TMSJ
TURKISH MEDICAL STUDENT JOURNAL

Turk Med Stud J 2023;10(1):23-5
DOI: 10.4274/tmsj.galenos.2023.2022-9-3

CASE REPORT

SWOLLEN LIMBS AND DELAYED ECCHYMOSIS: UNEXPECTED ENCOUNTER WITH ACQUIRED HEMOPHILIA A

Muhammad Ihsan Bin Mohd Tusirin, Johan Abdul Kahar

University Putra Malaysia School of Medicine, Department of Orthopedics and Traumatology, Selangor, MALAYSIA

ABSTRACT

Acquired hemophilia A is a rare disorder and may be first encountered anywhere from the primary care setting, emergency departments, and like in this case report, orthopedic clinics. This case report is about an elderly patient with comorbidities not usually associated with acquired hemophilia A, initially presented with left wrist swelling following a bee sting, which later turned into ecchymosis. The later presentation of ecchymosis prompted the clinician to investigate the coagulation profile, which led to a referral to the hematology team for further workup, and the subsequent diagnosis of acquired hemophilia A. Considering the high mortality rate of AHA, high index of suspicion, early management, and prompt referral to a hematology team are very important.

Keywords: Autoimmunity, ecchymosis, hemophilia A

INTRODUCTION

Acquired hemophilia A (AHA) is a rare disorder with an annual incidence of 1.48 cases per 1 million healthy individuals per year in the United Kingdom (UK) (1). The usual initial presentation of patients diagnosed with AHA is bleeding events, which may be spontaneous, or associated with trauma, surgery, and the peripartum period (2). Skin, deep muscle, and mucosal tissues are common sites of bleeding (2). Given the rarity of the disease and its unfamiliarity among clinicians, diagnosis is challenging and often delayed (2). While AHA is rare, patients presented with swollen limbs are common with vast differentials. This is a case report of an elderly patient diagnosed with AHA who initially presented with vague swelling of limbs with delayed ecchymosis.

CASE REPORT

A 64-year-old male patient with a history of diabetes mellitus, hypertension, and dyslipidemia initially presented to the clinic with complaints of left forearm swelling associated with intermittent neuropathic pain from elbow toward the hand following a bee sting one week ago. Initial examinations of the left upper limbs revealed a firm, erythematous, and warm diffuse swelling over the wrist extending to distal forearm. It was associated with numbness over the ulnar aspect of the left hand and forearm. He was initially treated for forearm cellulitis and completed a course of antibiotics. Following the treatment, the swelling reduced, but the numbness persisted although it was intermittent and had less frequency. The patient underwent electromyography, which revealed normal results.

At the patient's follow-up visit, the ulnar nerve neuropathy symptoms were found to be resolved. Although patient's ulnar nerve neuropathy symptoms were resolved, he had vague discomfort over his left leg and both of his forearms. There were multiple ecchymoses of varying ages and sizes seen in the bilateral upper limb and left thigh (Figure 1). Diffuse swelling over the anterior aspect of the left leg was also present. The patient denied any prior trauma. Blood investigations revealed an isolated prolonged activated partial prothrombin time (APTT) of 85.2 seconds (normal range 32.4-42 seconds). Ultrasound of the left leg revealed no focal lesion or collection. He was referred to the hematology team to investigate further the cause of

Address for Correspondence: Muhammad Ihsan Bin Mohd Tusirin, University Putra Malaysia School of Medicine, Department of Orthopedics and Traumatology, Selangor, MALAYSIA
e-mail: ihsantusirin@gmail.com
ORCID iDs of the authors: MIBMT: 0000-0002-9870-4836; JAK: 0000-0002-8579-6946.
Received: 27.10.2022 Accepted: 17.02.2023

Cite this article as: Bin Mohd Tusirin MI, Kahar JA. Swollen limbs and delayed ecchymosis: unexpected encounter with acquired hemophilia A. Turk Med Stud J 2023;10(1):23-5.

