Bleeding sites in turn vary with the age and activity of the child.[1] The possible indicators of a congenital bleeding disorder from the neonatal period through the first two years of life include cephalhaematoma, subgaleal haemorrhage, prolonged post-circumcision bleeding, soft tissue/intramuscular haematoma, oral/nasal bleeding and joint haemorrhage.[5,6]

The clinical presentation and/or complications of the disease depend on the sites and extent of the bleeding. These bleeding sites are generally classified into three categories:

(a) Life-threatening bleeding sites such as intracranial haemorrhage, airway haemorrhage leading to obstruction, and gastrointestinal haemorrhages; iliopsoas haemorrhage.

(b) Common sites: spontaneous bleed into other muscles, and joints (haemarthrosis) when crawling, walking, climbing, or falling.

(c) Other sites: include haematuria, scrotum or penile shaft.[5,6]

Atypical clinical presentations and clinical features have been reported by some authors[8-10] in paediatric populations. Although rare, oropharyngeal and penile bleeding are documented complications in patients with haemophilia.[10] Oropharyngeal bleeds typically arise following an acute neck injury induced either by trauma, or dental or oral surgical procedures.

Spontaneous haemorrhages at these sites, as they occurred in the index patient, are extremely rare, and require that clinicians have a high index of suspicion, especially in patients with an established history of bleeding disorder, to prevent untoward complications.

Case presentation:

AO. is a 12-year-old known haemophilia A patient who presented to the Children Emergency Room on account of progressive jaw and neck swelling, drooling of saliva and difficulty opening the mouth of about 12 hours duration. There was no preceding history of trauma, dental procedure, fever, cough or sore throat. Physical examination revealed a firm, non-tender swelling in the mandibular area extending to the cricoid cartilage area inferiorly **(Figure 1).** Oral examination revealed no evidence of bleeding from the gums and oral mucosa; other systemic examination findings were essentially normal. A diagnosis of submental and submandibular haematoma in a known haemophilia A patient was made.

He had presented five months earlier following a progressive painless non-traumatic bleeding into the penile shaft (penile haematoma). The penile shaft was ecchymotic and oedematous; there was no associated scrotal oedema (Figure 2). He had complete resolution of symptoms within two weeks of recombinant factor VIII concentrate.

His first contact with our facility was however during the neonatal period (20th day of life) when he was referred from a primary health care (PHC) facility on account of severe anaemia following prolonged bleeding post-circumcision. There was also examination evidence of a previous cephalhaematoma. Results of laboratory investigations showed deficient factor VIII (<1% of normal value) and prolonged PTTK. Other laboratory test results were unremarkable.

He is the second child in a monogamous family setting with no history suggestive of bleeding disorder from the maternal pedigree. He has received clotting factor concentrates (CFCs) on different occasions at our facility for recurrent bleeding episodes. These included gum bleeds, subdural haematoma following a fall during infancy and haemarthrosis involving the ankle, knee, and elbow joints.

Management and Outcome:

At index presentation, available FVIII concentrates were immediately administered intravenously along with tranexamic acid following which he was promptly referred to the National Haemophilia Foundation Centre on account of worsening of his symptoms and the attendant risk of respiratory compromise. He received further doses of recombinant FVIII concentrates and tranexamic acid at the haemophilia centre. The jaw swelling subsequently regressed over 72 hours and he was discharged to our facility

