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Acquired Hemophilia A Associated with Autoimmune Bullous Dermatosis: Persistent Factor VIII Inhibitor and Prolonged Clinical-Laboratory Discrepancy

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Abstract **Case Report**

Introduction: Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder caused by the development of inhibitory autoantibodies directed against coagulation factor VIII (FVIII). It may occur in association with various underlying conditions, including autoimmune diseases, malignancies, pregnancy, and drugs. However, its association with autoimmune bullous dermatosis remains exceptional. ***Case report:*** We report the case of a 60-year-old woman with a history of longstanding psoriasis and autoimmune bullous dermatosis, who developed severe bleeding manifestations. Laboratory investigations revealed an isolated prolongation of activated partial thromboplastin time (aPTT) and a high-titer FVIII inhibitor (748 Bethesda units/mL). Reduced activities of intrinsic pathway coagulation factors (FVIII, FIX, FXI, and FXII) were observed, likely related to analytical interference of one-stage clotting assays in the presence of a high-titer FVIII inhibitor. Immunological evaluation showed persistent triple positivity for antiphospholipid antibodies without clinical criteria for antiphospholipid syndrome. After initial treatment with corticosteroids combined with cyclophosphamide, followed by rituximab and maintenance therapy with mycophenolate mofetil, an initial decrease in inhibitor level was achieved, followed by secondary re-elevation without recurrence of bleeding manifestations. ***Conclusion:*** This observation highlights the complexity of AHA associated with autoimmune bullous dermatosis, characterized by challenges in laboratory interpretation and a prolonged discrepancy between FVIII inhibitor levels and clinical evolution. Clinical assessment should remain central to therapeutic decision-making, beyond isolated biological parameters.

Keywords: Acquired hemophilia A; factor VIII inhibitor; autoimmune bullous dermatosis; antiphospholipid antibodies; clinical-laboratory discrepancy.

INTRODUCTION

Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder caused by the development of autoantibodies directed against coagulation factor VIII (FVIII) in individuals with no personal or family history of bleeding disorders. Its annual incidence is estimated at 1–1.5 cases per million population, with a bimodal age distribution characterized by a predominance among older adults and a second peak during the postpartum period. Diagnosis is based on an isolated prolongation of activated partial thromboplastin time (aPTT) that fails to correct on mixing studies, together with reduced FVIII activity and confirmation of a specific FVIII inhibitor using the Bethesda assay [1–3].

Approximately 50% of AHA cases occur in association with an underlying condition, including autoimmune diseases, malignancies, pregnancy, or drug exposure, whereas the remainder are considered idiopathic. These associations are thought to reflect a breakdown of immune tolerance leading to the production of pathogenic autoantibodies. Among the autoimmune disorders associated with AHA, autoimmune bullous dermatoses, particularly bullous pemphigoid, have only rarely been reported, suggesting shared immunopathogenic mechanisms involving abnormal B-cell activation [1,4–6].

The concomitant presence of antiphospholipid antibodies (aPL), including lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein I

antibodies, may indicate a broader autoimmune background. Persistent triple positivity for aPL is recognized as a high-risk laboratory profile for thrombosis in antiphospholipid syndrome (APS), although its clinical significance in the absence of APS-defining manifestations remains uncertain [7,8].

Managementof AHA relies on prompt control of bleeding and eradication of the FVIII inhibitor through immunosuppressive therapy. However, inhibitor titers do not consistently correlate with bleeding severity, and marked clinical–laboratory discrepancies have occasionally presenting with an exceptionally high FVIII inhibitor titer, persistent triple positivity for antiphospholipid antibodies, apparent reductions in multiple intrinsic pathway coagulation factors, and a been reported [1,2,9].

Herein, we describe a patient with acquired hemophilia A associated with autoimmune bullous dermatosis, presenting with an exceptionally high FVIII inhibitor titer, persistent triple positivity for antiphospholipid antibodies, apparent reductions in multiple intrinsic pathway coagulation factors, and a prolonged clinical–laboratory discrepancy despite immunosuppressive therapy.

Case Report

A60-year-old woman was referred to the internal medicine department for severe bleeding manifestations. Her medical history included longstanding psoriasis since childhood and autoimmune bullous dermatosis diagnosed in 2018, treated with systemic corticosteroids.

