DOI: https://doi.org/10.47275/2332-4864-121
Volume 7 Issue 1
Case Studies

Scholit Publishers

Journal of Clinical & Anatomic Pathology

Haemophilia in Cam: Allopathic Perspective

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Abstract

Acquired hemophilia A (AHA) is a rare acquired bleeding disorder. It is caused by factor VIII autoantibodies which neutralize factor VIII. Acquired hemophilia differs from congenital hemophilia A where there are alloantibodies to factor VIII products after repeated exposure to plasma-derived or recombinant factor VIII products. Nearly 50% of cases are idiopathic. The hallmark of AHA is mucocutaneous bleeding; ecchymosis, melena, hematoma, and hematuria. Diagnosis is based on isolated prolonged aPTT, normal PT, absence of lupus anticoagulant, and a mixing test for the presence of inhibitors, finding neutralizing antibodies against VIII lead to a diagnosis. Our discussion revolves around a young male with a history of complementary and alternative medicine (CAM) with no history of anticoagulant use presenting with hematuria, bruises, and hematoma. His laboratory investigations were significant for isolated prolongation of aPTT and subsequent testing revealed low factor VIII levels with factor VIII inhibitors which led to the diagnosis of HA. He was managed with medications and withdrawal of the offending drug resulted in the normalization of aPTT. We believe CAM might be the culprit since withdrawing that medication relieved all symptoms and there is no recurrence. Further research is needed to confirm the association between complementary alternative medicine and AHA.

Keywords: Acquired Hemophilia A; Complementary and Alternative Medicine; Isolated aPTT Factor VIII; Bethesda Assay

Introduction

Acquired hemophilia A (AHA) is a rare acquired bleeding disorder that occurs due to autoantibodies against different epitopes of factor VIII molecule. AHA mimics congenital hemophilia A. Alloantibodies of congenital hemophilia A occur after repeated exposure to plasma-derived or recombinant factor VIII. AHA occurs due to the breakdown of immune control mechanisms for both genetic and environmental factors. These autoantibodies are IgG-type. Generally, AHA occurs in patients without a personal or familial history of bleeding manifestations, and symptoms may range from the mild to mod, to severe. The incidence of AHA is around 1.2 to 1.48 cases per million people per year, with a mortality of 20%. The incidence of AHA increases with age and AHA may be associated with pregnancy, autoimmune disease, and cancer. AHA differs from congenital hemophilia A presence of antibodies that neutralize factor VIII in AHA [1]. AHA patients have cutaneous and intramuscular hemorrhages more commonly while congenital hemophilia A has hemarthrosis as a common presentation [2]. AHA presents with recurrent gastrointestinal, intramuscular, or intracranial bleeding in elderly patients in contrast to hemarthrosis in younger patients with congenital hemophilia A. Laboratory tests of coagulation and mixing studies are needed to diagnose AHA. Control of bleeding manifestations, treating the underlying cause, and immunosuppression when needed has an excellent prognosis and includes the mainstay of treatment.

Case Report

Here we present the case of a 44-year-old male who came with hematuria, bruises, and hematoma for 18 days following ingestion of complementary and alternative medicine for 1 month. No significant oral and parenteral anticoagulant/recent antibiotics/anti-epileptic drug history, past family, and surgical (valvular replacement) history. On examination: no lymphadenopathy, no other visible swellings, no organomegaly. Routine investigations such as CBP, LFT, RFT, Chest X-ray, USG Abdomen, and pelvis were normal. Bleeding time was normal whereas clotting time was prolonged. There was an isolated prolongation of aPTT. He was screened for inhibitors by mixing studies (inhibitors screening test) which turned out to be positive (aPTT was not corrected). His factor VIII activity was measured and detected as 1%, and the inhibitor to factor VIII was 4.8 Bethesda units by Bethesda assay (Table 1).

The patient underwent further workup for secondary causes of AHA, no cause was identified (negative for ANA, RA Factor, lupus anticoagulant; CT chest, Abdomen, and pelvis; peripheral smear-negative for malignancy). Then the patient was diagnosed with AHA - probably secondary to complementary and alternative medicine (CAM). The patient was treated with corticosteroids 1mg/kg (50mg/day) for 3 weeks and advised not to

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Citation: Nichenametla N, Kumar KA and Sri Ram Charan G (2022) Haemophilia in Cam: Allopathic Perspective. J Clin Anat Pathol, 7(1): 121. DOI: https://doi.org/10.47275/2332-4864-121

Received: January 21, 2022; **Accepted:** February 25, 2022; **Published:** March 02, 2022

Table 1: Details regarding the investigations done.

Sample type	Result	Method
Prothrombin time	12.3 seconds	Clotting time with ca thromboplastin
aPTT	76.9 seconds	Activation of clotting time by phospholipids
Factor Vlll	1.0%	Endpoint clotting assay using deficient plasma
Inhibitor screen	Positive	37ºC incubation method
Inhibitor to factor Vlll	4.8	

take the offending medication. His aPTT returned to normal with no further complaints. The patient is under follow up and there is no recurrence of symptoms as of now.

Discussion

Hemophilia is a hemorrhagic disorder and is grouped into three types based on the pathophysiology. Types of hemophilia are hemophilia-A, B, and C caused by defects in factors VIII, IX, and XI, respectively [1]. The most common is the hereditary form of hemophilia and a rare variety is the acquired type. Acquired hemophilia is secondary to the autoantibodies which occur against the coagulation factors, most commonly against factor VIII, hence called AHA [3]. Half of the cases of acquired hemophilia have no precipitating factors. In the other half, the underlying cause can be identified. Following factors have been identified in the development of AHA, immunological disorders form 18% of the total incidence in AHA: SLE, RA, SS, CTD, autoimmune thyroiditis, grave disease, APLA, MS, MG, etc. Obstetrical causes are 8.4%, presenting in the postpartum period, sometimes needing a hysterectomy to control PPH. Hematological and Oncological causes: Solid tumors of the lung, prostate, pancreas, breast, hematological malignancies, CLL, multiple myeloma, NHL, MGUS, etc. Dermatological conditions: psoriasis, pemphigus, Medications: β-lactams, penicillin, NSAIDs, amiodatone, heparin, phenytoin, methyldopa, and fludarabine, etc. [4].

