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Diagnostic and Management of Severe Hemophilia a in an Infant Complicated with Compartment Syndrome: A Case Report

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Abstract **Case Report**

Introduction: Acquired Hemophilia A (AHA) is a rare coagulopathy characterized by the development of autoantibodies that inhibit factor VIII activity. Diagnosis is often delayed due to the absence of personal or familial bleeding history, increasing the risk of life-threatening complications, as demonstrated in this clinical case. ***Case Report:*** We present the case of a 7-month-old male infant with no relevant personal or family medical history, who was admitted for spontaneous ecchymosis in the right upper limb and signs of pain upon movement. Laboratory findings revealed severe microcytic hypochromic anemia (Hb 3.1 g/dL), prolonged activated partial thromboplastin time (aPTT, 67.9 s), and factor VIII activity <1%. An urgent fasciotomy was performed due to compartment syndrome, revealing pale muscle tissue and intramuscular coagulated blood. Management included red blood cell transfusions, fresh frozen plasma, cryoprecipitate, and replacement therapy with factor VIII. The patient showed favorable clinical evolution, achieving 90% factor activity without new bleeding episodes. ***Discussion:*** Hemophilia A is an X-linked recessive bleeding disorder that predominantly affects males. Clinical severity correlates directly with residual factor VIII activity (1). The severe form may manifest within the first months of life with spontaneous muscular or joint hemorrhages (11). Diagnosis relies on clinical history, coagulation studies, and specific factor assays (14). Early detection and comprehensive, multidisciplinary management are essential to prevent disabling complications and long-term sequelae. ***Conclusion:*** This case underscores the importance of early recognition and prompt therapeutic intervention in severe Hemophilia A. The combination of emicizumab and immunosuppressive therapy proved to be a safe and effective strategy, enabling functional recovery without recurrence of bleeding episodes.

Keywords: Acquired Hemophilia A; Factor VIII Inhibitors; Spontaneous Hemorrhage; Compartment Syndrome; Emicizumab; Pediatric Hematology.

Quick Guide to Hemophilia

- Haemophilia is a genetic bleeding disorder where blood doesn't clot properly
- Haemophilia is usually hereditary and can be passed down from parent to child
- In people with haemophilia bleeding continues for longer but it is not faster than someone else
- There are effective treatments to manage and prevent bleeding
- There is support and advice available at all stages of life if issues arise
- With knowledge and planning most people live well with haemophilia and lead active and independent lives.

1. INTRODUCTION

Acquired haemophilia A (AHA) is a rare disease believed to be caused by spontaneous inhibition of clotting Factor VIII by autoantibodies. This is in contrast to the more common congenital haemophilias which are largely due to an absolute deficiency in coagulation factors. It has a prevalence of approximately one per million per year. However, this figure may be underestimated because there are many undocumented cases due to a lack of recognition. Patients who develop this disease may present with catastrophic bleeding despite having no previous bleeding history. In this study, we report a case of acquired Haemophilia A presenting with spontaneous unprovoked bruising and discuss the approach to diagnosis and how to alert the clinician to suspect this potentially rare but devastating disease

2. CASE REPORT

A 7-months-old male patient without history of chronic diseases or pathological family history was hospitalized following an episode of spontaneous ecchymosis two hours before at arrival time in the right arm and pain to the active and passive movements.

Upon arrival at our institution, the patient appeared pale and irritable but had no fever. Normal respiratory rate (30/min) and heart rate (148/min) together with normal blood pressure (111/66 mmHg) were noted and the oxygen saturation was within the normal range. Ecchymosis and edema at the distal right arm and proximal forearm with asymmetrical appearance compared to the left arm were presented, the pulses are preserved in both upper extremities. There were no other abnormal findings in the physical exam.

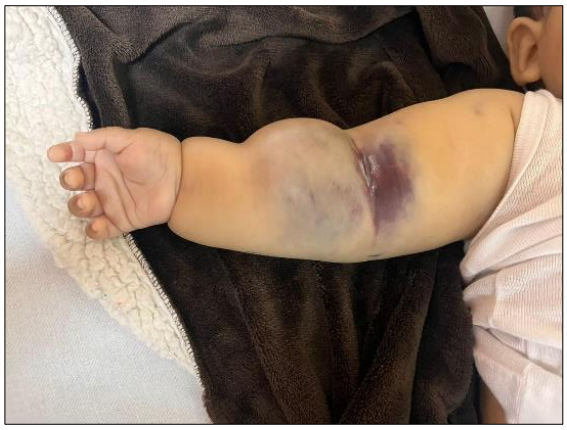

Fig.1: Ecchymotic and edema lesions in upper right arm

A blood analysis revealed a severe microcytic hypochromic anemia (Hb = 3.1 gr/dl), (MVC = 67.2 fL), (MHC = 20.2 pg), decreased levels of iron (5.27 ug/dl) and ferritin (21.83 mg/dl), increased LDH levels (318.4 U/L), and elevated count of reticulocytes (4.04 mg/dl). The coagulation test showed normal range of TP and INR but elevated levels of aTTP (67.9 s), platelets count were within normal levels and peripheral blood smear showed not significant findings. An occult blood test in feces was positive and urinalysis had no relevance.

