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CASE REPORT

Postpartum Acquired Hemophilia A

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Abstract

Acquired hemophilia A (AHA) is a bleeding disorder that occurs from aberrant production of autoantibodies that target factor VIII. The underlying cause of AHA is unclear but can present postpartum. Very few cases have reported instances of AHA coexisting with other hematological disorders, such as sickle cell trait (SCT). Although rare and no direct correlation between the two, critical situations involving intractable bleeding can intensify the severity of these disorders. A 31-year-old pregnant female with a medical history significant for SCT presented to the hospital for a C-section. Shortly after the procedure she experienced intractable bleeding from multiple sites. Initial lab work yielded an isolated increase in activated partial thromboplastin time (aPTT). Further investigation showed abnormal mixing studies, reduced factor VIII activity and the presence of factor VIII antibodies. The patient was diagnosed with postpartum AHA (PAH) and treated with activated Factor VII and prednisone. PAH is an uncommon bleeding disorder that commonly occurs one to four months postpartum and presents as excessive bleeding elevated aPTT, abnormal mixing studies, and reduced factor VIII levels with abnormally high inhibitor levels. Despite an unknown identifiable etiology, treatment hinges upon establishing hemostasis and eradicating the aberrant generated factor VIII inhibitors. The association of AHA and other hematological disorders is not yet elucidated.

Keywords: Factor VIII deficiency, Acquired, Hemophilia A, Sickle cell trait, Postpartum

1. Introduction

Acquired hemophilia A (AHA) is a rare bleeding disorder that occurs when the immune system produces autoantibodies that target factor VIII (factor VIII inhibitor), resulting in its destruction and causing dysfunction in the intrinsic coagulation pathway, thereby increasing the risk of bleeding.[1] The incidence of AHA is 1.4 cases per million individuals per year.[12] This condition is typically characterized by an isolated increase in activated partial thromboplastin time (aPTT), which assesses the intrinsic coagulation pathway.[2] Patients with AHA may be asymptomatic or experience severe bleeding. In postpartum acquired hemophilia A (PAH) cases, transplacental transfer of IgG antibodies to factor VIII can result in serious complications for both the mother and neonate.[7] The underlying cause of AHA remains unclear, but risk factors include autoimmune disorders, malignancies, dermatological disorders and pregnancy.[1] The predominant antibody is polyclonal IgG with most being IgG4 which lacks the ability to fix complement, thus making AHA a non-immune complex disease. In very rare situations, there have been reported instances of AHA coexisting with other hematological disorders, such as sickle cell disease (SCD) and sickle cell trait (SCT).[9] SCD is an autosomal recessive disease whereas SCT is a heterozygous variant involving the short arm of chromosome 11 and with less severe clinical presentation and symptoms as compared to SCD. SCT is a prothrombotic state, whereas hemophilia leads to increased bleeding tendencies, the combination of these 2 conditions is unique given the hypothesis that patients with hemophilia should have lower frequency of bleeding in presence of SCT, but again there are very rare cases reported regarding

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coexistence of both AHA and SCT making this case very rare.[10,11] Early identification of AHA is crucial for optimal patient outcomes and treatment should be focused on eradicating the antibodies. We present a case of a 31-year-old patient with SCT, no history of bleeding episodes, and diagnosed with PAH after significant intractable bleeding following an uncomplicated C-section for preeclampsia.

