

Case Report

Treatment of Patients with Mild Hemophilia-A and Low Titer Inhibitor during Operations: Report of a Case

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- Inhibitor
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Abstract

There is little data for the management of patients with mild hemophilia-A and inhibitors concerning prophylaxis before operations and in the postoperative period. We report a case of an adult with mild hemophilia-A and a low-titer inhibitor who successfully underwent hemorrhoidectomy without post-operative bleeding. An increased dose of F-VIII concentrate was given before operation and a bypassing agent with desmopressin were given after operation. The main challenge in that case was not to trigger the inhibitor and change the clinical phenotype to severe.

ABBREVIATIONS

FVIII: Factor VIII; INH: Inhibitor; rFVIII: recombinant Factor VIII; aPCC: activated Prothrombin Complex Concentrate

INTRODUCTION

Patients with non-severe hemophilia-A [Factor VIII (FVIII) levels above 1%] usually present with bleeding episodes after trauma or surgery and rarely for spontaneous bleeding. Replacement with FVIII concentrate is preserved for patients with severe bleeding episodes. For minor bleeding episodes the treatment includes antifibrinolytics and desmopressin. The development of anti-FVIII antibodies (inhibitors) reduce the efficacy of treatment and could convert the non-severe phenotype into severe with spontaneous bleeding [1].

There is little data for the management of patients with mild hemophilia-A and low-titer inhibitors (INH) concerning prophylaxis before operations and in the postoperative period. As experience is limited a clinician can follow the common practice used in patients with severe hemophilia-A and INH or mild hemophilia-A and high-titer INH [2-4]. We present a case of a man with mild-hemophilia A and a low-titer INH and discuss the therapeutic approach before a scheduled operation.

CASE PRESENTATION

We report a case of a 58-year-old man with mild hemophilia-A and low-titer INH. The diagnosis of hemophilia-A was made at 4 years old and he had rarely received fresh frozen plasma or plasma-derived FVIII concentrate upon bleeding episodes. After 1990 he was switched to recombinant F-VIII (rFVIII) concentrate

that occasionally received for large hematomas and on surgery procedures (varicose vein surgery). However, he had never been infused with rFVIII concentrate for more than 5 consecutive days. In 2015, clinical response and the recovery of infused rFVIII was not the optimal. Blood test revealed that he had developed low titer INH of 3.5 Bethesda units. However, he was retaining his own levels of FVIII (5-6%). At this period, he suffered from painful hemorrhoids and rectal bleeding and since topical treatment was ineffective, hemorrhoidectomy was thought to be the best treatment approach. As the response to bypassing agents was unknown and could not be predicted to this patient, we decided that best prophylactic treatment before operation was increased dose of recombinant FVIII (90 IU/Kg). Intraoperatively no bleeding was observed and in the postoperative period he received activated prothrombin complex concentrate (aPCC-FEIBA®) (50 IU/Kg) every 8 hours the first day reducing the frequency to every 12 hours the second and third postoperative day. Since no bleeding was observed he continued aPCC alternate with desmopressin for four days in an attempt to minimize the risk of triggering the INH. The clinical recovery was excellent. Six months after operation, he is asymptomatic, he retains FVIII at 5% and the INH is detected at a level below 5 BU.

DISCUSSION

Surgery in patients with INH poses several therapeutic dilemmas because low levels of F-VIII cannot be overcome by factor replacement except in cases with low titer INH (<5BU). Therapy with bypassing agents (aPCC-FEIBA® and recombinant F-VIIa-NovoSeven®) is an effective strategy for the management of bleeding episodes in hemophilia-A patients who have high-titer INH.

F-VIII INH bypassing activity with FEIBA® is both effective and safe when used for non-surgical hemostatic control in hemophilia patients who have high INH titers [2-4]. Experience with perioperative use of FEIBA® is more limited, but has resulted in good hemostatic efficacy in major and minor surgical procedures. According to SURF study the overall hemostatic efficacy of FEIBA® during the study period was judged as excellent or good for 91.2% of all surgical procedures, in agreement with previously reported findings [5]. The FEIBA-NovoSeven comparative study (FENOC study) revealed comparable hemostatic effects of both products. However, individual responses were variable and it could be difficult to predict a patient's treatment response [6]. Thus, a patient could show different response to either aPCC or VIIa.

In a recent published study by INSIGHT study group including 100 patients with mild hemophilia-A and INH development, 89% required treatment for bleeding episodes or operations. Most of the patients with bleeding episodes were treated with one type of treatment (either FVIII concentrate, bypassing agents, desmopressin). Both patients with high titer INH and FVIII levels < 1% were mostly treated with bypassing agents. Treatment with FVIII concentrates was preferred for patients with low-titer INH. Some patients who were treated with desmopressin experienced bleeding episodes, thus this approach could be offered in non-severe cases that have endogenous FVIII levels above 1% [1].

CONCLUSION

In conclusion, treatment of patients with mild hemophilia-A and low-titer INH is a major challenge because there is a risk of triggering the titer of the INH and changing the clinical phenotype from mild to severe. The benefit of an increased dose of FVIII concentrate is to insure the immediate hemostasis needed at the operation field and then both bypassing agents are able to bypass the FVIII dependent step and promote hemostasis through

thrombin generation during the post-operative period. Patients could respond differently to by passing agents and it is important to have both agents available in order to early adjust treatment to non-responders [6]. Adjuvant therapy with desmopressin has been successful in the treatment of episodic minor bleeds and for minor surgical procedures without anamnesis, alone or alternate with a bypassing agent [1,2].

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