International Journal of Advances in Medicine
Gulati S et al. Int J Adv Med. 2024 May;11(3):249-251
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20241021

Case Report

A rare case of acquired hemophilia A

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Received: 01 January 2024
Revised: 25 January 2024
Accepted: 04 March 2024

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ABSTRACT

Acquired hemophilia A (AHA) is a rare bleeding disorder characterized by IgG autoantibodies directed against circulating coagulation factor (F) VIII neutralizing its coagulant function. The usual clinical presentation of AHA is spontaneous or provoked bleeding in a person with a negative personal or family history of a coagulopathy and can lead life threatening bleeding especially in older patients. Here we report a case of 54-year-old male patient presenting with blood and passage of clots in urine. He was treated with recombinant factor VII and VIII with steroid as eradication therapy. Underlying cause remained unclear in this case.

Keywords: Bleeding, Coagulopathy, Ecchymotic patches, Hematoma

INTRODUCTION

Acquired hemophilia A (AHA) is a rare bleeding disorder associated with formation of autoantibodies to factor VIII. Incidence of AHA is approximately 1.5 cases per million per year.[2] Bleeding in AHA usually manifests as spontaneous subcutaneous haematomas, extensive bruising, haematuria, epistaxis, GI bleeding and intracranial hemorrhage. Diagnosis is made by presence of low factor VIII level. Commonly associated with auto immune disorder (systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and Sjogren syndrome), malignancies, medications (penicillin, sulphonamides, and methyldopa), hepatitis B and C infections and postpartum. Approximately 50% of the cases are idiopathic.[3] Mortality rate range between 8–22%.[3]

Most frequently treated with by passing agent (recombinant activated factor VII (rFVIIa) or activated prothrombin complex concentrate (aPCC)) or FVIII replacement therapy with concentrates or induction of FVIII release using 1 desamino-8-D arginine vasopressin (DDAVP) along with steroids and immunosuppressive agents.

CASE REPORT

A 54-year-old male patient known diabetic and hypertensive presented with complaints of blood in urine associated with passage of clot in urine. He also complained of pain in lower back radiating to anterior aspect of right thigh. Positive finding on systemic examination were pallor present, multiple ecchymotic patches over both upper limbs and palms, ecchymotic patch over right loin, vitals were stable. Laboratory evaluation revealed haemoglobin (Hb) 6.8 gm%, total leucocyte count (TLC) 14000/µl, platelet 279000/µl, blood urea nitrogen (BUN) 44.19 mg/dl, serum creatinine 5.19 mg/dl, sodium 125 mEq/l, potassium 7.6 mEq/l, activated partial thromboplastin time (aPTT) 74.4 sec, prothrombin time (PT) 13.0 sec. aPTT mixing test revealed clotting time in test plasma 75.6 sec, normal plasma 30.9 sec, 1:1 mix (normal: test plasma) 38.6 sec. aPTT based inhibitor screen showed clotting time in test plasma 63.2 sec, normal plasma 30.9 sec, 1:1 mix (normal: test plasma) not

incubated 38.8 sec, 1:1 mix (normal: test plasma) incubated (2 hours) 53.2 sec. Coagulation factor VIII assay was 2.7% (normal-50 to 150%), Von Willebrand factor (VWF-Ag) was 208.5%, Bethesda assay for FVIII inhibitor was 3.94 BU. ANA (IF) was 1+, in ANA profile anti SCL-70 was positive. drVVT, SCT, B_2GPI IgG, IgM, ACA IgG, IgM were all negative. ASCA was positive but colonoscopy was normal. Positron emission tomography-computed tomography (PET CT) showed non FDG avid hyper densities in bilateral bulky iliacus and psoas muscle, left pelvicalyceal system and left ureteric lumen likely hematoma (Figure 1). Patient was given four doses of NoVo seven (rVIIa), one dose of recombinant FVIII, pulse therapy of dexamethasone followed by oral prednisolone. He was also given two units of FFP, 4 units of packet red blood cell (PRBC). Patient improved gradually; haematuria subsided slowly. aPTT showed decreasing trend, FVIII level improved from 2.7% to 131.2%. Repeat Bethesda assay showed fall in inhibitor level from 3.9 BU to 1.4 BU. Later he was started on azathioprine, but it was stopped in view of leukopenia and thrombocytopenia. He was discharged on tapering dose of steroids.

