Case Report

Report 2 Cases of Congenital Factor XII Deficiency: A Rare Coagulation Disorder

Somjai Kanjanapongkul MD*

** Hemato/Oncology Unit. Queen Sirikit National Institute of Child Health, College of Medicine, Rangsit University, Bangkok, Thailand*

Factor XII (F.XII, Hageman factor) is one of the contact system factors which initiates an intrinsic coagulation pathway. But its definite role is still unclear, because many cases of severe F.XII deficiency experience thrombotic events instead of a bleeding problem. Moreover, most of them are asymptomatic. There have only been a few reports of F.XII deficiency in Thailand. The author reports two cases of congenital F. XII deficiency in Thai children.

***Keywords**: Prolonged aPTT, Factor XII deficiency, Thrombosis*

J Med Assoc Thai 2011; 94 (Suppl. 3): S231-S232
***Full text. e-Journal:** http://www.mat.or.th/journal*

Factor XII (F.XII, Hageman factor) deficiency is an extremely rare congenital prothrombotic disorder that might contribute to a thromboembolic event, especially during adulthood[1]. Even F.XIIa is involved in the initiation of the intrinsic coagulation pathway; however, several patients with inherited F.XII deficiency, who were identified through findings of activated partial Thromboplastin time (aPT) prolongation, did not result in drastic bleeding symptoms *in vivo*[2-5]. The author described 2 cases of hereditary F.XII deficiency. The laboratory findings showed a very low level of F.XIIa in both cases.

Case 1

A 6-year old girl was admitted to the hospital due to ecchymosis over her legs and arthritis of the left ankle. Numerous red blood cells were found in her urine examination. She was diagnosed as Henoch-Schonlein purpura (HSP). There was no history of bleeding tendency or hypercoagulability in her parents and siblings. After receiving symptomatic treatment, her clinical condition was going well. Her blood tests were as follows: Hb 12.6 g/dl, Het 36.8%, WBC 11,500/mm^3, aPTT > 150 sec (control 29.6 sec), prothrombin time 15.0 sec (control 14.9 sec), thrombin time 5.5 sec (control 5.8 sec), albumin 4.57 g/dl globulin 2.99 g/dl, ALT 19 u/l, AST 8 u/l, ANA profile negative, C3 1,343 mcg/ml (normal 750-1,400), CH50 100%. Two repeated tests for aPTT were performed and the results were prolonged as well. Lupus anticoagulant screening tests were also negative. Factor levels were also done. The results were as follows: vW antigen 128%, ristocetin co-factor activity 100%, F.VIII > 100%, F.IX 60% and F.XI 94%. F.XII activity was found to be less than 1%. During the follow-up period, she underwent minor surgical procedure such as dental extraction without prolonged bleeding symptom. Her family's genetic mutation on F.XII gene was studied.

Correspondence to:
Kanjanapongkul S, Hemato/Oncology Unit, Queen Sirikit National Institute of Child Health, Bangkok 10400, Thailand.
Phone & Fax: 0-2354-8439
E-mail: somjaik@childrenhospital.go.th

Case 2

A 14-year old female was referred to investigate the problem of prolonged aPTT > 180 sec. The abnormal aPTT was accidentally found during the course of her admission due to a dengue viral infection. One month after recovery from illness, aPTT was still prolonged > 140 sec, with normalized CBC and PT. She had not experienced abnormal prolonged bleeding symptom. Her family history had no bleeding tendency. The laboratory findings showed correctable aPTT by mixing test 1: 1 vWF antigen was 70.7%. F.XII level was 3%.

Discussion

The biological role of F.XII is not yet fully understood. Because F.XII is one of the contact system factors that initiates fibrinolysis[8], there was a suspicion that deficiency of F.XII could paradoxically

result in hypercoagubility. Thus, there is the possibility that F.XII deficiency might be related to thrombotic events, such as thromboembolism, acute coronary syndromes[1,5,6,9], or recurrent fetal loss. However, some studies suggested that there was an association between F.XII deficiency and thrombotic events[10,11]. Even heterozygous F.XII deficiency is common in Caucasian populations[6,7], but homozygous F.XII deficiency is rare. Severe F.XII deficiency in Asian people is usually asymptomatic. There are only a few reports of clinical data and genetic mutation of the F.XII gene in Thai people[12]. Here, the author described two pediatric patients of hereditary F.XII deficiency.