The patient presented with a severe hemorrhagic syndrome characterized by recurrent epistaxis, gingival bleeding, hematuria, extensive ecchymotic purpura, muscular hematoma, and persistent bleeding from venipuncture sites.

Clinical examination revealed no lymphadenopathy or organomegaly. Musculoskeletal examination showed a large right knee effusion. The remainder of the physical examination was unremarkable.

Laboratory investigations showed regenerative normocytic anemia,hospholipid antibodies, including lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein I antibodies, confirmed on two separate samples obtained 12 weeks apart. Antinuclear antibodies were negative. Rhe neutrophilic leukocytosis, normal platelet count, normal prothrombin time (PT), and isolated prolongation of activated partial thromboplastin time (aPTT) with a ratio of 3.

Immunologicalevaluation revealed persistent triple positivity for antiphospholipid antibodies, including lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein I antibodies, confirmed on two separate samples obtained 12 weeks apart. Antinuclear antibodies were negative. Rheumatoid factor (latex agglutination and Waaler–Rose tests) was negative. Direct antiglobulin test was negative, and fibrinogen levels were normal.

Coagulation factor assays showed markedly reduced activities of intrinsic pathway factors, including FVIII, FIX, FXI, and FXII, associated with the detection of coagulation factor inhibitors. The FVIII inhibitor level was markedly elevated at 748 Bethesda units (BU)/ml. Low inhibitor titers were also detected against FIX (3 BU/ml), FXI (5 BU/ml), and FXII (1 BU/ml).

Aradiologicalassessment performed to investigate an underlying malignancy, including thoraco-abdomino-pelvic computed tomography and breast imaging, showed no evidence corticosteroids combined with cyclophosphamide. However, persistent FVIII inhibition with recurrence of bleeding manifestations was observed. A second-line treatment with rituximab was initiated at a dose of 500 mg weekly for four consecutive weeks, combined with systemic corticost of neoplastic disease.

Based on the clinical presentation and laboratory findings, the diagnosis of acquired hemophilia A associated with autoimmune bullous dermatosis was established.

Thepatient initially received a 3-month course of systemic corticosteroids combined with cyclophosphamide. However, persistent FVIII inhibition with recurrence of bleeding manifestations was observed. A second-line treatment with rituximab was initiated at a dose of 500 mg weekly for four consecutive weeks, combined with systemic corticosteroid therapy, followed by maintenance treatment with mycophenolate mofetil at a dose of 2 g/day.

Follow- up evaluation demonstrated an initial decrease in FVIII inhibitor level from 748 BU/ml to 12.8 BU/mL, followed by a secondary increase to 85.76 BU/ml. The most recent assessment performed on April 2, 2026, showed a further increase in FVIII inhibitor level to 153.6 BU/ml.

Despite the persistent and increasing FVIII inhibitor titer, the patient has remained free of bleeding manifestations, with clinical remission maintained for more than six months, illustrating a prolonged discrepancy between biological inhibitor persistence and clinical outcome.

DISCUSSION

The main strength of this case lies in the rare association between acquired hemophilia A (AHA) and autoimmune bullous dermatosis in a patient with a complex autoimmune background. Although AHA is commonly associated with autoimmune diseases, malignancies, pregnancy, or certain medications, its association with autoimmune bullous dermatosis remains exceptional. Among these disorders, bullous pemphigoid is the most frequently reported entity, although only a limited number of cases have been described in the literature.

Qiu *et al*. reported a case of acquired hemophilia associated with bullous pemphigoid, suggesting shared immunopathogenic mechanisms involving B-cell activation and autoantibody production [10]. Similarly, Sourdeau et al. described the association of acquired hemophilia A with bullous pemphigoid and multiple myeloma, highlighting the complex interplay between autoimmunity, autoimmune skin disease, and the development of coagulation inhibitors [11]. More recently, Abakarim et al. reported another case of bullous pemphigoid associated with AHA, further emphasizing the rarity of this association and the importance of considering AHA in patients presenting with unexplained bleeding manifestations in the setting of autoimmune disease [12].

