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Acquired Postpartum Hemophilia A Presentation of Severe Hematuria: A Case Report

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Abstract

BACKGROUND: Acquired hemophilia A (AHA) is a rare, severe bleeding disorder caused by the development of autoantibodies against FVIII that may be idiopathic or secondary to medical conditions. Postpartum AHA can occur as early as 1–4 months after delivery or as late as 1-year postpartum.

CASE REPORT: A 20-year-old female presented with vaginal bleeding 20 days after delivery, then ecchymotic patches developed 2 months later, followed by hematuria 2 months after that. Laboratory investigation revealed isolated, prolonged partial thromboplastin time that was not corrected by mixing 50:50 with fresh normal plasma. FVIII activity was markedly deficient, with a high titer of immediate-acting FVIII inhibitor antibodies.

CONCLUSION: The case was diagnosed as postpartum AHA with a good response to the combined steroids and cyclophosphamide treatment.

Introduction

Acquired hemophilia A (AHA) is considered one of the rarest bleeding disorders, with an incidence of <2 in every one million of the worldwide population [1]. It is caused by autoantibodies against factor VIII that impair its function as a cofactor in the activation of FIX in the intrinsic pathway [2]. These autoantibodies are high-affinity immunoglobulin G (IgG) antibodies belonging mainly to subclasses IgG1 and IgG4 [3]. AHA may occur without an underlying cause in up to 50% of the reported cases or be accompanied by pregnancy and postpartum status, drugs, autoimmune diseases, malignancies, or infections [4]. Postpartum AHA is a potentially rare, severe complication of pregnancy that accounts for 7% of AH cases [5]. Isolated prolonged activated partial thromboplastin time (PTT) is the hallmark of its laboratory diagnosis and is not corrected by fresh normal plasma [6]. Glucocorticoids and immunosuppressive agents are effective in its management [7].

Methods

The study was conducted in accordance with the Declaration of Helsinki (ethical principles for medical research involving human subjects). A written informed consent was obtained from the participant.

A 20-year-old female was given her first healthy baby on April 20, 2022. Twenty days later, she developed a vaginal bleeding attack, on which vaginal ultrasound revealed a normal status of the uterus with no retained perception. The bleeding was controlled by anti-hemorrhagic drugs.

On the 1st week of July, a purperic eruption and large ecchymotic patches were developed on both upper and lower limbs with a drop in hemoglobin (Hb) to 9 g/dL, on which she received anti-hemorrhagic drugs in the form of dicynon, alphintern, and hemoclar gel.

- Hb: 9 g/dL
- Plts: 340 × 10^3/mm^3
- White blood count (WBCs): 12.3 × 10^3/mm^3
- PC: 88%
- INR: 1.11

- PTT: >120 s.

The condition is progressive, with more ecchymotic patches that have not responded to treatment and need to be hospitalized on July 26 for 10 days and discharged on demand. During her hospitalization, she received anti-hemorrhagic drugs (dicynon, alphintern, capron, and thromogel) and 4 units of fresh frozen plasma transfusion. Routine investigations revealed normal liver and kidney functions. She had no medical diseases. There is no family history of similar conditions with positive consanguinity.

- Hb: 10 g/dL
- Plt: 370 × 10^3/mm^3
- WBCs: 13.7 × 10^3/mm^3
- PC: 78%
- INR: 1.14
- PTT: >120 s.

No further investigations were done to reach the proper diagnosis.

On August 14, she was presented with ecchymotic patches and a recent onset of hematuria. RBCs in urine were more than 100. Abdominal and pelvic computed tomography with contrast revealed no abnormalities. Normal CD55 and 59 flow cytometry results were detected.

Platelet dysfunction was suspected, so a platelet function test was done that revealed normal studies with ADP, ristocetin, collagen, and adrenaline.

- Hb: 9.5 g/dL
- Plt: 364 × 10^3/mm^3
- WBCs: 14.7 × 10^3/mm^3
- PC: 100%
- INR: 1
- PTT: 86 s.

The patient's aPTT after immediate mixing 50:50 with control normal plasma (aPTT = 36 s), not corrected, was 74.0 s (immediate acting inhibitor).

