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Review

Unexplained hemorrhagic syndrome? Consider acquired hemophilia A or B

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ABSTRACT

There is a dire need to develop an algorithm to improve the recognition of acquired hemophilia A and B (AHA and AHB) in clinical practice. Initial and intensive care unit (ICU) management of the disorder is particular and represents a challenge for the internist/hematologist and the ICU physician. A delay in the proper treatment of bleeding episodes can lead to a life-threatening event. Expert advice should be sought as soon as possible. Succesful resolution involves accurate diagnosis, bleeding control with hemostatic and immunotherapy, and eradication of the autoantibodies to improve overall survival. Current treatment guidelines are based on the literature in the form of cases and observational studies due to a lack of randomized controlled trials. AH can be triggered by many pathologies, presenting as a paraneoplastic syndrome in case of malignancies or as surgical associated acquired hemophilia (SAHA). We have reviewed the literature from 2015 to 2021 regarding the new case reports to further assess if there is an improvement in the clinical approach.

1. Background on diagnosis and underlying causes

Acquired hemophilia (AH) is an autoimmune disorder of a rare entity, which consists of the onset of abnormal spontaneous bleeding in patients without a medical record of a bleeding disorder, in consequence, it can be suspected by the clinical manifestations [1]. Coagulation tests can confirm the disease by revealing an isolated prolongation of the activated partial thromboplastin time (aPTT – factors VIII, IX, XI, XII) both in acquired hemophilia A (AHA) and B (AHB), with normal prothrombin time (PT- factors I, II, V, VII, and X). When the factor VIII activity is less than 50%, a measurement of anti-factor VIII titers should be determined to check whether an inhibitor is present. The patient is potentially diagnosed with AH if the inhibitor levels are over 0.6 Bethesda Units/mL (BU/mL) [2,3]. This disease affects both of the sexes with the same percentage and it is most often found in the elderly (60–80 years old) and *peri*/postpartum women, with rare encountering in children population [4,5].

The mechanism by which this disorder develops is based on immunoglobulins (IgG) autoantibodies (also known as inhibitors due to inhibition of clotting factors), produced by a triggered immune system, that target the following clotting factors: clotting factor VIII – AHA; clotting factor IX –AHB. Still, some case reports are linking AH to other clotting factors as well [6]. To exclude the genetic factor deficiencies, a mixing study is proposed in which a sample of blood can be withdrawn from the patient and mixed with blood from the control. The lack of resolution of prolonged aPTT confirms the presence of an inhibitor [7]. Inhibitors to factor VIII can be time and temperature-dependent and may correct immediately but prolong with two hours of incubation, and also show second-order nonlinear inactivation pattern with detectable residual FVIII activity – usually less than 15% [8]. Other reasons for

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