In our patient, the occurrence of AHA in the setting of long-standing autoimmune bullous dermatosis and childhood-onset psoriasis supports the hypothesis of an underlying immune dysregulation favoring the development of multiple autoantibodies. However, no specific pathophysiological mechanism directly linking these two disorders has been demonstrated. The prevailing hypothesis involves a breakdown of immune tolerance leading to aberrant B-cell activation and the production of autoantibodies directed against multiple self-antigens [1,2].

Another distinctive feature of our case was the persistent triple positivity for antiphospholipid antibodies (aPL), including lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein I antibodies. This profile reflects a broad autoimmune activation but does not fulfill the classification criteria for antiphospholipid syndrome (APS) in the absence of thrombotic or obstetric manifestations. According to the classification criteria proposed by Miyakis et al. and the recommendations of the European Alliance of Associations for Rheumatology (EULAR), APS requires the combination of persistent laboratory abnormalities and compatible clinical manifestations [7,8]. Therefore, in our patient, persistent triple aPL positivity should be interpreted as a marker of extensive autoimmune dysregulation rather than definite APS.

Thelaboratory findings also raised an important diagnostic challenge. Initial coagulation testing demonstrated markedly reduced activities of several intrinsic pathway coagulation factors (FVIII, FIX, FXI, and FXII), initially suggesting the presence of multiple acquired coagulation factor inhibitors. However, these findings should be interpreted with caution because of the well-recognized limitations of one-stage clotting assays in the presence of circulating inhibitors.

One-stage clotting assays are particularly susceptible to assay interference caused by potent coagulation inhibitors. As reported by Favaloro *et al*., a high-titer inhibitor may lead to falsely reduced activities of several coagulation factors, particularly those measured within the same coagulation pathway [13]. Consequently, a high-titer FVIII inhibitor may produce an apparent reduction in FIX, FXI, and FXII activities, thereby mimicking multiple acquired coagulation factor deficiencies [13,14].

In our patient, the extremely high FVIII inhibitor titer (748 Bethesda units/mL) strongly supports the hypothesis that the apparent reductions in FIX, FXI, and FXII activities resulted from assay interference rather than from true inhibitors directed against these coagulation factors. This observation underscores the importance of interpreting coagulation assays in conjunction with the clinical presentation, mixing study results, inhibitor assays, and the known analytical limitations of one-stage clotting assays [13,14].

The management of AHA is based on two major objectives : controlling acute bleeding and eradicating the FVIII inhibitor. Current international guidelines recommend early immunosuppressive therapy with corticosteroids alone or combined with cyclophosphamide according to the patient's clinical characteristics and prognostic factors [1]. Rituximab, through selective depletion of CD20-positive B lymphocytes, has become an established therapeutic option, particularly in patients with persistent inhibitors or an inadequate response to first-line immunosuppressive therapy [1,2].

In ourpatient, first-line treatment with systemic corticosteroids combined with cyclophosphamide failed to achieve complete eradication of the FVIII inhibitor, leading to the introduction of rituximab followed by maintenance therapy with mycophenolate mofetil. This therapeutic strategy was also appropriate for the underlying autoimmune bullous dermatosis, for which these immunosuppressive agents may provide additional clinical benefit. The favorable clinical outcome further supports the value of an individualized therapeutic approach in patients with complex autoimmune disorders.

The most remarkable feature of this case was the prolonged discrepancy between the persistence of the

FVIII inhibitor and sustained clinical remission. After an initial decline in the inhibitor titer from 748 to 12.8 Bethesda units/mL, a subsequent increase to 85.76 and later 153.6 Bethesda units/mL was observed, despite the absence of bleeding manifestations for more than six months.

A similar dissociation between inhibitor titers and clinical outcome has previously been described in AHA. Data from the European Acquired Haemophilia Registry (EACH2) demonstrated that clinical outcomesatory mechanisms within the hemostatic system. Although the Bethesda assay provides a standardized measurement of inhibitory activity, it does not fully reflect the complexity of the interaction between autoantibodies and coag are influenced by multiple factors and cannot be predicted solely on the basis of inhibitor titers [9]. Likewise, current international guidelines emphasize that although FVIII inhibitor titers are essential for diagnosis and biological monitoring, they do not accurately predict individual bleeding risk [1].

