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Acquired Hemophilia A in Older Adults: A Case Series and Practical Diagnostic Approach

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ABSTRACT

Background: Acquired Hemophilia A (AHA) is a rare autoimmune bleeding disorder caused by autoantibodies against factor VIII (FVIII), with an incidence of 1–4 cases per million annually and a mortality rate exceeding 20%. It typically presents as spontaneous bleeding in individuals without personal or familial history of coagulation disorders.

Case Illustration: Three elderly patients (aged 52–75 years) with spontaneous bruising and no prior trauma, comorbidities, or bleeding history. They presented with isolated prolonged aPTT ranging from 69 to 78.8 seconds, severely reduced FVIII activity (1 IU/dL), and high-titer FVIII inhibitors between 35 and 213 Bethesda Units. All patients were treated with FVIII concentrate and corticosteroids.

Discussion: AHA results from immune-mediated inhibition of FVIII, leading to uncontrolled bleeding in soft tissues, muscles, and mucosa. Symptoms range from hematomas and ecchymosis to potentially fatal hemorrhages. Half of cases are idiopathic, while others are linked to underlying conditions.

Conclusion: Due to its rarity and diagnostic complexity, AHA requires high clinical suspicion and prompt management. Early recognition and targeted therapy are essential to control bleeding and eliminate inhibitors, improving patient outcomes. This study supports Sustainable Development Goal (SDG) 3 on Good Health and Well-being, particularly by promoting early diagnosis and effective management of rare autoimmune bleeding disorders to reduce morbidity and mortality.

KEYWORDS: Acquired Hemophilia, AHA, bleeding disorder, aPTT, Good Health and Well-being

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INTRODUCTION

Acquired hemophilia A (AHA) is an uncommon condition, with registry data estimating its annual incidence at approximately 1.48 cases per million individuals. It primarily affects older adults (Tian *et al*., 2023). AHA can be life-threatening, resulting from the development of autoantibodies targeting coagulation factor VIII (FVIII), leading to its accelerated clearance and functional inhibition. In contrast to congenital hemophilia A—which is hereditary and usually presents in early childhood, AHA arises in individuals without any prior personal or familial history of bleeding tendencies. Without timely recognition and appropriate treatment, AHA carries a high risk of serious complications and death (Lehoczki *et al*., 2025).

Individuals diagnosed with AHA commonly exhibit clinical signs of bleeding accompanied by an isolated prolongation of activated partial thromboplastin time (aPTT). The severity of bleeding manifestations ranges widely, from mild superficial ecchymosis to life-threatening hemorrhagic events (Tiede *et al*., 2020).

This case series is descriptive in nature and cannot establish causality; however, our findings support early suspicion of AHA in cases of spontaneous bleeding with isolated prolonged aPTT.

CASE PRESENTATION

In this report, we present three cases of patients diagnosed with AHA, each exhibiting characteristic spontaneous bleeding

manifestations in the absence of significant trauma, underlying comorbidities, or a family history of bleeding disorders. All three patients were elderly—two females and one male—ranging in age from 52 to 75 years. They presented to healthcare facilities with chief complaints of extensive bruising and progressive subcutaneous hematomas that developed suddenly, without any identifiable physical or procedural triggers. All images were de-identified and published with written patient consent.

Case 1: A 61-year-old female presented with severe pain and swelling in the posterior region of her right thigh, accompanied by spontaneous bruising in multiple areas of the body, most prominently on the forearms and elbow region. There was no history of abnormal bleeding, either during menstruation or childbirth, and no use of anticoagulant or anti-inflammatory medications. Physical examination revealed extensive hematomas on both thighs and marked ecchymosis on the upper and lower arms, particularly the forearms. Laboratory findings showed normochromic normocytic anemia (hemoglobin 8.5 g/dL), markedly prolonged activated partial thromboplastin time (aPTT) of 69 seconds, and severely reduced factor VIII activity (1%). Mixing test was performed both immediately and after 2-hour incubation at 37 °C, with persistently prolonged aPTT. Lupus anticoagulant was excluded using dRVVT and LA-sensitive aPTT assays, both of which yielded negative results. The presence of a factor VIII inhibitor was confirmed with a titer of 85 Bethesda Units. The patient was treated with factor VIII concentrate, systemic corticosteroids, and packed red cell transfusions to address the anemia. Clinical improvement was observed within one week, including reduced pain, decreased hematoma size, and increased hemoglobin levels.