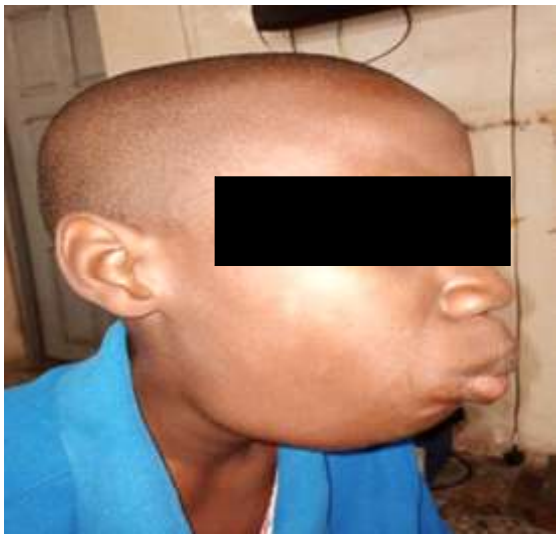

Figure 1: Submandibular and submental haematoma

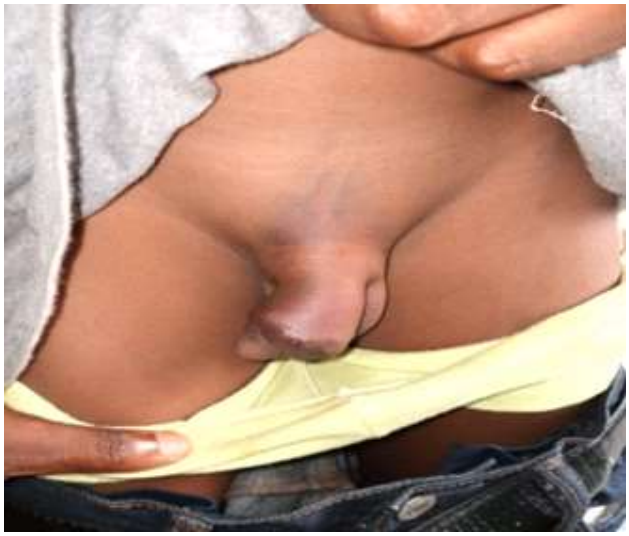

Figure 2: Penile shaft hematoma

for follow-up care. He is still on regular follow-up at our paediatric haematology clinic and has been event-free in the six months preceding this report. The administration of prophylactic FVIII concentrates has however remained erratic due to financial constraints.

Discussion:

Reported cases of unusual presentation in the literature especially after the advent of CFCs are few. Aliyu *et al*[7] reported a case of axillary haematoma in a 7-month-old infant. Other reported uncommon presentations include neck and cranial haematoma,[8] superficial fibromatosis in an adolescent following a sprained ankle[9] and spontaneous penoscrotal haematoma.[10]

Spontaneous oropharyngeal bleeding is a rare but documented complication in patients with haemophilia. Bleeding at this site may arise following an acute neck injury induced by trauma, dental or oral surgical procedures.[11] Spontaneous haemorrhages have also been reported and may occur with or without prodromal symptoms. Yamamoto *et al*[12] reported an acute upper airway obstruction in a 16-year-old patient with haemophilia following spontaneous retropharyngeal haemorrhage, despite being on routine factor VIII replacement therapy. The submental and the submandibular bleeds in the index child were also spontaneous, although he had not been regular CFCs due to financial constraints. Also, there was a disruption in the supply of the concentrates occasioned by the COVID-19 pandemic in the year (2020).

The rapidity of progression of the submandibular swelling in the highlighted case despite the administration of recombinant factor VIII may be connected to the fibrinolytic activity of saliva which has been noted with oral bleeding. Such bleeds, therefore, require adjunct therapy with antifibrinolytic agents such as tranexamic acid, which was also administered to the patient before referral.

Oropharyngeal bleeds in haemophilia patients are potentially life-threatening and require prompt diagnosis and interventions. Inappropriately treated oral bleeding can lead to excessive blood loss and symptomatic anaemia on one hand, while extension of the bleeds into the surrounding structures may result in pharyngeal, facial, or dissecting neck haematomas which could compromise breathing, and ultimately lead to death. Penile or penoscrotal haematomas have also been reported following trauma or surgical procedures such as circumcision or repair of an inguinoscrotal hernia in a known patient with haemophilia A.[13] Spontaneous penile haemorrhage as reported by Siddiqui and Tomar,[10] and which occurred in our patient, is however extremely rare.

This report also highlights the inadequate supply of CFCs, as well as other blood products (such as Fresh frozen plasma and cryoprecipitate), in resource-poor countries like ours. This was evident in this present case, who had to be referred to the closest Haemophilia Centre, which was located over a hundred kilometres from our facility for further treatment despite the risk of further bleeding.

Conclusion:

Oral or neck bleeds in haemophilia patients are categorized as life-threatening bleeding episodes and require prompt CFC replacement therapy and other adjunctive treatments as required. Hence, prompt recognition and institution of management are crucial as delay or inadequate treatment could lead to complete upper airway obstruction and possible fatality. Inadequate access to CFCs, selective blood products and supportive care, especially in patients with life-threatening conditions in most health facilities, still constitutes a huge challenge in their management in resource-poor countries.

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CONTRIBUTION DETAILS

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