Antiphospholipid antibodies were excluded due to negative anticardiolipin, antiB2 glycoprotien, and lupus anticoagulant antibodies. An autoimmune profile was conducted with negative antinuclear antibody and rheumatoid factor. FVIII activity was determined to be 4.5%. FVIII inhibitor titer was found to be high titer (24.5 Betheda unit [BU]).

The case was diagnosed as postpartum-AHA. The patient underwent conservative treatment for 2 months with no improvement in FVIII activity as a follow-up. She started prednisone (1 mg/kg/day) for 2 weeks with improvement in bleeding symptoms, but unfortunately, that returned with tapering of the corticosteroids.

Cyclophosphamide was added (100 mg/day) in addition to the original dose of prednisone for 1 month, followed by gradual tapering by a quarter of the dose every 2 weeks with no recurrence of symptoms. A coagulation profile and FVIII activity were done during the follow-up (Table 1). The patient was noticed for 2 months after the stoppage of treatment with no renewal of the bleeding attacks.

Discussion

AHA is a relatively rare severe bleeding disorder [1]. It has a bimodal age of presentation, as it occurs postpartum at 20–40 years of age, but it is commonly developed after the age of 50 with no sex difference [8].

It is caused by polyclonal IgG autoantibodies against factor VIII with proteolytic capabilities. FVIII inhibitors are usually time-dependent antibodies, with the rare reported presence of immediate-acting ones [9]. It occurs either primary or secondary to medical conditions such as pregnancy, drugs, malignancies, or autoimmune disorders [4]. Postpartum AHA can occur as early as 1–4 months after delivery or as late as 1-year postpartum [10]. It has a good prognosis with a high incidence of recurrence in subsequent pregnancies [11].

The pattern of bleeding is distinct from congenital hemophilia as it occurs as spontaneous, unexpected attacks in the form of severe large ecchymosis or soft-tissue hematomas, as well as sometimes muscle, vaginal, gastrointestinal, or urogenital bleeding, in contrast to hemarthrosis in congenital hemophilia [12].

Although the etiology of inhibitors development in the puerperium is unknown [13], the disorder is thought to develop from a defect in the adaptive immune system. Normal, healthy individuals have endogenous antibodies to FVIII, suggesting that immune tolerance mechanisms, such as regulatory T cells, keep such antibodies inactive. Hence, the autoantibodies may arise from disturbances of these immune tolerance mechanisms [14].

The laboratory diagnosis of AHA depends on an isolated prolonged PTT that is not corrected by mixing 50:50 with fresh normal plasma. This failure of correction excludes factor deficiency and indicates the presence of inhibitors that are measured by BU as

Table 1: Laboratory and treatment response on patient follow-up

Laboratory tests	After 2 months of conservatives treatment	Steroid treatment response						
		2 weeks	4 weeks	8 weeks	10 weeks	12 weeks	14 weeks	10 weeks
aPTT (s)	120	45	90	40	38	37	37	36
FVIII activity %	1.5	65	8.0	75	80	85	90	95
Cyclophosphamide (mg)	none	None	None	100	75	50	25	None
Prednisone (mg)	60	60	45	60	45	30	15	none

aPTT: Activated partial thromboplastin time, mg: Milligram, %: Percent, sec: Second.

inhibitor titer [15].

The management of AHA relies on the achievement of two steps: First, controlling the active bleeding depends on the inhibitor titer; if it is <5, the use of desmopressin and recombinant factor VIII can be effective. If the titer is >5, using by-passing agents such as prothrombin complex concentrate or recombinant human FVII is the choice [16].

The second step is the elimination of the inhibitor by glucocorticoids, cyclophosphamide, rituximab, or a combination of these agents, which have all shown efficacy [7]. FVIII inhibitor titer>20 is usually an indicator of the need for immunosuppressive drugs to achieve remission [17].

Postpartum AHA is usually resolved spontaneously within 30 months. Conservative treatments, as well as immunosuppressive drugs, are considered [18].

Conclusion

Postpartum AHA is a rare bleeding disorder with a good prognosis. Its frequency may be low due to missed or undiagnosed cases. Our case study started its presentation 20-day postpartum with vaginal bleeding, followed by ecchymosis, and progressed to hematuria. Her final diagnosis is established after 4 months since her first presentation with high-titer, immediate-acting acquired FVIII inhibitors. The patient responded to the combined steroids and cyclophosphamide after failing conservative treatment.

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