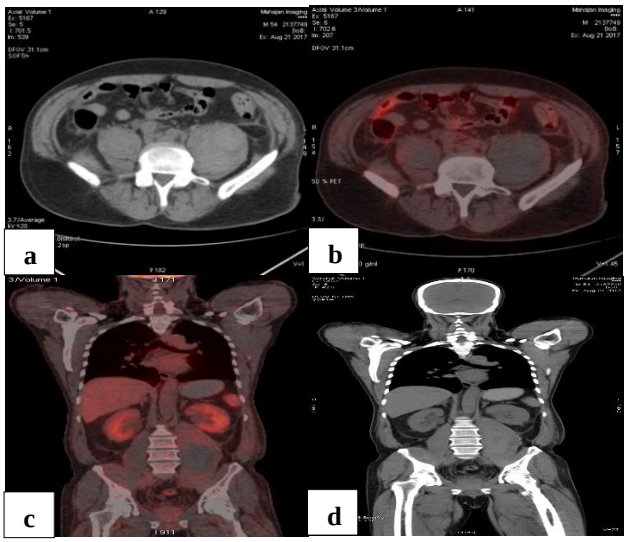

Figure 1: (a-d): PET scan images.

DISCUSSION

AHA is an anticoagulation defect against FVIII to the presence of inhibitory autoantibodies. The incidence is higher with age and the median age of diagnosing AHA is 75 years.[2] Many risk factors contribute to AHA and the most common being the pregnancy and postpartum (2% to 21%).[2,4,5] There are no risk factors associated with high incidence of AHA like autoimmune disorders (20%), malignancies (12%), dermatological disorders (2%), and medications. It can also be associated with infections and blood transfusions rarely, however, the majority of the cases are still considered idiopathic.[6] Approximately 50% of the cases have no underlying cause and is found equally in males and females.

It is challenging to diagnose AHA due to non-specific presentation and being a rare disorder. Coagulation profile shows isolated prolonged aPTT (typically by 2-3 times). Due to presence of coagulation factor inhibitors, it could be presenting disorder like intrinsic coagulation factor (FVIII, FIX, FXI, FXII). Therefore, quantitative measurement assays of coagulation factor and coagulation factor inhibitor level is necessary.[2,4] Pivotal diagnostic step is mixing study which differentiates between coagulation factor deficiency and the presence of coagulation factor inhibitor. This step is done by mixing plasma of the patients with the normal plasma in 1:1 ratio, which should correct aPTT if there is coagulation factor deficiency and if mixing study failed to correct aPTT[7], this is the indicator of presence of coagulation factor deficiency inhibitor. FVIII activity and inhibitor titers are neither co-related nor associated with bleeding severity.[3,6,8]

Management of AHA includes two strategies, first is control of bleeding initially and second is inhibitor eradication.[2,9] Anti-hemorrhagic treatment strategies include rFVIIa replacement therapy and aPCC (bypass coagulation agent), alternative treatment includes human FVIII given if inhibitor levels are low (<5 BU), for minor bleeding desmopressin can be used (DDAVP).[1] Inhibitor eradication strategies include corticosteroids, corticosteroids + cyclophosphamide, rituximab. Alternative treatment includes azathioprine, mycophenolate, cyclosporine.[2,6,10] Relapse is common up to 20% in the first two years and thus close follow up is required and patient should be followed up with FVIII activity every month for first six months, every two to three months for next six months and every six months later.[1,9,10]

CONCLUSION

AHA is rare auto immune hematologic disorder. Diagnosis is challenging, may go undetected. Patient presenting with bleeding symptoms and hematomas with isolated prolonged aPTT should be further evaluated for AHA.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Gulati S, Dessai R, Chawla K, Pandey A. A rare case of acquired hemophilia A. Int J Adv Med 2024;11:249-51.