Auto Antibody Mediated Acquired Haemophilia: A Case Report

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Abstract:

Autoantibody mediated acquired haomophilia is a rare disease. Hereditary haemophilia usually presents with traumatic or spontaneous bleeding in a young male with positive family history in maternal side.In this case study we described an elderly male patient presenting with short history of recurrent ecchymosis with no similar history in the past and no family history of similar illness. He ultimately turned out to be a case of acquired Haemophilia due to SLE.

Key Word : Auto Antibody, Hemophilia.

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Introduction:

Haemophilia is usually an X linked coagulation disorder due to deficiency of factor VIII, but rarely it can develop due to autoantibody to factor Vlll in response to some underlying pathological condition , presentation of which differ from that of hereditary haemophilia and require high degree of clinical suspicion to diagnose the disease and its treatment is also a challenge. This disease is seen in one to two personper million population annually.[1]

Case Report:

A 70 year old farmer from Kalihati,Tangail attended BSMMU on 5.12.2015 with generalized ecchymosis and a huge hematoma in his right hand . Patient stated that he was reasonably alright four months back and developed reddish discolouration of skin over flexor aspect of right forearm which gradually became brown and finally black. It was not associated with any trauma, appeared spontaneously. There was no tenderness and the local temperature was not raised. It even disappeared spontaneously. After one month he again developed same type of skin discoloration in flexor surface ofright thigh and swelling of both knee joints , also swelling of both calf muscles.He gradually improved. After three months he suffered from skin discoloration of same type in same area and also involved both shoulders, both upper limbs moreon the right side. Also there wasan erythema in both thighs and upper chest. He had mild swelling and tenderness in his right knee joint and left ankle joint, which initially restricted his movement but it improved spontaneously later on. He was hospitalizedand was advised forblood transfusion. During transfusion he developed a huge hematoma over dorsum of his right hand and slight oozing of blood from cannula insertion site. He was then referred to BSMMU for further evaluation and better management.

No history of recent drug administration or herbal medication preceding this episode of illness.He never suffered from jaundice or ascites. Patient never experienced unusual bleeding episode like this before. No history of such type of event in his family .

On examination , he was found to be moderately anaemic. He also had arthralgia of right knee joint . Skin survey revealed extensive ecchymosis involving both shoulders , both arms and also both hands more on right side. Also there was erythema in right thigh and upper chest. Ecchymosis did not blanch on pressure,non tender, local temperature was not raised. He also had huge hematoma over dorsum of his right hand and slight oozing of blood from cannula insertion site of transfusion.

His investigation reports revealed dimorphicanaemia, neutrophilic leukocytosis and eosinophilia and also raised

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ESR. His Hb% was 6 gm/dl.His platelet count was found normal. His liver and renal functionswere within normal limit. Viral markers were negative for hepatitis B & hepatitis C. Evaluation ofhis coagulation profile revealed that his bleeding time wasnormal but his clotting time was prolonged. His prothrombin time was normal but APTT was found prolonged. D-dimer level was normal. We were surprised to see his factor VIII activity which was found to be 1.6% .

The patient had no previous history of prolonged bleeding episode following tooth extraction, circumcision and never experienced hemarthosis during heavy daily works as a farmer.Hedenied any kind of abnormal bleeding problem in his maternal side. We thought that he might have mild form of hereditaryhaemophilia which was not evident overtly but his clinical presentation was not a usual one.Normally a patient with haemophilia present with joint swelling or prolonged bleeding after minor injury.Then we thought of acquired haemophilia which can present with ecchymosis.At that time we thought of both the possibilities. To confirm we performed mixing test with patient's plasma and normal plasma 50:50 mix which was uncorrected and proved our suspicion of having factor VIII inhibitory antibody. In a mixing test if APTT is found prolonged due to lack of factor VIII (hereditary haemophilia), it is corrected when patient's plasma is mixed with normal plasma.

