

A Case Report of a 80-Year-Old Woman with A Life-Threatening Hemorrhage as a Result of Acquired Hemophilia

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Abstract: *Acquired hemophilia (AH) is a bleeding disorder involving development of autoantibodies directed against plasma coagulation factors. It is a rare, but potentially life-threatening disease. Therefore, establishment of an early diagnosis with subsequent initiation of an appropriate treatment is crucial. Case Report: We present a case of an 80-year-old woman with a clinical presentation of progressive ecchymosis and hematomas spread all over her body at the time of admission. The patient has not been taking anticoagulants or nonsteroidal anti-inflammatory drugs previously and both her medical and family history were negative for occurrence of a clotting disorder at any point before. Regarding the diagnosis, several coagulation studies have been performed including: activated partial thromboplastin time (APTT), APTT mixing assay, clotting factors level and the Bethesda assay. The latter, confirmed the diagnosis of acquired hemophilia A. Consequently, appropriate immunosuppressive treatment with Cyclophosphamide and corticosteroids (Cyclophosphamide 200mg given on alternative days and Dexamethasone 8mg/daily) has been initiated. This resulted in apparent clinical improvement in two weeks.*

Keywords: acquired hemophilia, inhibitors, Bethesda units

1. Introduction

AH is a rare bleeding disorder caused by development of autoantibodies directed against plasma coagulation factors, most frequently factor VIII. The clinical presentation involves occurrence of spontaneous hemorrhages generally in soft tissues such as: the skin, muscles, other soft tissues and mucosal membranes in patients with no previous medical and/or family history of a bleeding disorder (1). The bleedings are often very heavy and potentially life-threatening in more than 70% of cases. AH is an autoimmune disorder which differs greatly from congenital hemophilia with alloantibodies against FVIII (2). The latter completely inactivate factor VIII through type 1 kinetics and this inactivation is not dependent on the inhibitor titer. On the other hand, the autoantibodies in AH typically develop type 2 kinetics. This is more complex and results in remaining a residual factor VIII which may be laboratory detected but has no substantial efficiency (3). The majority of patients present as an idiopathic condition without evidence of coexisting disorder. However, sometimes AH might be associated with underlying conditions including: pregnancy, autoimmune disorders, inflammatory bowel disease, dermatologic conditions, respiratory diseases as well as allergic reactions, diabetes, hepatitis, solid tumors and malignant hemopathies (4). Epidemiologically, the incidence of this disease is 0.2 to 1.0 cases per million annually but, one should always consider that some cases remain misdiagnosed due to the complexity of the condition. The main spade of distribution is over the age of 60 (5). Typical laboratory finding is an isolated prolongation of the APTT (activated partial thromboplastin time). The "APTT mixing tests" with normal plasma distinguish between persisting inhibitor and other causes for factor deficiency. The priority treatment involves a prompt management of the acute hemorrhage syndrome using by-passing agents such as recombinant FVIIa (Novoseven) and activated prothrombin

complex concentrates (FEIBA) (7,8). In addition, immunosuppressive treatment aiming eradication of the inhibitors is recommended in all patients with AH. This involves using corticosteroids alone or in combination with cytotoxic medications such as Cyclophosphamide (9). Recently Rituxumab occurred as a promising new agent for this purpose.

2. Case Report

An 80 year old woman was admitted to our hospital with massive skin and muscles hematomas that had appeared two weeks before. Her current medical history included regular antihypertensive and cardio-protective treatment without including anticoagulant or nonsteroidal anti-inflammatory drugs. The patient had no history of any liver disease neither personal nor family history for coagulation disorder. On physical examination she was afebrile and with stable vital signs: heart rate of 85bpm, blood pressure 145/86mm Hg. She had big hematomas on both arms, on the neck, thorax and the back. She did not reveal any epistaxis, hematuria, hematemesis, melena, hemoptysis neither haemarthrosis. The laboratory findings asserted hemoglobin level of 6.0g/dl, red blood cells (RBC) 2.7×10^9 , hematocrit 22.3%, white blood cells 8700 per cubic millimeter and platelet count 316×10^9 . Liver and renal functional tests were in normal range as well as the glucose level. Screening haemostasis tests revealed: prothrombin time (PT) 61% (INR 1.20), APTT significantly prolonged-85" and normal thrombin time (TT). The mixing APTT test with equal volume of patient's and control plasma after incubation of 2 hours on 37°C showed an APTT correction to 33". The factor VIII concentration was 1.25%. The Bethesda assay asserted inhibitor titer of 1.7 BU which eventually established presence of an acquired hemophilia in this patient.

3. Photographs



Figure 1: The figure presents large hematoma on the right arm



Figure 2: The figure presents presence of hematomas on both the thorax and the back



Figure 3: The figure shows presence of hematoma on the left arm

4. Treatment

In the absence of by-passing products the acute bleeding was treated with fresh frozen plasma (FFP), 400ml daily for several days and transfusion of 2 units red blood cells. The immunosuppressive treatment was started with Amp.Dexason 8mg daily and Cyclophosphamide 200mg on alternative days. The clinical condition substantially improved in two weeks. This was accompanied by normalization of the values of the laboratory tests: APTT to 45" and increased FVIII level to 60%.

One month following treatment initiation, the patient had no signs of a new bleeding and the existing ecchymosis and hematomas disappeared substantially. The doses of corticosteroid therapy were decreased from the 10-th treating day on, and after one month the patient continued with 40mg Decortin (Prednisolone) daily.

5. Discussion

This is a case report of an 80 years old woman with acquired hemophilia who was successfully treated with a combination of Cyclophosphamide and corticosteroids. On physical examination and with laboratory tests we did not assert any coexisting condition. Therefore, idiopathic acquired hemophilia A was established as diagnosis. In the absence of by-passing agents, the acute bleeding was controlled with FFP (10). The patient had low inhibitor titer (<5 BU) and a good hemostatic effect was achieved with this therapy. The immunosuppressive treatment for eradication of inhibitors with Cyclophosphamide and Dexason was started promptly and within two weeks the APTT decreased and the FVIII level increased greatly.

6. Conclusion

Acquired hemophilia must be considered in all patients with sudden onset of bleeding and a prolonged APTT with normal PT, TT and platelet number. The prompt diagnosis and appropriate treatment are essential for efficient control of the condition.

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