An osteo-muscular ultrasound with doppler showed an hyperechogenic pattern and increased the volume of the interstitial fluid and conserved but reduced flow of the brachial arteries.

An Urgent Fasciotomy of the anterior compartment of the upper right forearm was performed due to the high suspicious of Compartment Syndrome showed clothes and pale muscular and cellular tissue, the surgery passed without complications with minimal bloody, the surgical wound was left open to be closed in the second instance. In the same surgery the patient had a central venous line placed due to difficult peripheral access.

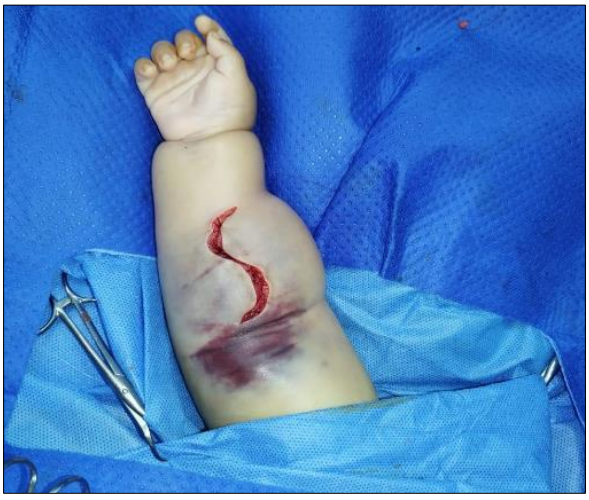

Fig. 2: Fasciotomy of the anterior compartment of the upper right extremity

Based on the obtained results, there was a robust suspicion of a secondary hemostatic disease, that was causative of the compartment syndrome and the severe anemia, analysis of the VIII, IX, and Von Willebrand factor was performed showed a severe deficiency of activity of the Factor VIII (less than 1%), the rest of factors were in normal parameters.

The patient was transferred to intermediate pediatric care, with the proper correction of the severe anemia (15 ml/kg of red blood cells reduced-leucocytes) and urgent correction of factor deficiency with fresh frozen plasma (10 ml/kg), additionally management of the pain with acetaminophen (15 mg/kg/dose every 8 hours) and neurovascular control of the intervened extremity.

After three days the patient was transferred to the pediatric care floor, the patient received another packet of red blood cells reduced-leucocytes (15 ml/kg) and a three day schedule of fresh frozen plasma (10 ml/kg/day) along with a dose of cryoprecipitate (10ml/kg), the closed of the surgery wound of the upper right forearm was performed without complications.

Due to inability of peripheral access the patient was collocated a central venous line of peripheral implantation through of which the patient received 500 UI of factor VIII three times per week reached a percentage of activity of the factor of the 90%.

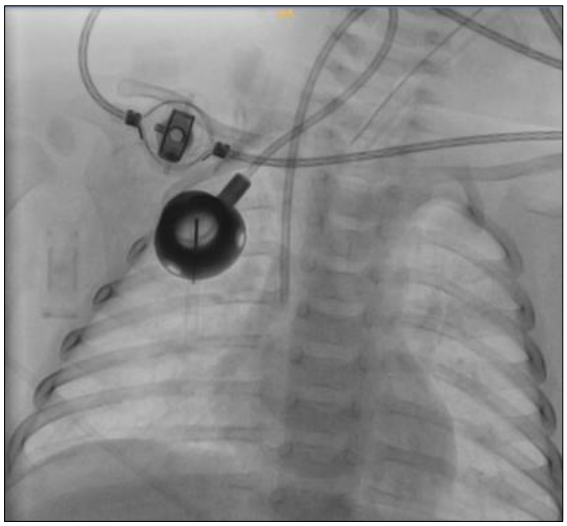

Fig. 3: Central venous line of peripheral implantation

The patient underwent through outpatient follow-up evaluations over the subsequent months and his overall health status remained satisfactory.