Then we started searching for cause of development of Factor VIII antibody. It is usually due to alloantibody in Haemophilia A after frequent exposure of factor VIII ,which was not possible in this case. Rare other causes are autoimmune disease like SLE, RA,some dermatological cause like Psoriasis, Pemphigus vulgaris,in peripartum period,sometimes in lymphoproliferative disease , plasma cell dyscrasias also in non haematologicalmalignancys and some drugs like Penicillin, Phenytoin and sometimes cause remain obscure.

When we started searching we focused on lymphoproliferative disease or secondary to underlying malignancy considering his age but we found no clinical clue as there was no organomegaly , no lymphadenopathy even no significant weight loss or fever.Imaging also revealed no clue.To complete check list we sent ANA and RA test.Interestingly ANA test report was found positive.Then we sent anti ds DNA test and it was also positive.HisCoomb's test was positive and reticulocyte count was raised. Clinically the patient had arthritis of both knee joints. Ultimately we found a 70 year old man who presented with generalized ecchymosis as a case of acquired Haemophilia due to SLE with autoimmune haemolyticanaemia. We started prednisolone 1 mg/kg/day and also fresh frozen plasma to combat bleeding and patient responded after about one week. His haematoma disappeared and there was no new ecchymosis. He was discharged home and advised for follow up after 3 weeks.

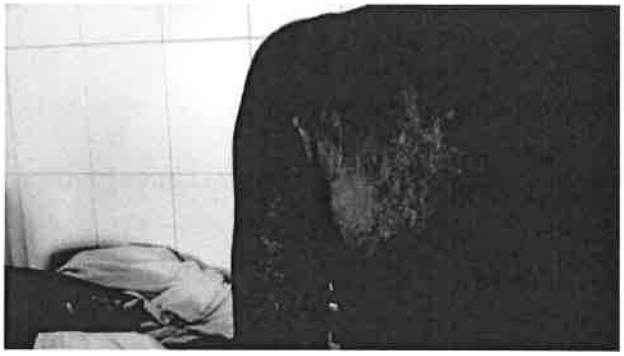


Fig-1: Extensive ecchymosis in arm.

Fig-2: Extensive ecchymosis in thigh.

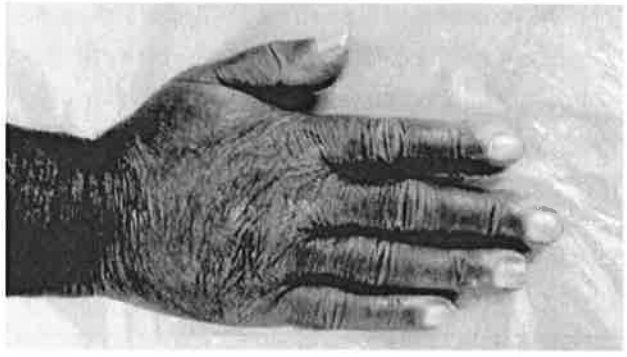


Fig-3: Hemotoma on the dorsum of hand.

Discussion:

It is estimated that acquired factor VIII autoantibodies are seen in to 1 to 2 person per million population annually.[1] Monospecific antibodies to factor VIIIcan arise spontaneously in association with various autoimmune and chronic inflammatory diseases such as systemic lupus erythematosus, rheumatic arthritis, and ulcerative colitis.[2] Antibodies to factor VIII can develop in the puerperium , usually appearing at term or within several months after first pregnancy.Acquired haemophilia may also be seen in association withhaematologic malignancies and solid tumors, certain medications such as penicillin sulfa antibiotics, chlorpromazine and phenytoin and dermatological such as psoriasis and pemphigus vulgaris. Most often acquired factor VIII antibodies are idiopathic particularly in older person.[1]

