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RESEARCH ARTICLE

ACQUIRED HEMOPHILIA A REVEALING A PEMPHIGUS: A CASE REPORT

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Abstract

Background: Acquired hemophilia A (AHA) is a rare bleeding disorder that affects one to two cases per million people annually and results from the development of autoantibodies directed against coagulation factor VIII.

Case presentation: We report the case of a 63-year-old woman admitted for surgical management of a knee fracture associated with a large hematoma. Laboratory investigations revealed an isolated prolongation of activated partial thromboplastin time (aPTT) not corrected by normal plasma, with a factor VIII activity of 1% and an inhibitor titer of 12.8 BU/mL. One month later, the patient developed cutaneous and mucosal hemorrhagic bullous lesions, and skin biopsy confirmed the diagnosis of pemphigus. She received recombinant factor VIII and high-dose corticosteroids, followed by cyclophosphamide and rituximab.

Conclusion: This case highlights an exceptional association between acquired hemophilia A and pemphigus, emphasizing the importance of early diagnosis and coordinated multidisciplinary management to prevent severe hemorrhagic complications.

Introduction:-

Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder characterized by the development of neutralizing antibodies against coagulation factor VIII (1). Its incidence is estimated at 1–2 cases per million people per year. Unlike congenital hemophilia, which is hereditary, AHA occurs later in life and affects both men and women equally.The clinical presentation varies from mild spontaneous bruising to life-threatening bleeding, often involving muscles or internal organs. Because of its rarity, diagnosis is frequently delayed or mistaken for other conditions (2). The patient care pathway remains complex, often requiring hospitalization, although outpatient management strategies are emerging.The objective of this work is to describe a case of acquired hemophilia A revealing pemphigus in a 63-year-old woman, and to review the relevant literature.

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Case Report:-
A 63-year-old woman, with no notable medical history, was admitted for surgical management of a right knee fracture accompanied by an extensive hematoma. She reported the recent onset of cutaneomucosal papules and spontaneous ecchymotic lesions prior to the trauma.

Laboratory investigations:
Preoperative blood work showed hemoglobin 10.3 g/dL, leukocytes 9.8 × 10⁹/L, and platelets 256 × 10⁹/L. Prothrombin time (PT) was 82%, while activated partial thromboplastin time (aPTT) was prolonged (ratio = 2.9). The mixing test (Rosner index = 75%) confirmed the presence of an inhibitor (table1). Lupus anticoagulant testing was negative. Coagulation factor assays revealed factor VIII = 1%, factor IX = 113%, factor XI = 74%, and factor XII = 71%. Anti-FVIII antibodies were detected by the Nijmegen method (inhibition = 98%, titer = 12.8 BU/mL), confirming the diagnosis of AHA.

Table 1. Laboratory Findings Supporting the Diagnosis of Acquired Hemophilia A

Parameter	**Result**	
Hemoglobin (Hb)	10.3 g/dL	
Leukocytes	9.8 × 10⁹/L	
Platelets	256 × 10⁹/L	
Prothrombin Time (PT)	82%	
Activated Partial Thromboplastin Time (aPTT)	Ratio = 2.9	
Mixing Test (Rosner Index)	75%	
Lupus Anticoagulant	Negative	
Factor VIII activity	**1%**	
Factor IX activity	113%	
Factor XI activity	74%	
Factor XII activity	71%	
Anti-FVIII antibodies (Nijmegen method)	Inhibition = 98% ; Titer = 12.8 BU/mL	

Management:
The patient received recombinant factor VIII and high-dose corticosteroids to control the bleeding and immune response.

Further investigations:
Autoimmune screening was initially negative. One month later, she developed hemorrhagic bullous lesions on the skin and mucosa. Skin biopsy and direct immunofluorescence showed intraepidermal cleavage with intercellular IgG deposition, confirming pemphigus vulgaris.

Outcome:
She was treated with a combination of cyclophosphamide and rituximab, resulting in complete resolution of the hematoma, normalization of the coagulation profile, and improvement of the skin lesions. A relapse occurred during corticosteroid tapering, requiring adjustment of immunosuppressive therapy. The patient was discharged on oral corticosteroids with close follow-up.The case presented above illustrates a rare and challenging clinical situation. To better understand its pathophysiology, diagnostic approach, and management strategies, we discuss below the relevant literature and highlight the key learning points.

Discussion:-

Hemophilia refers to a bleeding disorder caused by an isolated deficiency of a coagulation factor—factor VIII in hemophilia A and factor IX in hemophilia B. These plasma glycoproteins are essential for thrombin generation and fibrin clot formation. Their deficiency leads to delayed and reduced clot formation, resulting in hemorrhagic manifestations.Acquired hemophilia develops later in life and affects both sexes equally. It is caused by neutralizing autoantibodies directed against coagulation factors, particularly FVIII or FIX. Most patients present with spontaneous or post-traumatic bleeding of varying severity (1).Because of its rarity, AHA is often underdiagnosed. Patient management is complex due to diverse hemorrhagic presentations and frequent comorbidities (2). AHA is the most common acquired coagulation disorder, with an incidence of about 1.5 per million per year (3). Although rare, acquired FVIII deficiency is more frequent than acquired FIX deficiency (4,5). Two incidence peaks are described: one between 20 and 30 years (often postpartum) and another after 60 years. Rare pediatric cases have been reported, sometimes linked to transplacental transfer of maternal antibodies (6–8).Approximately 50% of AHA cases are idiopathic, while the rest are associated with autoimmune diseases, malignancies, pregnancy, or drug exposure (1,7,9).

Among autoimmune causes, pemphigus is exceptional. It is characterized by autoantibodies targeting epithelial adhesion proteins(desmosomes),leading to blistering of the skin and mucosa.The coexistence of pemphigus and AHA likely reflects shared autoimmune mechanisms involving loss of immune tolerance and concurrent antibody production against FVIII and epithelial adhesion proteins (1,7).The coexistence of acquired hemophilia A and pemphigus may reflect a shared autoimmune background characterized by loss of immune tolerance, Treg dysfunction, and B-cell hyperactivity. Both diseases are mediated by IgG4 autoantibodies driven by Th2 cytokines and share common HLA class II susceptibility alleles. Cross-reactive immune activation and elevated BAFF levels may further promote the simultaneous emergence of multiple autoantibody specificities. This overlap supports the hypothesis of a systemic autoimmune dysregulation rather than two coincidental entities (8,10).The treatment requires an individualized and multidisciplinary approach combining hemostatic therapy (rFVIIa, FEIBA®, or FVIII concentrates) and immunosuppression (corticosteroids, cyclophosphamide, or rituximab) to eradicate inhibitors and control autoimmunity.

Conclusion:-

The association between acquired hemophilia A and pemphigus highlights the interplay between autoimmune disorders and coagulation defects. Early recognition and multidisciplinary management are essential to prevent life-threatening hemorrhagic complications. Moreover, this case underlines the need for clinical vigilance and early screening for autoimmune hematologic complications in patients with autoimmune dermatologic diseases. Further studies are needed to elucidate the immunopathological links between these rare entities and to optimize therapeutic strategies.

Conflict of Interest:-

The authors declare no conflict of interest.

Author Contributions:-

All authors contributed to patient management, manuscript preparation, and literature review. All have approved the final version of this article.

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