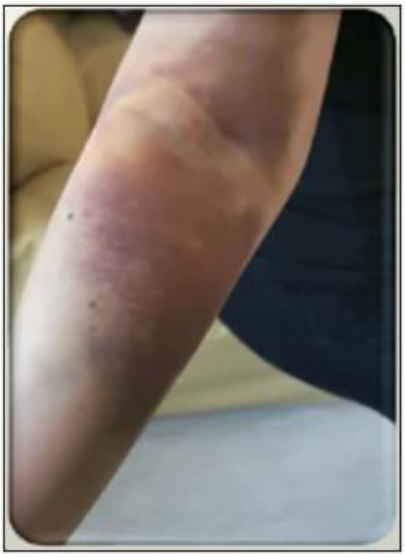

Figure 1. Subcutaneous Bruising on the Forearm of Patient 1 Diagnosed with AHA.

Case 2: A 52-year-old female presented with spontaneous bruising around the left periorbital region and left thigh, without any history of trauma, underlying medical conditions, or routine medication use. Physical examination revealed periorbital ecchymosis and a large subcutaneous hematoma on the lower left thigh. Laboratory investigations showed a markedly prolonged activated partial thromboplastin time (aPTT) of 72.2 seconds, severely reduced factor VIII activity (1%), and a high-titer factor VIII inhibitor of 213 Bethesda Units. Mixing studies were performed both immediately and after 2-hour incubation at 37 °C, with persistently prolonged aPTT. Lupus anticoagulant was excluded using dRVVT and LA-sensitive aPTT assays, both of which were negative. The diagnosis of acquired hemophilia A (AHA) was confirmed. The patient was treated with a combination of factor VIII concentrate and activated prothrombin complex concentrate (aPCC), along with oral corticosteroids. Clinical response was favorable, with cessation of bleeding within seven days and a subsequent decline in inhibitor titer on follow-up evaluation.

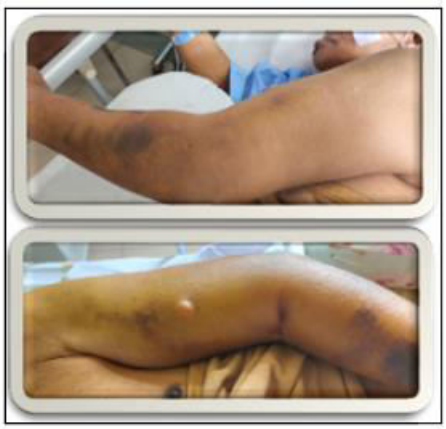

Figure 2. Periorbital ecchymosis and subcutaneous hematoma on the left thigh of patient 2 diagnosed with AHA

Case 3: A 75-year-old male presented with spontaneous bruising involving both the upper and lower arms, without any prior

history of trauma, abnormal bleeding, or anticoagulant use. He had no known comorbidities such as hypertension, diabetes mellitus, or hepatic disease. On physical examination, extensive subcutaneous hematomas were observed in the upper extremities, with no clinical signs of compartment syndrome. Laboratory investigations revealed severe normocytic normochromic anemia (hemoglobin 6.8 g/dL), markedly prolonged activated partial thromboplastin time (aPTT) of 78.8 seconds, factor VIII activity of 1%, and a factor VIII inhibitor titer of 35 Bethesda Units. Mixing studies were performed both immediately and after 2-hour incubation at 37 °C, with persistently prolonged aPTT. Lupus anticoagulant was excluded using dRVVT and LA-sensitive aPTT assays, both of which were negative. The patient was treated with factor VIII concentrate and systemic corticosteroids, along with packed red cell transfusions to manage the anemia. Clinical improvement was noted within ten days, characterized by a reduction in hematoma size and an increase in hemoglobin levels.

Figure 3. Subcutaneous hematoma on the upper and lower arm of patient 3 diagnosed with AHA

Table 1. Laboratory Findings of Three Patients Diagnosed with AHA

Laboratory Test	Result			Reference Value
	P1	P2	P3	
Hb (g/dL)	8.5	14	6.8	11.7-15.5
Leukosit (×10³/µL)	18.7	6.8	11.2	4-11
Plt (×10³/µL)	317	353	532	150-440
PT (seconds)	10.8	12.8	11.9	9-12
aPTT (seconds)	69	72.2	78.8	23-33
FVIII (IU/dL)	1	1	1	60-150
FIX (%)	80	66	70	60-150
von Willebrand factor (%)	242	156	162	50-160
Mixing studies	Not corrected	Not corrected	Not corrected	-
Inhibitor FVIII (BU)	85	213	35	Negative

Hb : Hemoglobin
Plt : Platelet
PT : Prothrombin Time
aPTT : Activated Partial Thromboplastin Time
FVIII : Factor VIII Activity
FIX : Factor IX Activity
BU : Bethesda Units

DISCUSSION

Acquired Hemophilia A (AHA) is a rare autoimmune bleeding disorder characterized by the development of autoantibodies against coagulation factor VIII (FVIII) (Lehoczki *et al*., 2025). Unlike congenital hemophilia A, which is hereditary and typically manifests in early childhood, AHA occurs sporadically in individuals with no personal or family history of bleeding disorders. This condition most commonly affects the elderly population and carries a high risk of mortality if not promptly diagnosed and appropriately managed (Sridharan and Pruthi, 2022).