Characteristics of Factor VIII Antibodies

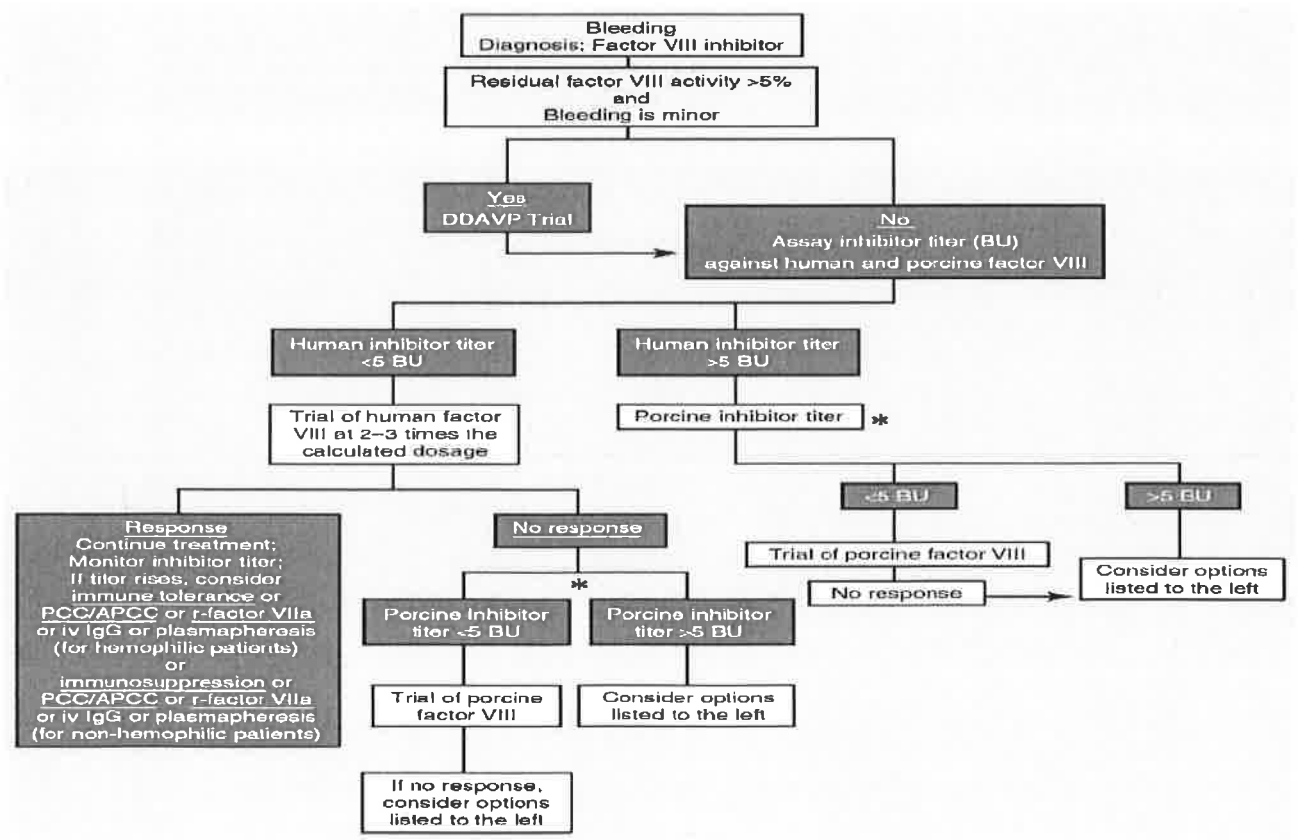
The majority of antibodies are IgGimmunoglobulins that appear to be specific for the coagulant subunit of the factor VIII complex (VIIIc). It neutralizes the function of VIII protein or result in increased clearance or both.[3]

Methods for detection and quantification of antibody. Bethesda assay- in vitro tests are performedat 37o c using two hour incubation mixtures of various dilutions of patient plasma with normal plasma.The inhibitor titre is the reciprocal of the dilution of inhibitor plasma that neutralizes 50% of normal factor VIII activity.[4]

Clinical Manifestations

Prolonged or unexpectedly severe hemorrhage may occur after comparatively trivial trauma,soft tissue or muscle hematomas,hematuria,spontaneous and intractable epistaxis.For unknown reasons, hemarthrosis is relatively less common.

Treatment of spontaneous Factor VIII inhibitor1



A strategy for management of factor VIII inhibitors in hemophilic and nonhemophilicpatiients

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