Several mechanisms may account for this clinical–laboratory discrepancy, including residual FVIII activity, the functional properties of the inhibitor, antibody kinetics, and compensatory mechanisms within the hemostatic system. Although the Bethesda assay provides a standardized measurement of inhibitory activity, it does not fully reflect the complexity of the interaction between autoantibodies and coagulation in vivo [1,9].

Accordingly, management of AHA should not be guided solely by FVIII inhibitor titers. Therapeutic decisions should integrate the patient's clinical status, bleeding phenotype, treatment tolerance, and the risk–benefit balance of prolonged immunosuppressive therapy.

CONCLUSION

Acquired hemophilia A associated with autoimmune bullous dermatosis represents an exceptional association reflecting a complex immune dysregulation. Our observation highlights the challenges in interpreting laboratory tests in the presence of a high-titer FVIII inhibitor, which may result in an apparent reduction of several intrinsic pathway coagulation factors due to analytical interference. It also illustrates the possibility of a prolonged discrepancy between persistent biological inhibitor activity and favorable clinical evolution, emphasizing that patient management should incorporate clinical assessment beyond biological parameters alone.

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Conflict of Interest

The authors declare that they have no conflicts of interest related to this publication.

REFERENCES

1. Tiede A, Collins P, Knoebl P, Teitel J, Kessler CM, Shima M, et al. International recommendations on the diagnosis and treatment of acquired hemophilia A. *Haematologica*. 2020 ;105(7):1791-1801.
2. Kruse-Jarres R, Kempton CL, Baudo F, Collins PW, Knoebl P, Leissinger CA, et al. Acquired Hemophilia A: Current Guidance and Experience from Clinical Practice. *J Blood Med*. 2022 ;13:221-245.
3. Collins PW, Hirsch S, Baglin TP, Dolan G, Hanley J, Makris M, et al. Acquired hemophilia A in the United Kingdom : a 2-year national surveillance study by the UK Haemophilia Centre Doctors' Organisation. *Blood*. 2007;109(5):1870-1877.
4. Franchini M, Mannucci PM. Acquired haemophilia A: a 2020 updates. *Thromb Haemost*. 2020 ;120(11):1541-1548.
5. Hadi A, Chen Y, Elmariah S. Bullous pemphigoid associated with acquired hemophilia A: a systematic review. *Int J Dermatol*. 2021;60(5):e181-e188.
6. Sugiyama S, Tanaka R, Hayashi H, et al. Acquired haemophilia A in DPP-4 inhibitor-induced bullous pemphigoid as immune reconstitution syndrome. *Acta Derm Venereol*. 2020 ;100: adv00178.
7. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006;4(2):295-306.
8. Tektonidou MG, Andreoli L, Limper M, Amoura Z, Cervera R, Costedoat-Chalumeau N, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. *Ann Rheum Dis*. 2019;78(10):1296-1304.
9. Baudo F, Collins P, Huth-Kühne A, Levesque H, Marco P, Nemes L, et al. Management of

bleeding in acquired hemophilia A: results from the European Acquired Haemophilia Registry (EACH2). *Blood*. 2012;120(1):39-46.

10. Qiu X, Zhang G, Xiao R, Zhang J, Zhou Y, Li G, et al. Acquired hemophilia associated with bullous pemphigoid: a case report. *Int J Clin Exp Pathol*. 2012;5(1):102-104.
11. Sourdeau É, Clauser S, Prud'Homme R, Bardet V, Calmette L. Acquired hemophilia A associated with bullous pemphigoid and multiple myeloma: a case report. *Ann Biol Clin (Paris)*. 2019;77(2):179-183.
12. Abakarim O, Lahlimi FE, Tazi I. Association of bullous pemphigoid with acquired hemophilia A: a case report. *Pan Afr Med J*. 2024;48 :27.
13. Favaloro EJ, Pasalic L, Curnow J. Laboratory testing for factor inhibitors. *Semin Thromb Hemost*. 2016 ;42(6):638-649.
14. Kitchen S, McCraw A, Echenagucia M. *Diagnosis of Hemophilia and Other Bleeding Disorders: A Laboratory Manual*. 2nd ed. Montreal: World Federation of Hemophilia; 2010.