The three patients described in this report exhibited classic features of AHA, including extensive spontaneous bleeding without any preceding trauma or invasive procedures, and no underlying comorbidities or medication use that could trigger hemorrhage. Clinical manifestations included subcutaneous hematomas in the upper and lower extremities, periorbital ecchymosis, and severe pain that impaired mobility. Hemarthrosis, which is typical of congenital hemophilia, was not observed, further supporting the diagnosis of AHA (Perotti-Abad *et al*., 2025).

The diagnosis of AHA requires a systematic laboratory approach combined with careful clinical interpretation. One of the key tools in the diagnostic process is the evaluation algorithm for isolated prolongation of activated partial thromboplastin time (aPTT). This flowchart (**Figure 4**) begins with the identification of prolonged aPTT in the absence of prothrombin time (PT) abnormalities, followed by exclusion of pharmacologic anticoagulant use. If no clear cause is identified and the patient presents with bleeding symptoms, the next step is to perform an aPTT mixing study (Tiede *et al*., 2020; Platton *et al*., 2023).

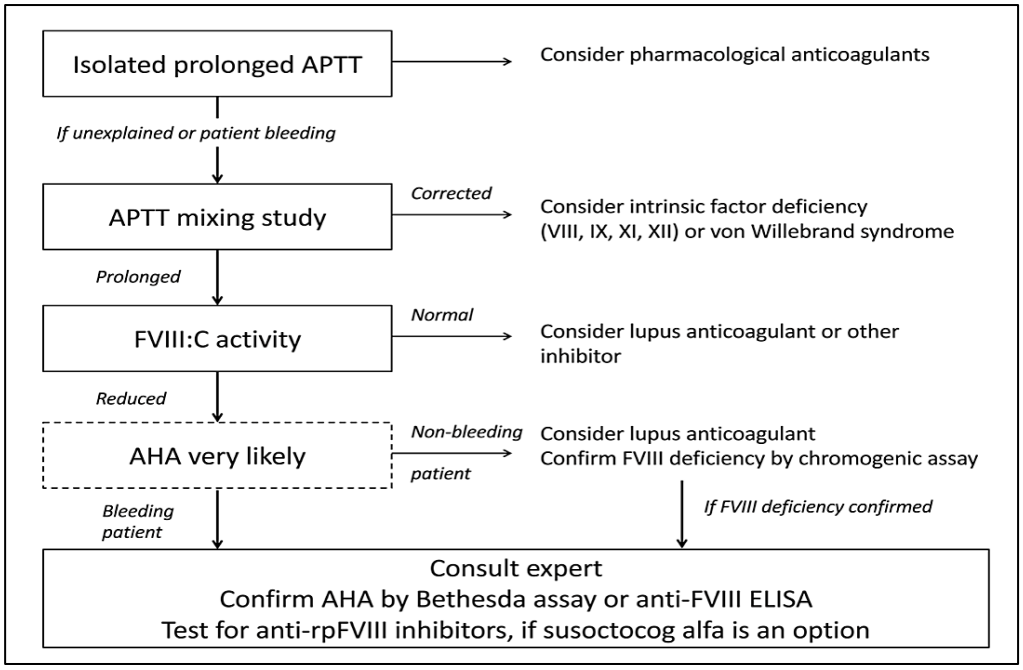

Figure 4. Diagnostic Flowchart for Isolated Prolonged aPTT in Suspected AHA (Tiede *et al.*, 2020)

