Abstract

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When Cause Can Also Be The Cure. Hemophilia A and Inhibitors

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Background: Hemophilia A is an inherited blood clotting disorder that occurs when clotting factor VIII is either absent or not present in sufficient amounts. People with hemophilia may experience excessive bleeding or bruising in the joints, muscles, or soft tissue. While there is no cure for hemophilia A, there are a number of effective treatment options available. One common treatment is called factor replacement therapy, which is an injectable treatment that helps replace the clotting factor VIII (fVIII). Prevention and treatment of bleeds with fVIII replacement products have greatly improved the quality of care for patients with hemophilia A. However, development of neutralizing antibodies, or inhibitors, against infused factor remains a challenging complication of hemophilia treatment. Approximately ~30% of patients with severe hemophilia A will develop inhibitors, in addition to 5% of patients with mild and moderate hemophilia A. Inhibitors significantly increase the cost of care, intensify the financial and psychosocial stressors on patients and their families, and have a negative effect on disease morbidity and mortality by making bleeding episodes more difficult to treat. Bypassing agents (BPAs) are the primary treatment modalities currently available for patients with inhibitors. Traditionally, the use of BPAs during ITI has been reserved for patients with inhibitor titers higher than 10 BU/mL and persistent bleeding symptoms despite high doses of fVIII replacement. Recombinant FVIIa is often chosen as the first-line BPA for patients with hemophilia A and B with inhibitors before the start of ITI because of the potential risk for anamnesis and allergic reaction with a PCC resulting from small amounts of fVIII and the presence of fIX, respectively. Patients with low titer and low responding inhibitors (<5 Bethesda units BU/mL) can often continue receiving factor replacement therapy, albeit at higher doses, for prophylaxis and treatment of bleeds.

Case History: Male, 46yo, entered ER for severe anaemia (Hb 4gr/dl) due to gingival haemorrhage, secondary to tooth extraction. Patient did not practice antihemorrhagic prophylaxis before and after the dental procedure. Test performed showed a picture compatible with his diagnosis of moderate Hemophilia A (aPTT ratio 3.2, FVIII 4.5%). In our department, blood transfusion is administered with antihemorrhagic prophylaxis (FVIIa 3000IU bid) and anti fibrinolytics, also performing local haemostasis of the bleeding site. Following days, however, in absence of clinical and laboratoristic improvement (constantly reduced circulating FVIII levels even after supplementation, continuous need for transfusion support) we requested inhibitor dosage, which was confirmed to be present. Considering low inhibitor titer (4.1 BU/ml n.v, <0.5), we decided to continue higher dose replacement therapy, antifibrinolytics and blood transfusions, obtaining in a few days normalization of Hb values and optimal bleeding control with a gradual reduction in the level of inhibitor, which was eradicated after about 3 months.

Discussion: Inhibitors remain a challenging complication of treatment in patients with haemophilia. Several questions remain regarding the optimal therapeutic approach in poor-risk patients. Nonetheless, there are several novel therapies in development or active clinical trials that may potentially lessen the burden of disease and reduce bleeding risk in patients with haemophilia with or without inhibitors.