

Research Article

43 Years Old Female with Acquired Hemophilia Presented with Pseudotumor

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ABSTRACT

Introduction: Acquired-haemophilia A in women is rare. This disorder is caused by the formation of auto-antibodies to factor VIII. Pseudo-tumor is a complication of hemophilia caused by recurrent bleeding which forms mass due to the presence of blood and necrotic tissue. A woman, 43 years old with complaints of left thigh lumps for 2 weeks before admitted to the hospital. Physical examination found a mass in the left thigh, with a thigh circumference of 34 cm, cystic. Laboratory tests showed coagulation disorders in the form of normal APTT lengthening after a mixing study, 2% factor VIII and 7.12 BU inhibitor levels. The ultrasound results of the femoral region showed heterogeneous cystic lesions with multi-inoculated internal echo and septa in the subcutaneous, the impression involved a muscular layer. Vascularity did not appear in it. The patient was improved with conservative therapy of 500mg corticosteroids and recombinant factor VIII. Pseudotumor hemophilia must be followed up immediately since it may cause further complications in the form of compartment syndrome. A biopsy is contraindicated in pseudotumor hemophilia. Simple imaging modalities are able to distinguish pseudotumor from other tumors. The patient was improved with conservative corticosteroid pulse dose 500g for inhibitor and recombinant factor VIII therapy. Due to limited costs, Recombinant activated factor VIII combined with activated prothrombin complex concentrate was not given. Acquired hemophilia A is a hemorrhagic disease with reduced coagulation factor VIII (F.VIII) activity due to the appearance of autoantibodies (inhibitors) against F.VIII. Hematoma is generally diffuse and very painful (Pseudomotor). In contrast to congenital hemophilia, where joint bleeding rarely occurs in AHA. The two strategies used for the management of AHA with pseudotumor in this patient is hemostatic therapy and immunosuppression.

Keywords: Acquired hemofilia A, high titer inhibitor, pseudotumor

Introduction

Acquired hemophilia A (AHA) is very rare in women [1, 2]. It is a hemorrhagic disease with decreased coagulation factor VIII (FVIII) activity due to the appearance of autoantibodies (inhibitors) against FVIII. The body's immune control mechanism speculates to cause this disease. AHA is very rare, and annual incidents are around 1.48/1 million populations [3]. In most patients with AHA, they experience sudden

and spontaneous bleeding, even in 25% of patients, bleeding occurs after a trauma or invasive procedures [4]. Most patients with AHA do not experience previous coagulation disorders [3].

Many risk factors contribute to AHA, pregnancy and postpartum are the most common risks (2% up to 21%). Other risk factors associated with a high incidence of AHAs are autoimmune disorders (20%), malignancy (12%),

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dermatological disorders (2%), and drug effects [5]. AHA is rarely associated with infection and blood transfusions. However, the majority of cases are still considered idiopathic. Pseudotumor is a complication of hemophilia caused by recurrent bleeding which forms mass due to the presence of blood and necrotic tissue.

This case is a very interesting case because AHAs are a very rare disorder which occurs at 43 years old with manifestations of pseudotumor [6]. The epidemiological study of AHA in the incidence of AHA at this age is still relatively low. The purpose of this case is to introduce manifestations that occur in young women and the therapy of AHA.

Material and Methods

A 43-year-old woman came to the emergency room with a lump in her left thigh which had grown in size for 2 weeks. Previously, there was no recurrent bleeding. There are no families with bleeding disorders. About the history of her pregnancy, the patient was pregnant 4 times with the first child died due to the umbilical cord but patient didn't remember and she said that pass out the blood from vagina, the other three children live. This patient always gives birth to spontaneously with physiological post-partum bleeding.

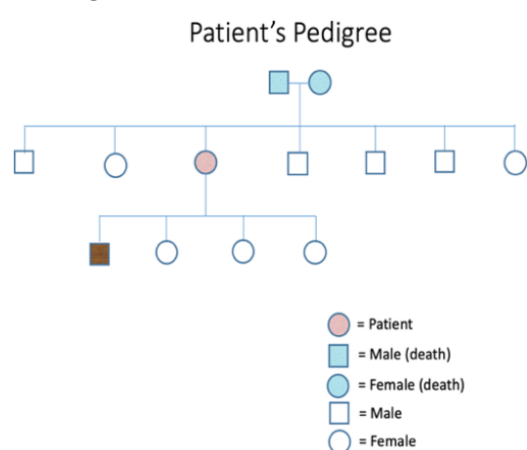


Figure 1. Patient's Pedigree. In pedigree, we didn't find risk factor from genetic

The physical examination found a mass in the left thigh, a cystic consistency, encircling the thigh with a diameter of 34 cm. An investigation by APTT and a lengthy mixing study obtain

APTT value of 66.7 seconds (25.0-31.3 seconds) which improved with the value of the mixing study 48.8 seconds (25.0-31.3 seconds). Factor VIII (2%) decreased (normal value 60-150%) with a 7.12 BU inhibitor value. The results of the musculoskeletal ultrasound examination revealed heterogeneous cystic lesions with multiloculated internal echo and septa in the subcutaneous and involved the muscular layer. Vascularity did not appear in it.