In all three patients, the aPTT mixing study revealed persistent prolongation following the addition of normal plasma, both in the immediate phase and after 2-hour incubation at 37 °C, indicating the presence of an inhibitor. Lupus anticoagulant was excluded using dRVVT and LA-sensitive aPTT assays, both of which yielded negative results. Subsequent testing showed markedly reduced FVIII activity (1%), and the Bethesda assay confirmed high-titer FVIII inhibitors ranging from 35 to 213 Bethesda Units. Based on the diagnostic algorithm for isolated prolonged aPTT, the combination of active bleeding, non-corrected aPTT, and low FVIII levels strongly supports the diagnosis of acquired hemophilia A (AHA). In such cases, the flowchart recommends expert consultation and confirmation through Bethesda assay or anti-FVIII ELISA, with consideration of recombinant porcine FVIII inhibitor testing if susoctocog alfa is being considered as a therapeutic option (Kruse-Jarres *et al*., 2017; Mazzuconi *et al*., 2020)

The management of AHA involves two primary components: bleeding control and eradication of FVIII inhibitors. In patients with low inhibitor titers (<5 Bethesda Units), FVIII concentrate can be effectively used to achieve hemostasis. For those with high-titer inhibitors (≥5 BU), first-line hemostatic agents typically include bypassing agents such as recombinant activated factor VIIa (rFVIIa), activated prothrombin complex concentrate (aPCC), or recombinant porcine FVIII (rpFVIII). Nevertheless, human FVIII concentrate may still be considered in selected high-titer cases when close clinical and laboratory monitoring is feasible. In this report, all patients received FVIII concentrate as initial therapy, and one patient with a very high inhibitor titer was additionally treated with aPCC. The therapy section was revised to emphasize the rationale behind drug selection and to provide clinical justification for the continued use of FVIII concentrate (Collins *et al*., 2010).

Inhibitor eradication in AHA is primarily achieved through systemic corticosteroid therapy, which serves as the first-line immunosuppressive treatment. In the present cases, all patients received oral prednisone at a dose of 1 mg/kg/day for 3–4 weeks, followed by gradual tapering based on the decline in inhibitor titers and recovery of FVIII activity. Although combination regimens involving cyclophosphamide or ritauximab have been shown to improve remission rates, their use must be carefully considered in elderly patients due to the increased risk of adverse effects such as sepsis, neutropenia, and metabolic disturbances. All patients in this series demonstrated favorable clinical responses to corticosteroid monotherapy, with a reduction in inhibitor titers and symptomatic improvement within less than two weeks. Complete remission was defined as FVIII activity >50 IU/dL, normalization of aPTT, and undetectable inhibitor levels (Collins *et al*., 2012). Therapy for each patient is presented in **Table 2**.

Table 2. Therapies Administered and Outcomes in Three AHA Patients (bleeding control and inhibitor eradication)

Actual Therapies		**Patients**			**Patient Outcome**		
		P1	**P2**	**P3**	**P1**	**P2**	**P3**
Hemostatic Treatment/ Control of Bleeding	Recombinant FVIIa	-	-	-	• Bleeding stop • Increase FVIII • Decrease FVIII-inhibitor		
	Activated Prothrombin Complex Concentrate	-	+	-			
	Recombinant porcine FVIII	-	-	-			
	FVIII concentrate	+	+	+			
Eradication of antibodies / inhibitor	Corticosteroid	+	+	+			
	Cyclophosphamide	-	-	-			
	Rituximab	-	-	-			

P1: Patient of Case 1; P2: Patient of Case 2; P3: Patient of Case 3

Therapeutic response in AHA is primarily monitored through clinical observation, as no laboratory parameter can directly assess the efficacy of bypassing agents (Chaireti *et al*., 2024). Therefore, changes in hematoma size, intensity, hemoglobin levels, and mobility serve as the main indicators of treatment success (Kishi *et al*., 2024). In all three cases, patients demonstrated gradual improvement, including cessation of bleeding, increased hemoglobin levels, and significant pain reduction.

This report underscores the importance of clinical vigilance in identifying AHA, particularly in elderly patients presenting with unexplained spontaneous bleeding. The diagnostic algorithm based on isolated prolonged activated partial thromboplastin time (aPTT) is instrumental in differentiating between factor deficiencies, specific inhibitors, and lupus anticoagulants. Early diagnosis and appropriate management are critical to preventing severe complications and improving patient outcomes. Although AHA is a rare condition, a thorough understanding of its immunological mechanisms and therapeutic strategies can enable clinicians to manage cases effectively and safely (Tiede *et al*., 2020).

CONCLUSION

Acquired Hemophilia A (AHA) remains a rare and diagnostically challenging condition, particularly in elderly patients with unexplained spontaneous bleeding. Prompt recognition through structured evaluation of isolated prolonged aPTT, followed by timely intervention, is essential to reduce morbidity and mortality. Effective management hinges on achieving hemostasis and eradicating FVIII inhibitors, supported by a clear understanding of the immunopathology and therapeutic options available.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose

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