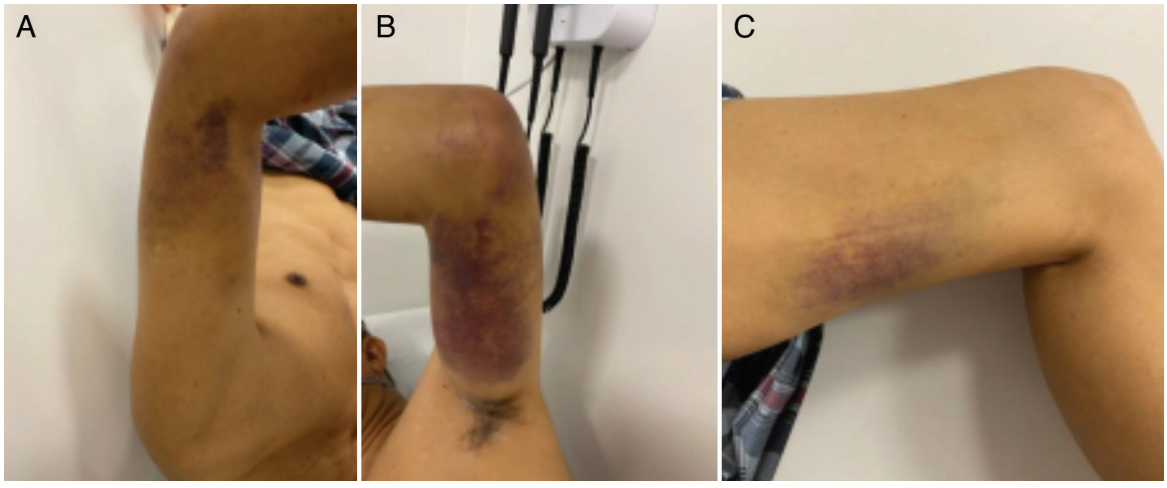

Figure 1: Multiple ecchymoses during first follow-up visit noted at the lateral and medial aspect of left arm, and medial aspect of left thigh.

isolated prolonged APTT and was investigated as an outpatient.

One month later, he presented to the emergency department with a complaint of worsening left forearm swelling and pain. Symptoms were associated with extensive ecchymosis over the left upper limb, which was extending from forearm to mid-arm. The patient denied any trauma. He still had vague discomfort over his left leg. Examination of his left upper limb showed diffuse swelling of left upper limb from forearm distally to mid-arm proximally, which was firm, and tender upon deep palpation, limiting his elbow range of motion. Extensive ecchymosis over the medial aspect of the forearm to the mid-arm was also present. Neurovascularity of the left upper limb was intact. There was also ecchymosis over his left thigh, which did not worsen since previous visit. He was admitted to the ward for observation of the swelling. Ultrasound of the left forearm revealed an intramuscular hypoechoic lesion that was likely an intramuscular hematoma. Blood investigations revealed persistent isolated prolonged APTT, non-correctable mixing study, low factor VIII of 1.3% (normal range 50-150%) with the presence of factor VIII inhibitor at 18.4 Bethesda unit. The hematology team reviewed him in the ward and diagnosed him with AHA with bleeding tendency. Initial treatment started by the hematology team included intravenous vitamin K and tranexamic acid, transfusion of fresh frozen plasma, cryoprecipitate, prothrombin complex concentrate, oral prednisolone, and cyclophosphamide. He was then transferred to a hematological center for further treatment and workup for the diagnosis of AHA.

DISCUSSION

Initial presentation of a swollen limb with a precipitating factor such as an insect sting, as seen in this report, usually does not require the clinician to investigate any hematological disorder. The extensive bruising that the patient later developed was the eliciting factor behind the clinician's investigation of the coagulation profile, which lead to a referral to the hematology team for further workup, and, subsequently, the diagnosis of AHA. The exact period that the patient developed the disease is not known.

Acquired hemophilia A is a rare disorder with an incidence of 1.48 cases in 1 million healthy individuals per year in the United Kingdom (1). According to a UK study, 63% of the cases are elderly with ages between 65 to 80 years old (1). 43% to 63% of the patients who do not have underlying diseases are at risk of getting AHA (1, 2). In terms of gender, there is a higher incidence in females compared to males, with incidence rates of 57% and 42%, respectively; although in older age groups, incidence of AHA is higher in males (1, 2). In the female age group between 20-40 years old, most cases of AHA are pregnancy related (1-3). Development of AHA can be linked to multiple factors such as malignancies, autoimmune diseases, pregnancy, infections, and drugs (1-3). However, more than half of the time AHA is idiopathic (1-3).