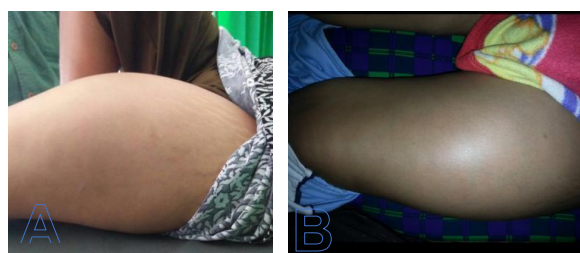


Figure 2. The clinical picture of tumor mass when the patient was admitted to the hospital, (A) in day 1, (B) day 2

The physical examination found a mass in the left thigh, a cystic consistency, encircling the thigh with a diameter of 34 cm. An investigation by APTT and a lengthy mixing study obtain APTT value of 66.7 seconds (25.0-31.3 seconds) which improved with the value of the mixing study 48.8 seconds (25.0-31.3 seconds). Factor VIII (2%) decreased (normal value 60-150%) with a 7.12 BU inhibitor value. The results of the musculoskeletal ultrasound examination revealed heterogeneous cystic lesions with multiloculated internal echo and septa in the subcutaneous and involved the muscular layer. Vascularity did not appear in it.



Figure 3. Results of the musculoskeletal ultrasound of the left femur. We found a hypoechoic in muscle and volume ± 20 cc

The patient was diagnosed with acquired hemophilia A, a high titre inhibitor with a left femoral region pseudotumor.

The patient received methylprednisolone pulse therapy with a dose of 500 mg in 0.9% 100 cc NaCl before injection human anti-haemophilic factor VIII was conducted. The dose of anti-haemophilic factor VIII given was 2400 iu for 3 days. The tumor shrank and the skin returned to normal Figure 3. The tumor shrink and the skin returned to normal.

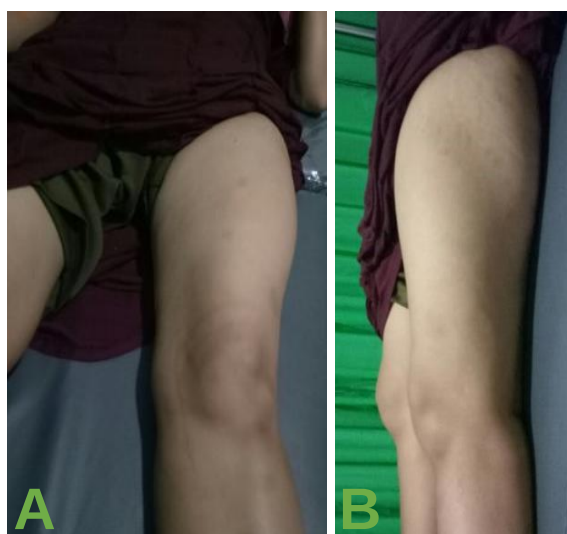


Figure 4. Clinical photos 2 weeks after treatment (during the patient's control) (A) anterior view, (B) lateral view, in this condition.

Results and Discussion

AHA is a very rare case with a high number of morbidity and mortality. The occurrence of incident is 1.48/one million people/year, the incidence rate is 14.7% in the elderly, in this patient it is 43 years old [7]. In a survey of 215 non-hemophilic patients with an increase of inhibitors to factor VIII, most patients were over 50 years old, 8% had rheumatoid arthritis, and 7% were at several peripartum phases. Other diseases that can cause this occurrence include asthma, malignancy, allergies to penicillin, and other autoimmune diseases [8]. Lymphoproliferative and solid malignancy is related to AHA; the most common malignant health problems are chronic lymphocytic leukemia and prostate cancer, followed by lung cancer [6]. Recently the CTLA 4 inhibitor, Ipilimumab has been reported to lead to the development of inhibitors to factor VIII. It is not

yet known the risk factors that cause AHA in this patient because some autoimmune screening that is carried out is negative.