2. Case presentation

A 31-year-old G21010 African American female with a past medical history significant for SCT presented to the hospital for treatment of diagnosed preeclampsia. Upon receiving initial treatment, she delivered a healthy baby via an uncomplicated C-section. However, shortly after the procedure both her epidural and IV sites began to bleed significantly. Despite conservative management, the patient continued to bleed and developed an incisional hematoma. MRI of the lumbar spine showed concurrent epidural hematoma (Figs. 1 and 2). Lab work showed aPTT of 83.5 s and a prothrombin time (PT) of 11.5 s. This was elevated from her baseline coagulation profile five months prior which yielded aPTT of 25 s and PT of 12 s. Other diagnostics such as platelets, LDH, haptoglobin, and total bilirubin were all within normal limits. A peripheral smear showed rare schistocytes consistent with a microangiopathic process. The patient denied any family or personal history of any bleeding disorders or previous bleeding episodes. A prior pregnancy was aborted, where she obtained a dilation and curettage (D&C) with minimal bleeding and no blood transfusions. Her current prenatal and antenatal care was uneventful, and she received routine RHogam at 28 weeks. During her present admission, she was placed on regular heparin, for DVT prophylaxis. Hematology suggested a fresh frozen plasma (FFP) infusion to correct bleeding. However, despite four units of FFP, her aPTT remained elevated. This prompted further investigation which led to the ordering of mixing studies, factor VIII, IX, XI, and factor VIII inhibitor levels, anticardiolipin, anti-glycoprotein, and lupus anticoagulant. Fibrinogen, lactate dehydrogenase (LDH), uric acid, antiphospholipid antibodies were also ordered to rule out disseminated intravascular coagulation (DIC) and antiphospholipid antibody syndrome. All of these came back negative except for the mixing studies and VIII inhibitor levels, which were abnormal. Mixing study tests that failed to correct her aPTT suggested the presence of autoantibodies against factor VIII. After determination of autoantibodies, titers were measured using Bethesda assay and a diagnosis of PAH was finalized.

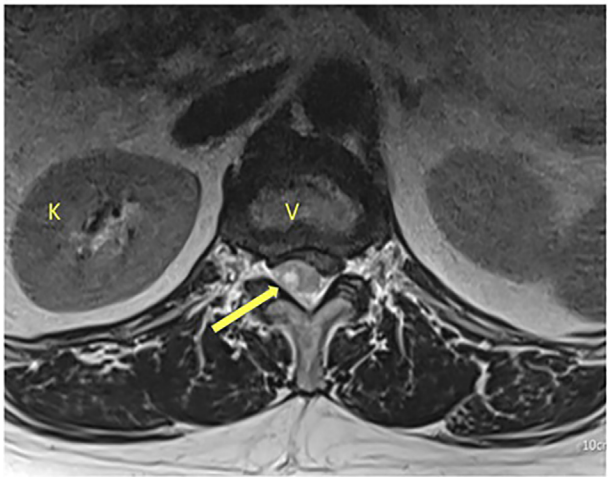

Fig. 1. Lumbosacral MRI without contrast, axial view showing epidural hematoma occupying the spinal canal with compression of spinal cord (arrow). V: vertebrae, K: kidney.

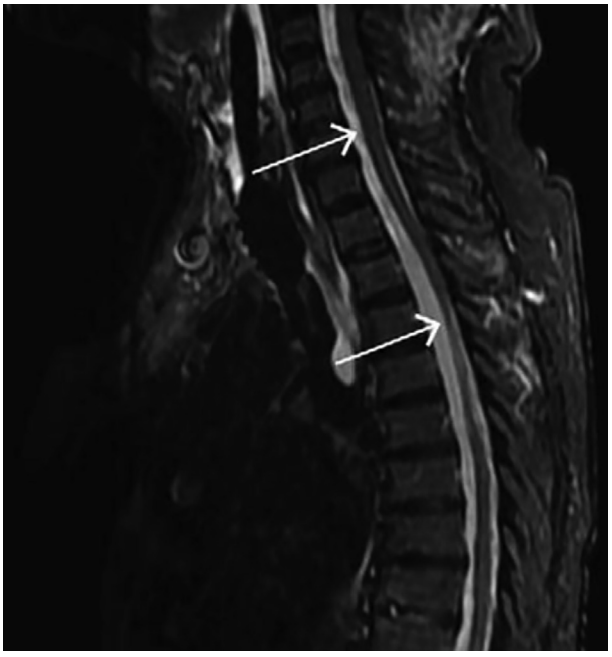

Fig. 2. T2 weighted MRI image showing epidural hematoma (arrow).