3. DISCUSSION

Hemophilia A is usually an X-linked recessive inherited bleeding disorder in which the blood does not clot properly due a deficiency of factor VIII activity [1], males are predominantly affected, females are predominantly carrier but in rare cases such as loss of X chromosome, skewed lyonization, chromosomal translocations or pathogenic variants in the XIST gen could express the disease [2]. In rare cases HA could present as an acquired disease due to malignancy, autoimmunity, pregnancy, medications or could be idiopathic [3].

The prevalence of HA per 100.000 people is 17-21 cases being the more common type of Hemophilia with 80% of the cases, approximately one-half to two-thirds have a severe disease, sporadic disease (without a positive family history due to the novo mutation), causes 30% of cases of mild to moderate disease and 55% of severe disease [4]. HA occurs in all racial and ethnic groups, and throughout the world, it is estimated that 43% of the world's hemophilia population lives in India, Bangladesh, Indonesia and China of which only 12% have been diagnosed [5]. In Latin-American approximately 57.000 people are diagnosed with hemophilia of which 75-90% have HA [6]. In Ecuador until 2015, 535 people were diagnosed with HA [7], updated data are necessary.

The clinical manifestations of HA are related to bleeding from impaired homeostasis and are correlated with the degree of activity levels of factor VIII and the site of bleeding, in severe disease these symptoms appears spontaneously or with a minimal injury and include subgaleal and intracerebral hemorrhage, gastrointestinal bleeding, genitourinary tract hemorrhage, muscles bleeding (quadriceps, iliopsoas, biceps), and hemarthrosis (most common in elbows, ankles and knees) [1-9], in moderate disease these symptoms appear with an intercurrent trauma and are more prevalent in muscles and joints, and in mild disease the patient could be asymptomatic or just have oral or mucosal bleeding due an injury or surgery and bleeding may not become clinically apparent until later in life [1-

10]. The initial presentations of the symptoms vary depending of the degree of the disease being 1-6 months for severe HA, > 8 months for moderate HA and > 36 months for mild HA [11].

The diagnostic evaluation of HA begins with patient`s personal bleeding history and family history, then with screening tests such as count blood cells (CBC), platelet count, prothrombin time (TP), activated partial thromboplastin time (aPTT) and thrombin time (TT). The patient with HA usually presents with normal levels of TP, TT, and platelet count, the aPTT is prolonged in moderate and severe disease, and could be normal in mild disease because aPTT is not affected with factor VIII levels above 15% [12]. If the aPTT is prolongued mixing studies measuring the aPTT patient´s blood, with external plasma that is known to contain sufficient clotting factors are done if the result of the aPTT is corrected, the patient suffers of hemophilia, but if the aPTT is in the same range before the test, the development of an inhibitor is possible [12]. Factor activity levels should be measured in patients with prolonged aPTT levels that correct in mixing studies and those with normal PT, aPTT, TT, and platelet count who have a clinical history, compatible with hemophilia and known family history of hemophilia. The chromogenic assays based on release of a colored product are preferred because have less variability and is more sensitive for identify the activity of the specific factor [13]. The degree of bleeding and therefore, severity of HA depends on residual activity levels of factor VIII, mild hemophilia (> 5% and <40% or > 0.05 UI/ml and < 0.40 UI/ml), moderate hemophilia (> 1% and <5% or > 0.01 UI/ml and < 0.05 UI/ml) and severe hemophilia (< 1% or < 0.01 UI/ml), the normal refence activity is more than 50% or 0.50 UI/ml [1].

Genetic testing is appropriate in most patients and helps to predict the risk of inhibitor formation in the patient and facilitates carrier identification in female members. HA families with mild to moderate disease are more likely to have in 90% of the time a point of mutation in the gene F8 and in the severe disease have an inversion in intron 22 in 50% of the cases and mutation in intro 1 in 5% of the time [14]. A son or daughter of a mother who is a carrier has 50% chance of being a carrier, daughters of a father with HA will be obligate carriers of the familial F8 variant and sons of a father with HA cannot be a carriers because the F8 gene are located on the X chromosome [14].

4. CONCLUSION

In this AHA case, no new clinically relevant bleeds were observed after initiation of emicizumab in conjunction with standard immunosuppressive therapy.

The results of this study provide further evidence of the efectiveness and safety of emicizumab. A variety of exercise types were recorded throughout this study, with only two events being associated with one bleeding occurrence each. These results suggest that the health benefits of physical activity for PwHA receiving emicizumab may outweigh the associated bleeding risk, which appears to be minimal.

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6. Funding: This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

7. Declaration of Competing Interest: None

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