The clinical condition of patients with AHA occurs subcutaneous hematoma, mucosal bleeding, intramuscular bleeding, retroperitoneal bleeding, and postoperative bleeding. Hematoma is commonly diffuse and severe. Unlike congenital hemophilia, in AHA joint bleeding is rarely happened [5,9]. Family relationships, a history of abnormal bleeding, and the use of anticoagulation or antiplatelet drugs can help differentiate AHA from other bleeding disorders [8]. From the reported case, we found muscle bleeding or often called as a pseudotumor. This is in accordance with the theory that the most common manifestations of AHA are the occurrence of intramuscular bleeding. There is no sign of joint bleeding in the reported patient so it was most likely that they diagnosed with AHA.

The ability to make a diagnosis of AHAs is a challenge itself, given the low presentation and prevalence all over the world [11]. In laboratory tests, the assessment of the coagulation profile shows a prolonged aPTT that can be caused by a lack of intrinsic coagulation factor (FVIII) or due to the presence of inhibitors to coagulation factors [2, 12]. Therefore, measuring quantitative tests for the activity of coagulation factors and measuring the level of inhibitors to coagulation factors are considered as important diagnostic steps [13]. Mixing study is a screening test to assess whether the prolongation of aPTT is caused by a deficiency factor or because of the presence of an inhibitor. The results of mixing study in patient showed an improvement in aPTT from 66.7 seconds to 48.8 seconds even though it did not reach normal values (25.0-31.3 seconds). To seek the possibility of an inhibitor, we examined the presence of an inhibitor by using the Bethesda assay and obtained a high titer of 7.12 BU. We carried out the lupus anticoagulant test because it is the most common cause of inhibitors in women, and found negative results. We also conducted the confirmation step to find out the possibility of deficiency in this patient by measuring factor VIII levels. The test results of Factor VIII levels are very low in this case. The activity of factor VIII and inhibitors titer did not correlate

with each other and did not correlate with the severity of bleeding or the treatment outcomes [14]. With the results of a low factor VIII and a high inhibitor titer, it can be concluded that the diagnosis of this patient is AHA [15].

The Important management of the patient with AHA is stopping the bleeding, preventing further bleeding, treating the underlying causes, and overcoming the inhibitors to coagulation factors (antibodies). The two strategies used to treat AHA are hemostatic and immunosuppression. When acute bleeding occurs, the principle of hemostatics must be done as soon as possible. Hemostatic arm applies to patients with severe bleeding, including replacement therapy with active recombinant factor VIII if the inhibitor level is low (<5 BU), coagulation bypassing agents such as recombinant activated factor VII (90 $\mu\text{g/kg}$ every 2-3 hours), and activated prothrombin complex concentrates (50-100 IU/kg every 8-12 hours, maximum 200 IU/kg/day). For Minor bleeding, desmopressin can be used. Immunosuppression uses steroids (prednisone, 1 mg/kg/day for 4-6 weeks), and some immunosuppressants (such as cyclophosphamide, cyclosporine, azathioprine, 6-mercaptopurine, vincristine, and Mycophenolate Mofetil). The main line treatment recommended for use lately is single corticosteroids, corticosteroids with a combination of cyclophosphamide, and corticosteroids with rituximab should be started as soon as possible, without delay to prevent the risk of fatal bleeding. Blood clotting (cessation of bleeding) will be reached when the factor VIII inhibitor is more than 50% and factor VIII inhibitor is undetectable, about 4 to 5 weeks after treatment [16].

Hemophilic pseudotumor must be followed up immediately because it can cause further complications in the form of compartment syndrome. A biopsy is contraindicated in hemophilic pseudotumor. A simple imaging modality but can distinguish pseudotumor from other tumors. The results of the consultation in the orthopedic section concluded that the pseudotumor in this patient did not require surgery and it was recommended to get conservative therapy so the steroids still became the choice of first-line therapy for inhibitors in the AHA patients. In this patient, the administration of 500 mg dose of

methylprednisolone was still able to control the inhibitor factor. Recombinant factor VIII is given as a therapy for hemostasis disorders in this patient. This combination of therapies provides satisfactory results with clinical improvement in this patient.

Conclusion

Acquired hemophilia A (AHA) is a hemorrhagic disease with a decrease in coagulation factor VIII (F.VIII) activity because of the emerging of autoantibodies (inhibitors) against F.VIII. Hematoma is generally diffuse and severe. In contrast to congenital hemophilia where joint bleeding rarely occurs in AHA. The two strategies used for the management of AHA with pseudotumor in this patient are hemostatic therapy and immunosuppression.

The dose of anti-haemophilic factor VIII given was 2400 iu for 3 days. The tumor shrank and the skin returned to normal.

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