Circumcision in a combined factor V and factor VIII deficiency using desmopressin (DDAVP)

Ömer Devecioğlu[1], Ertuğrul Eryılmaz[2], Dicle Çelik[1], Ayşegül Ünüvar[1], Zeynep Karakaş[1], Şema Anak[1], Leyla Ağaoğlu[1]

[1]Department of Pediatrics, İstanbul Faculty of Medicine, and [2]Our Children Leukemia Faundation, İstanbul University, İstanbul, Turkey

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Combined factor V and VIII deficiency is a rare inherited autosomal recessive single gene disorder commonly seen in the Middle East. Although the factor levels are between 5-30%, several authors have reported that these patients are more prone to bleeding compared to those having an isolated factor deficiency with the same levels. We report an eight-year-old boy with factor V and VIII deficiency who underwent a successful circumcision using desmopressin (DDAVP).

Key words: combined factor V and VIII deficiency, desmopression, circumcision.

Combined factor V and VIII deficiency was first described in 1954 by Oeri et al[1]. The total number of cases was mentioned as 89 in 58 families in a review by Ginsburg et al.[2] in 1998. The disease is an autosomal recessive single gene disorder with factor levels ranging from 5% to 30%[2].

It has been demonstrated that this combined deficiency is due to the absence of an intracellular transport protein named ERGIC-53 which is responsible for transporting factors V and VIII from the endoplasmic reticulum to the Golgi apparatus. ERGIC-53 is encoded on chromosome18[3]. There is no clear evidence that the severity of bleeding is heightened by the concomitant presence of two coagulation defects[4].

Circumcision, as a traditional procedure for Muslims and Jewish people, carries major risk of bleeding in factor VIII-deficient patients[5]. We report an eight-year-old boy with combined factor V and VIII deficiency who underwent circumcision without any significant bleeding with appropriate usage of desmopressin (DDAVP).

Case Report

The patient was an eight-year-old boy diagnosed as mild hemophiliac at one year of age. Diagnosis of combined factor V and VIII deficiency was made after finding factor V level as 28% and factor VIII level as 32%, in order to explain mildly prolonged hematologic parameters (PT=15.8 sec, Control=12.2 sec; apt=46.1 sec, Control=26.7 sec). Before admission, desmopressin test was performed giving 0.3 μg/kg intravenously. After one hour, factor VIII level was 130% and factor V level remained the same. One day before operation tranexamic acid (3x250 mg) and thioridazine (2x10 mg) were started and continued until the 7th day postoperatively. Before the operation, 0.3 μg/kg DDAVP in 100 ml normal saline was given in 15 minutes and 10 ml/kg fresh frozen plasma in 30 minutes. The circumcision was then performed with no bleeding problem. Fibrin glue was not used. DDAVP (0.3 μg/kg IV) was continued every 12 hours for nine consecutive doses. One day after the operation, DDAVP was being given every 12 hours, resulting in a level of factor VIII of 65% on the 2nd day and of 41% on the 4th day. The DDAVP was stopped on the 4th day, and the other medications (tranexamic acid and thioridazine) on the 7th day. The patient had no problems on the 10th day and the operation site had sufficiently healed.

Discussion

Combined factor V and VIII deficiency is a rare inherited coagulation disorder. The factor levels range between 5 to 30%. These patients are more prone to bleeding compared to those

having an isolated factor deficiency with the same levels[2]. Desmopressin (DDAVP) has been used for several years in mild hemophilia and von Willebrand's disease. It acts by mobilization of factor VIII depots and is very useful, especially for minor procedures and hemorrhages[6,7]. Circumcision is a traditional procedure for Muslims and Jewish people. Currently worldwide, one in seven males is circumcised. To achieve safer hemostasis in circumcision of hemophiliac patients, factor VIII level concentration must be 100% and afterwards must be held >50% for several days[5].

Because of high cost and possible transmission of viral diseases, the use of human origin factor concentrates have to be limited, especially in mild cases. For these cases desmopressin is a good alternative, and has been used with success in mild hemophiliacs and in von Willebrand's disease. The factor VIII levels are 2-12 times higher (commonly 3-5) than basal levels after DDAVP administration. In our case the increase of factor VIII level from 32% to 130% was as expected. The gradual decrease after the first dose was due to depletion of the storage sites, but the wound healing was good because the factor VIII levels were still sufficient on the 4th day.

Tranexamic acid as a fibrinolysis inhibitor was used successfully in many hemorrhages of hemophiliacs It is especially useful for bleeding in the oral cavity and has also been used successfully for circumcision[3,8]. Thioridazine was used to prevent erection which is the critical problem after circumcision. No adverse effect was s been with use of these drugs together with DDAVP.

We performed a circumcision in combined factor V and VIII deficiency patient using desmopressin. The level of factor VIII after one hour of DDAVP administration was four times higher as expected. On the 2nd day and 4th day the decrease in factor VIII levels was due to depletion of stores. We think that four days of factor VIII coverage for combined factor V and VIII deficiency is enough in the case of circumcision. If the initial level of factor VIII is not very low, as in mild hemophiliacs, desmopressin is a good alternative.

REFERENCES

1. Oeri J, Matter M, Isenschimid H, et al. Angeborener mangel an factor V (parahaemophilia). Verbunden mir echter haemophilie. A bein zwei brudern. Med Probl Paediatr 1954; 1: 575.
2. Gingburg D, Nichols WC, Zivelin A, Kaufman RJ, Seligsohn U. Combined factors V and VIII deficiency-the solution. Haemophilia 1998; 4: 677-682.
3. Montgomery RR, Scott JP. Hereditary clotting factor deficiencies. In: Behrman RE, Kleigman RM, Jenson HB (eds). Nelson Textbook of Pediatrics (16th ed). Philadelphia: WB Saunders; 2000: 1508-1516.
4. Peyvandi F, Tuddenham EG, Akhtari AM, Lak M, Manucci PM. Bleeding symptoms in 27 Iranian patients with the combined deficiency of factor V and factor VIII. Br J Haematol 1998; 100: 773-776.
5. Kavaklı K, Aledort LM. Circumcision and haemophilia: a perspective. Haemophilia 1998; 4: 1-3.
6. Manucci PM, Ruggeri ZM, Pareti FL, Capitanio A. 1-Deamino-8-d arginine vasopressin: a new pharmacological approach to the management of hemophilia and von Willebrand's diseases. Lancet 1977; 1: 869-872.
7. Manucci PM. Traetmant of von Willebrnad disease. Haemophilia 1998; 4: 661-664.
8. Lusher JM, Haemophilia A and B. In: Lillegman J, Hann I, Blanchette V (eds). Pediatric Hematology (2nd ed). London: Churchill Livingstone; 1999: 585-600.