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Congenital Coagulation Factor VII Deficiency: A Phenotype and Genetic Study in Taiwan

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Introduction:

- **Congenital factor VII (FVII) deficiency is a rare coagulation disorder inherited by autosomal recessive pattern with an estimated incidence of 1/500,000 in the general population.**
- **Its clinical and genetic studies in Asian countries are relatively limited than those from the West.**

Materials and methods:

- **From January 2009 to March 2014, there were 9 unrelated patients (6 men and 3 women) with congenital factor VII deficiency diagnosed and enrolled in this study.**
- **Their clinical manifestations, prothrombin time (PT), FVII coagulation activity and causative mutation of FVII gene were analyzed. All exons of FVII gene were amplified using polymerase chain reaction and followed by direct sequence.**

Results:

- **Their median age was 29 y/o; the mean age was 39.3 y/o with a range of 14-80.**
- **The clinical symptoms of this cohort were very variable, including no symptom, easy bruising, epistaxis, menorrahgia, prolonged bleeding after injury and life-threatening gastrointestinal bleeding.**
- **The median time of PT was 38.6 sec, the mean time of PT was 39.3 sec, with a range of 14.1 to 92.4 sec. The median coagulatioon FVII acitivity was 8.8%, the mean activity was 9.4%, ranging from 0.6% to 23.7%.**
- **There was no correlation between the circulating FVII activity and the clinical bleeding manifestations.**
- **Compound heterozygous and homozygous mutations were detected in four and three patients, respectively; and the rest of two patient was found to have heterozygous mutation in only one allele.**
- **Novel mutation: IVS5+2T>C found on Patient 5 and 6 is first reported.**
- **Two of the 3 patients with homozygous mutation were found to have double homozygous mutations (Patient 5 and 6).**
- **Seven of the 9 patients (77.8%) have Exon 8 coding mutations which were mostly found in our study.**

Table 1. Clinical informations, laboratory findings and genetic mutation site of the 9 patients with coagulation factor FVII deficiency

Patient	Age(Y) /Sex	Clinical manifestations	PT (sec)	FVII:C (%)	FVII:Ag (%)	Mutation site	comment
1	29/F	Easy bruising, menorrhagia,	45.2	9.5	8	IVS6+1G>T E8: c.1009C>T; R337C	Compound heterozygous
2	23/M	Epistaxis, prolonged bleeding after minor cut injury	63.4	2.8	77.8	E8: c.1091G>A, R364Q	Heterozygous
3	25/M	Colon bleeding	16.2	21.8	66.2	E8: c.1091G>A, R364Q -122C, -325ins10	Compound heterozygous
4	80/M	GI bleeding	22	8.8	9.7	E7: c.1009C>A;R337C	homozygous
5	69/F	Asymptomatic	44.2	4.1	10.2	IVS5+2T>C E8: c.1224T>G;H408Q	Double homozygous
6	53/F	Asymptomatic	92.4	0.6	ND	IVS5+2T>C E8: c.1165T>G: C389G	Double homozygous
7	43/M	Spontaneous GI bleeding	38.6	2.8	ND	E7:c.722C>A;T241N E8:c.1224T>G:H408Q	Compound heterozygous
8	14/M	Asymptomatic	17.4	13.5	ND	IVS5-1G>A E8:c.1091G>A, R364Q	Compound heterozygous
9	18/M	Ecchymosis over the site of venipuncture	14.1	23.7	ND	IVS6+1G>T -122C	Heterozygous

ND: not done

Conclusion:

- **FVII coagulation activity did not correlate with clinical bleeding symptoms.**
- **The most common genetic mutation were located in exon 8 including compound heterozygous and double homozygous mutations.**
- **More patients are needed to investigate further whether there is racial differences in genotypes and phenotypes of congenital FVII deficiency between Taiwanese and those in western countries.**

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