Pathophysiology: The autoantibodies bind to the domains of factor VIII in a time and temperature dependant manner. Breakdown of immune tolerance is the major factor in AHA and this is from a combination of genetic and environmental factors. Factor VIII deficiency leads to reduced thrombin on the surface of activated platelets. Diagnosis of AHA is confirmed by laboratory tests [5]. Laboratory testing shows an isolated rise in aPTT with a normal PT, platelets, and thrombin time. A mixing study will help to differentiate between factor deficiency vs inhibitors [6-8]. In factor VIII deficiency a mixing test shows corrected aPTT whereas in presence of inhibitors aPTT remains elevated. Serum factor VIII levels confirm the diagnosis. Bethesda assay measures the strength of inhibitors in the plasma.

Management of AHA includes securing hemostasis and inhibitor eradication. In case of minor bleeding observation is sufficient. Special cases improve with desmopressin. Major bleeding will need factor VIII, desmopressin when the patient has low titres, but in high titre cases bypassing agents will become the first line of treatment [5]. Bypassing agents are named so because they act by bypassing factor VIII in the coagulation pathway. The bypassing agents are activated prothrombin complex concentrate and recombinant activated factor VII [9,10]. Inhibitor eradication should be administered concurrently with hemostatic therapy; the first line includes prednisone (1mg/kg/day). Cyclophosphamide (50-100 mg/day) can also be added for better patient outcomes. When first-line immunosuppression is not effective second-line agents come into play, and rituximab can be used.

Complementary and alternative medicines are increasingly used to diagnose or treat allergic diseases/chronic pain. Organ toxicity has been observed associated with various herbal preparations involving the liver, kidneys, and heart. Some homeopathy, herbal medications like *Geum japonicum*, chondroitin, and Chinese peony may act at the level of the extrinsic pathway of coagulation and causes bleeding. Some have antiplatelet activities like Chinese agrimony, garlic, and *Arnica montana*. Cat's claw, celery, coleus, and guggul have unspecified antiplatelet and /or anti-coagulation activity. The pattern of side effects is similar to that observed by the use of conventional medicine. We were presenting a case of AHA after the use of complementary and alternative medicines. Further research is needed to confirm the association between complementary alternative medicines and AHA. Therefore, caution may be justified using both conventional and unconventional methods. Only if the benefit is proven and the side effects are established, should a given method be chosen.

In conclusion, it is likely that AHA is underdiagnosed and misdiagnosed in real-world clinical practice suggesting the need to raise awareness of this disease among health care practitioners. Patients presenting with bleeding manifestations with isolated aPTT on complementary alternative medication should be evaluated for AHA in India if others causes are ruled out. We believe CAM might be the culprit since withdrawing that medication relieved all symptoms and there is no recurrence. Further research is needed to confirm the association between complementary alternative medicine and AHA. Complementary and alternative medicine could interact negatively with our immune system causing detrimental side effects.

References

1. Mehta P, Reddivari AKR 2013. Hemophilia. Brenner's Encycl Genet Second Ed 2013: 426-429. https://doi.org/10.1016/B978-0-12-374984-0.00692-6

2. Franchini M, Vaglio S, Marano G, Mengoli C, Gentili S, et al. 2017. Acquired hemophilia A: a review of recent data and new therapeutic options. *Hematology* 22: 514-520. https://doi.org/10.1080/10245332.2017.1319115

3. Holme PA, Brosstad F, Tjønnfjord GE 2005. Acquired hemophilia: Management of bleeds and immune therapy to eradicate autoantibodies. *Haemophilia* 11: 510-515. https://doi.org/10.1111/j.1365-2516.2005.01136.x

4. Goldman L, Schafer AI 2012. Goldman's Cecil medicine. Twenty Fif. Elsevier Inc, United States. https://doi.org/10.1016/c2009-0-42832-0

5. Baudo F, Caimi T, De Cataldo F 2010. Diagnosis and treatment of acquired haemophilia. *Haemophilia* 16: 102-106. https://doi.org/10.1111/j.1365-2516.2010.02232.x

6. Reeves BN, Key NS 2012. Acquired hemophilia in malignancy. *Thromb Res* 129: S66-S68. https://doi.org/10.1016/S0049-3848(12)70019-1

7. Sborov DW, Rodgers GM 2013. How I manage patients with acquired haemophilia A. *Br J Haematol* 161: 157-165. https://doi.org/10.1111/bjh.12228

8. Huth-Kühne A, Baudo F, Collins P, Ingerslev J, Kessler CM, et al. 2009. International recommendations on the diagnosis and treatment of patients with Acquired hemophilia a. *Haematologica* 94: 566-575. https://doi.org/10.3324/haematol.2008.001743

9. Sallah S 2004. Treatment of acquired haemophilia with factor eight inhibitor bypassing activity. Haemophilia 10: 169-173. https://doi.org/10.1046/j.1365-2516.2003.00856.x

10. Hay CRM, Negrier C, Ludlam CA 1997. The treatment of bleeding in acquired haemophilia with recombinant factor VIIa: A multicentre study. Thromb Haemost 78: 1463-1467. https://doi.org/10.1055/s-0038-1665434