Potential conflicts of interest

None.

References

1. Taylor M, Mathew P, Grebe T, Martinez L, Berry K, Spector E. Genetic consideration in thrombotic disorders. Pediatric thrombotic disorders: Genetic Drift 2002; Fall: 7-10.
2. Kanaji T, Okamura T, Osaki K, Kuroiwa M, Shimoda K, Hamasaki N, et al. A common genetic polymorphism (46 C to T substitution) in the 5'-untranslated region of the coagulation factor XII gene is associated with low translation efficiency and decrease in plasma factor XII level. Blood 1998; 91: 2010-4.
3. Schloesser M, Zeerleder S, Lutze G, Halbmayer WM, Hofferbert S, Hinney B, et al. Mutations in the human factor XII gene. Blood 1997; 90: 3967-77.
4. Girolami A, Ruzzon E, Lombardi AM, Cabrio L, Randi ML. Thrombosis-free surgical procedures in severe (Homozygote) factor XII deficiency: report of four additional cases and literature review. Clin Appl Thromb Hemost 2004; 10: 351-5.
5. D'Uva M, Strina I, Mollo A, Ranieri A, De Placido G, Di Micco P. Acquired factor XII deficiency in a woman with recurrent pregnancy loss: working on a differential diagnosis in a single case. J Transl Med 2005; 3: 43.
6. Kitchens CS. The contact system. Arch Pathol Lab Med 2002; 126: 1382-6.
7. Bolton-Maggs PHB. The rare coagulation disorders. Treatment of hemophilia. Manchester: World Federation of Hemophilia; 2006.
8. Braat EA, Dooijewaard G, Rijken DC. Fibrinolytic properties of activated FXII. Eur J Biochem 1999; 263: 904-11.
9. Yamada H, Kato EH, Ebina Y, Kishida T, Hoshi N, Kobashi G, et al. Factor XII deficiency in women with recurrent miscarriage. Gynecol Obstet Invest 2000; 49: 80-3.
10. Koster T, Rosendaal FR, Briet E, Vandenbroucke JP. John Hageman's factor and deep-vein thrombosis: Leiden thrombophilia Study. Br J Haematol 1994; 87: 422-4.
11. Girolami A, Morello M, Girolami B, Lombardi AM, Bertolo C. Myocardial infarction and arterial thrombosis in severe (homozygous) FXII deficiency: no apparent causative relation. Clin Appl Thromb Hemost 2005; 11: 49-53.
12. Jinda W, Thongnoppakhun W, Limwongse C, Nakkinkun Y, Ruchutrakool T. A novel homozygous mutation (C54S) identified in the FXII (F12) gene of a Thai patient with coagulation factor XII deficiency. Siriraj Med J 2008; 60 (Suppl 1): 60.

รายงานผู้ป่วยเด็ก 2 รายที่ขาดปัจจัยการแข็งตัวของเลือด factor XII

สมใจ กาญจนาพงศ์กุล

Factor XII เป็นหนึ่งในปัจจัยการแข็งตัวของเลือดตั้งต้น แต่มีรายงานผู้ป่วยที่ขาด factor XII ในประเทศไทยน้อยมาก ผู้ป่วยมักจะไม่มีปัญหาเลือดออกง่ายแต่มีรายงานพบลิ่มเลือดอุดตันง่ายกว่าคนปกติ ซึ่งมักเป็นผู้ป่วยผู้ใหญ่ ผู้นิพนธ์ได้รายงานผู้ป่วยเด็กหญิง 2 ราย ที่ตรวจพบว่ามีค่า aPTT ยาวผิดปกติ โดยไม่มีอาการเลือดออกง่ายหรือมีลิ่มเลือดอุดตันจากการตรวจหาสาเหตุพบว่าผู้ป่วย 2 รายนี้มีระดับ factor XII ที่ต่ำมาก