After confirmation of the diagnosis, activated prothrombin complex concentrate (aPCC) at 50 units/kg was ordered. Following administration of aPCC her factor VIII was still low at <2% of normal function and she continued to bleed from multiple sites. Along with another aPCC dose, she was also given tranexamic acid (TXA) with two units of packed red blood cell (RBC). Due to the trivial effect of aPCC, it was decided to treat with activated factor VII (VIIa) and prednisone at 1 mg/kg. This

combined treatment led to the elimination of factor VIII inhibitors, and normalized her coagulation profile, which led to hemostasis. Once the patient was stable, she was discharged safely home with her newborn. Prednisone was subsequently tapered as an outpatient and patient followed up with hematology with undetectable titers of factor VIII inhibitors and subsequent normalization of aPTT and factor VIII levels.

3. Discussion

PAH is an uncommon bleeding disorder that typically occurs one to four months postpartum. Cases have been reported from the antepartum stage to 1-year postpartum.[3–6] Common clinical manifestations include ecchymosis, mucosal bleeding, soft tissue hematomas, and bleeding in joints, which are characteristics of congenital hemophilia and severe life-threatening hemorrhages.[4–6] Diagnosis of PAH can often be delayed due to unfamiliarity among clinicians towards the condition, especially when the patient has an absent bleeding-related history. In our case, the patient showed no signs of bleeding prior to undergoing a C-section. She developed incisional and epidural hematomas, along with continuous bleeding from IV sites. However, due to the heterogeneous nature of how PAH may present and similarities to other complications such as, DIC or antiphospholipid antibody syndrome, a diagnosis based on physical exam findings alone is limited, with confirmatory diagnostic lab work being required to rule out DIC and antiphospholipid antibody syndrome.[4]

PAH should be an important differential in postpartum patients with excessive bleeding and an isolated elevation of aPTT. Furthermore, laboratory test including abnormal mixing studies, low factor VIII levels and high factor inhibitor levels would help confirm the diagnosis. Inhibitor levels may correlate with the severity of the disease and bleeding. The severity of AHA is currently classified based on plasma levels of factor VIII activity: severe <1%, moderate between 1 and 5%, mild >5% and <40% normal.[8] Our patient was at the low end of moderate at <2% even following aPCC therapy.

Treatment of PAH involves two steps, firstly hemostasis should be achieved, then inhibitors should be removed. The treatment of choice for hemostasis depends on the intensity of bleeding and inhibitor titers. Factor VIII inhibitor bypassing activity or recombinant factor VIIIa are agents used in life threatening bleeding conditions, for non-life-threatening cases human factor VIII concentrates are used, and desmopressin acetate (DDAVP) is useful for minor bleeding. There are no known major side effects of factor eradication. In the absence of immunosuppression, complete remission has been observed. Combination therapy is commonly administered. Response to therapy has not been shown to correlate with baseline inhibitor levels nor with clinical severity. Immunosuppression with oral cyclophosphamide or rituximab, along with steroids, is the preferred treatment to remove autoantibody. IVIG and plasmapheresis are treatment options in refractory cases. Relapses can occur and unfortunately there is little correlation with inhibitor titers or response time. Careful monitoring is needed in later pregnancies as inhibitors can cross the placenta.[3]

There are few reported cases of congenital AHA in patients with SCD and SCT.[9] The coexistence of SCD or SCT and hemophilia is a rare combination with minimal presence in the literature, even in African American populations, where the prevalence of both conditions is higher, possibly due to the small number of reported cases. To our knowledge, very few cases have shown a patient with PHA and SCT.[10] In such cases, aberrant hematoma formation following delivery led to further workup and treatment once AHA was identified. Currently, AHA is not known to be related to genetic abnormalities, making this case quite unique.

4. Conclusion

This case describes a patient with SCT, no history of bleeding episodes, diagnosed with PAH and reports multiple diagnostic and treatment challenges. There are few cases of severe SCT and hemophilia with lower bleeding instances in the literature, and given SCT is a hypercoagulable state, the association and clinical outcomes are important to report. Despite the absence of an identifiable etiology, treatment should be focused on hemostasis and eradicating aberrantly generated factor VIII inhibitors. In severe bleeding cases, the combination therapy of factor VIIa along with immunosuppression and prednisone should be considered. Given the scarcity of known literature, this case is unique, intriguing, and therefore opens the door for consideration of future molecular, genetic studies.

Ethics information

Ethical review is not required, as this is a single case report.

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Conflicts of interest

The information provided has not been previously submitted for publication or presentation.

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