

The Use of Recombinant Factor VIIa in a Child with Glanzmann Thrombasthenia

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ABSTRACT

Glanzmann thrombasthenia is an autosomal recessive disorder of platelet aggregation that is characterized by a life-long bleeding tendency due to quantitative and qualitative abnormalities of the platelet membrane complex glycoprotein IIb/IIIa (Gp IIb/IIIa). Platelet transfusion is the standard treatment for severe bleeding and surgical support is necessary in these patients. However, repeated platelet transfusions can result in alloimmunization, which makes subsequent transfusions ineffective. Recombinant activated factor VIIa (rFVIIa) has recently been introduced as an alternative to platelet transfusion for treatment of bleeding episodes and to cover surgery in patients with hereditary platelet function defects. We report a 8-year-old child with Glanzmann thrombasthenia. The patient had been treated by nasal tampon placement because of epistaxis three years ago in another hospital. We detected perforation of nasal septum and deformation of nasal bone due to granulation tissue induced by forgotten nasal tampon. Forgotten tampon was removed and granulation tissue was resected. Bolus injections of rFVIIa (90 µg/kg) was given immediately before operation and three times with 2 hours intervals after the surgery. The patient was discharged from hospital without any bleeding complication or thrombocyte replacement.

Key Words: Glanzmann thrombasthenia, Recombinant activated factor VIIa, Child

ÖZET

Glanzmann Trombastenili Bir Çocukta Rekombinant Faktör VIIa Kullanımı

Glanzmann trombastenisi platelet membran kompleks glikoprotein IIb/IIIa (GpIIb/IIIa) daki kalitatif veya kantitatif anormallikler nedeni ile yaşam boyu kanamaya eğilim ile karakterize otozomal resesif olarak geçen platelet agregasyon bozukluğudur. Cerrahi esnasında ve şiddetli kanamalarda standart tedavi rejimi olarak platelet transfüzyonu uygulanmaktadır. Bununla birlikte tekrarlayan trombosit süspansiyonu transfüzyonları, ardışık transfüzyonların etkisiz hale geldiği alloimmünizasyona neden olabilmektedir. Rekombinant aktive faktör VIIa (rFVIIa) herediter platelet fonksiyon defektli hastalarda cerrahi de ve kanama episodlarının tedavisinde alternatif bir metod olarak son zamanlarda karşımıza çıkmaktadır. Biz glanzmann trombastenili sekiz yaşında bir vakayı sunduk. Hastamız, 3 yıl önce başka bir hastanede burun kanamasını durdurmak amacı ile nasal tampon uygulanarak tedavi edilmiş. Biz hastamızda unutulmuş nasal tampon nedeni ile oluşan granülasyon dokusunun nedeni olduğu nasal septum perforasyonu olduğunu belirledik. Unutulan tampon çıkarıldı ve granülasyon dokusu rezeke edildi. rFVIIa (90 µg/kg) operasyondan önce bolus injeksiyon tarzında ve operasyondan sonra da 3 kez 2 saatlik intervallerle verildi. Hasta, trombosit replasman tedavisi veya herhangi bir kanama komplikasyonu olmaksızın hastaneden taburcu edildi.

Anahtar Kelimeler: Glanzmann trombastenisi, Rekombinant aktive faktör VIIa, Çocukluk çağı

INTRODUCTION

Glanzmann's thrombasthenia (GT) is a rare autosomal recessive inherited disorder of platelet function caused by a quantitative or qualitative defects of the platelet membrane glycoprotein (GP) IIb-IIIa complex (1,2) Clinical manifestations include easy bruising, purpura, epistaxis, gingival bleeding, menorrhagia and, less frequently, gastrointestinal bleeding, hematuria, hemarthrosis, muscle hematoma and central nervous system bleeding. Local procedures and desmopressin, steroid, and antifibrinolytic agents can be useful for treatment (3). When bleeding does not respond to local measures and/or antifibrinolytic drugs, platelet transfusion is currently the standard treatment. However, repeated platelet transfusions may result in GP IIb-IIIa and/or HLA immunization, and development of platelet refractoriness (1). Blood products also carry other risks, including infections (4). Recombinant activated factor VIIa (rFVIIa) has recently been introduced as an alternative to platelet transfusion for treating bleeding episodes and to cover surgery in patients with hereditary platelet function defects.

We report our experience with the use of rFVIIa in a 8 years old boy for intranasal granulation tissue resection.

CASE REPORT

A 8-year-old boy diagnosed as Glanzmann thrombasthenia by other center was referred to our department in March 2005. He has been followed with Glanzmann thrombasthenia for 4 years. He complained difficulty in breathing and recurrent upper respiratory tract infections. We observed a big perforation at nasal septum and granulation tissue related with forgotten nasal tampon on nasal examination. Results of complete blood count were as follows: hemoglobin 8.9 g/dl, mean corpuscular volume (MCV): 64 fl, white blood cell count 4800/mm³, and platelet count 321.000/mm³. He was hospitalized for removal of the granulation tissue. In our patient alloimmunisation had developed due to frequent platelet transfusions to stop resistant nasal and gingival bleedings prior to the admission. The patient was operated with local anesthesia. Forgotten tampon was removed and granulation tis-

sue was resected. Bolus injection of rFVIIa (90 µg/kg) was given immediately before operation and three times with 2 hours intervals after the surgery. The patient was discharged one day after without any complication.

DISCUSSION

Glanzmann thrombasthenia, bleeding can be an extremely serious problem and difficult to solve. Sometimes conventional treatments cannot stop the bleeding (3). Local treatment for nostril bleeding, such as tampons or cauterization, may increase the risk of iatrogenic bleeding. In addition, recurrent platelet transfusions have risk for adverse reaction, infective agents, and alloimmunization (5). In our patient alloimmunisation had developed before admission. The treatments of choice for stopping the bleeding in Glanzmann thrombasthenia are very limited (3,5). In the literature, it has been demonstrated that rFVIIa is a one alternative treatment for bleeding and surgical support with a less adverse effect. In 1996 Tengborn and Petruson (6) reported successful treatment with rFVIIa of a 2-year-old child with GT who had not responded to conservative treatment for severe epistaxis. There are a Canadian pilot study (7) performed on four GT children and a British study of five GT patients (8), beside some case studies.

Recombinant factor (rF)VIIa is currently approved for the treatment of hemophilia patients with inhibitors (9). Nowadays, the clinical efficacy of rFVIIa in thrombasthenic patients is not clear. Thrombin generation is impaired in GT patients. The ability of high-dose rFVIIa to improve thrombin generation through direct binding to activated platelets and/or overcoming the inhibitory effect of zymogen FVII may contribute to its therapeutic efficacy in GT patients (10). The hypothesis on the mechanism of rFVIIa is that it may activate coagulation on the platelet surface (7). FVIIa is postulated to act on platelets to activate factors IX and X and thus enhance thrombin generation. Other experimental work has suggested that FVIIa can restore platelet adhesion defect by tissue factor-independent rFVIIa-mediated thrombin formation (11).

rFVIIa given as bolus injections appears to be a safe and the most effective alternative to platelet transfusion for the treatment and prevention of bleeding in patients with GT, particularly for those with antiplatelet antibodies and/or refractoriness to platelet transfusions. Until more data become available, the following treatment regimen for moderate to severe bleeding is suggested: bolus injections of 90 µg/kg per injection every 2 hours until the cessation of bleeding. One or more maintenance dose may be used to prevent recurrences. We used total 4 doses of rFVIIa as follows one dose was given immediately before operation and three times with 2 hours intervals after the surgery.

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