The exact pathophysiology of AHA remains unclear (4). However, it is known to be associated with the production of antibodies that affect the function of factor VIII in the coagulation cascades due to immune system dysfunction and the inhibition of thrombin generation and fibrin clot formation because of factor VIII deficiency (3, 4). These deficiencies will lead to the presentation of bleeding events in patients with AHA (3, 4). In AHA, the autoantibodies involved are mostly in the immunoglobulin G1 and immunoglobulin G4 classes. These antibodies will bind to factor VIII epitopes and affect the binding of factor VIII to von Willebrand factor, the formation of intrinsic rename complexes, and the interaction of factor VIII with phospholipids (3, 4).

Diagnosis of AHA is precipitated by bleeding events most of the time (89%) with most common being spontaneous bleeding (77.4%), while others are associated with trauma, surgery, and the peripartum period (2). With regards to sites of bleeding, common sites include skin, deep muscle, and mucosal bleeding, with incidence rates of 53.2%, 50.2%, and 31.6%, respectively

(2). Other sites of bleeding include hemarthrosis and intracranial bleeding, which are rare (4.9% and 1.1%) (2). The mortality rate is considerably high, which is up to 27.9% (2). In this case report, the patient developed a bleeding tendency following a bee sting, which may be considered a minor trauma precipitating the bleeding tendency. There are, however, some case reports with regards to insect sting or bites that lead to the diagnosis of AHA (5, 6).

A local case series of AHA summarizes that the disease has a different initial presentation. Two out of the 5 cases reported have initial presentations of spontaneous extensive skin bruising, while other cases have presented with prolonged bleeding after a dental procedure, post-natal vaginal bleeding, and bilateral lower limb weakness (7).

Treatment of AHA includes control of bleeding, inhibitor eradication, treating the underlying disorders, and prevention of trauma. Hemostatic management includes bypassing agents and strategies to increase the level of circulating factor VIII. Bypassing agents are commonly used as first-line treatment and it includes prothrombin complex concentrate. Inhibitor eradication with immunosuppressive therapy should be undertaken as soon as the diagnosis has been made. The options for immunosuppressive therapy include steroids, cytotoxics (cyclophosphamide, azathioprine, or combination therapy), rituximab, cyclosporin A, plasmapheresis, and FVIII immune tolerance (3).

Acquired hemophilia A is rare and it has a high mortality rate. This case report focuses on the importance of clinical suspicion, early management, and prompt referral to the hematology team.

Ethics Committee Approval: N/A

Informed Consent: An informed verbal consent was obtained from the patient.

Conflict of Interest: The authors declared no conflict of interest.

Author Contributions: Concept: M.I.B.M.T., J.A.K., Design: M.I.B.M.T., J.A.K., Literature Search: M.I.B.M.T., J.A.K., Writing: M.I.B.M.T., J.A.K.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Collins PW, Hirsch S, Baglin TP et al. Acquired hemophilia A in the United Kingdom: a 2-year national surveillance study by the United Kingdom Haemophilia Centre Doctors' Organisation. Blood 2007;109(5):1870-7. [Crossref]
2. Knoebl P, Marco P, Baudo F et al. Demographic and clinical data in acquired hemophilia A: results from the European Acquired Haemophilia Registry (EACH2). J Thromb Haemost 2012;10(4):622-31. [Crossref]
3. Collins PW, Percy CL. Advances in the understanding of acquired haemophilia A: implications for clinical practice. Br J Haematol 2010;148(2):183-94. [Crossref]
4. Windyga J, Baran B, Odnoczko E et al. Treatment guidelines for acquired hemophilia A. Ginekol Pol 2019;90(6):353-64. [Crossref]
5. Vinayek N, Kloecker GH, Riley BC. Acquired hemophilia after a spider bite. Blood 2012;120(21):4637. [Crossref]
6. Adeclat GJ, Hayes M, Amick M et al. Acute forearm compartment syndrome in the setting of acquired hemophilia A. Case Reports Plast Surg Hand Surg 2022;9(1):140-4. [Crossref]
7. Wan Ab Rahman WS, Abdullah WZ, Husin A et al. Epidemiology, spectrum of clinical manifestations and diagnostic issue of acquired haemophilia: a case series. Malays J Pathol 2019;41(2):185-9. [Crossref]