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Case Report

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Deficiency of coagulation factor VII in a 4 years old child with 13q deletion syndrome: a case report

Abstract

Background: Factor VII deficiency is rare inherited bleeding disorders, have been identified in the Factor VII gene located on chromosome 13 with very few cases reported. Factor VII deficiency was first described by Alexander et al. in 1951.The disorder has also been known as Alexander's disease. It is the rare inherited bleeding disorders' with an estimated incidence of 1 case per 3,00,000 to 5,00,000 individuals.

Objective and method: We did a case report and literature review for deficiency of coagulation factors VII was found in a 4 years patient who had chromosomal aberration 13q deletion syndrome (46, XX, del 13q32-13q33). This loci involved in synthesis or constitution of factor VII.

Results: A review of the gene map of chromosome 13 indicated that Factors VII and X are coded on the long arm of chromosome 13, within the deleted region.

Conclusion: Congenital Factor VII deficiency is a rare cause of bleeding disorder, which should be suspected in a bleeding child presenting in infancy when platelets and aPTT are normal with abnormal PT. Congenital Factor VII deficiency association with 46, XX, del (13q32– 13q33) syndrome is very rare disorder and further cases should be reported to know the outcome and the risk of complication in such a cases.

Keywords: 13q deletion syndrome, factor VII deficiency, factor 7 deficiency, partial monosomy of the long arm of chromosome 13, factor VII

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Introduction

Factor VII deficiency is rare inherited bleeding disorders, have been identified in the Factor VII gene located on chromosome 13 with very few cases reported.[1, 2] Factor VII deficiency was first described by Alexander et al. in 1951.[3] The disorder has also been known as Alexander's disease. It is the rare inherited bleeding disorders' with an estimated incidence of 1 case per 3,00,000 to 5,00,000 individuals.[4] Factor VII deficiency can be acquired during life; this report deals with the genetic form, which is present at birth (although symptoms may develop later).

Case presentation

A 4 year-old female presented with factor VII deficiency and 13 q deletion syndrome. She was the first child of a 30-year-old mother with no history of miscarriage and 29 year- old father with a second-degree consanguinity. This pregnancy was complicated by premature rupture of membrane for 36 hours prior C section due to oligohydramnios.

She was born at 37 weeks of gestational. Her birth weight was 2.1 kg (< 10th centile), height 46cm (10th centile), head circumference 29.5 cm (10th centile) and Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. At birth, she was noted to have facial dysmorphism, microcephaly and anterior anus displacement, so referred for genetics work-up, including karyotype revealed a deletion of chromosome 13(46, XX, del 13q32-13q33). Both an echocardiogram and a renal ultrasound showed ASD 3-5 mm with a left to right shunt and bilateral hydronephrosis and pelvictasia, respectively.

A generalized seizures had been developed at the age of 3 years, however brain MRI showed that the ventricular system appears slightly prominent with clear visualization of CSF spaces, but EEG revealed sub cortical epilepsy with right-brain predominance that have been successfully managed with antiepileptic medication. As part of her pre-operative work-up for dental abscess, she was discovered to have elevated Prothrombin 19.6 sec, so referred to pediatric hematology clinic for further assessment and the mother endorsed history of epistaxis twice per month in last two months that not require medical treatment and stopped spontaneously, but there was no family history of bleeding disorders or history of bleeding from other mucosal surfaces such as gum bleeding, hematuria, hematochezia, melena , swelling in joints, and spontaneous skin bruising.

On physical examination, the patient's height is 108 cm (50th centile), his weight is 17 kg (50th centile) and his head circumference is 43 cm (3rd centile). She has dysmorphic features microcephaly, broad nasal bridge and micrognathia. Her skin shows no ecchymosis or petechiae. His ears are normally placed without tags or pits. Her palate and uvula are normal without petechiae. She has normal heart rate, rhythm regular with grade 2 ejection systolic murmur audible over the left 2nd &3rd intercostals space .her lung, abdominal, back and rectal examination are unremarkable. Her neurological examination shows developmental delay, intellectual disability, behavioral problems, microcephaly, mild hypotonia, normal reflexes and walk incoordination.

Laboratory investigations demonstrated hemoglobin 80 g/L and platelet count 596×10^9/L. Liver and kidney function tests were normal; however, the Prothrombin time (PT) was prolonged 19.6 sec (12.6 -14.61 sec). The activated partial thromboplastin time (APTT) was 39.2 sec (normal range, 29.9 - 40.3 sec). Then Factor VII deficiency (24% of normal) was subsequently diagnosed after factor assays were done and summarized in table 1 and 2 below.

Table 1 Summary of coagulation studies and factor levels in patients

	Patient result	Normal range
Prothrombin time (PT)	19.6 sec	(12.6-14.61 sec).
The activated partial thromboplastin time (APTT)	39.2 sec	(29.98-40.39 sec).
International Normalized Ratio (INR)	1.5	(0.9 -1.15)
Fibrinogen	272mg/dl	(207.14-417.14)
Factor VII	low 24 %	(60-150)
Factor X	107%	(60-150)
Von will brand antigens	83%	(70-130)
Von will brand factors RCO	81%	(50-200)

Table 2 Summary of factor levels in the patient and her parents

	Patient	Father	Mother
Factor VII	24% (low)	112% (normal)	89% (normal)
Factor X	95% (normal)	117% (normal)	91% (normal)

Chromosome karyotyping was performed for the patient and her parents showed 13q deletion syndrome (karyotype 46, XX, del(13q32–13q33) on the long arm of one chromosome 13, father was a carrier for balanced translocation of chromosome 13 & 8 at the q arm and the mother's chromosome was normal, respectively.

A review of the gene map of chromosome 13 indicated that Factors VII and X are coded on the long arm of chromosome 13, within the deleted region. Functional Factor VII and X assays were performed for the patient and her parents. The index case demonstrated a Factor X level of 95% and a Factor VII level of only 24%. Factor VII deficiency was diagnosed. Maternal results were 91% (Factor X) and 89% (Factor VII), and paternal results were 117% (Factor X) and 112% (Factor VII).

Discussion

A review of the gene map of chromosome 13 indicated that Factors VII and X are coded on the long arm of chromosome 13, within the deleted region.[5] Pfeiffer[6] described two cases of 13q terminal deletion with associated subclinical deficiency of Factors VII and X (in each case activity of these factors was around 50% of the normal value). The genes for Factors VII and X were subsequently mapped to13q34 by Gilgenkrantz et al. It is probable that patients with 13q deletion syndromes involving the Factor VII region have a greatly increased rate of Factor VII deficiency compared to the general population, with a rate of Factor VII deficiency approximating the background frequency of the heterozygous or carrier state. Hewson and Carter described severe Factor VII deficiency in a case of 13q deletion syndrome.[7] Our patient factor Vll deficiency that manifested as elevated PT, would be 13q32-33 (similar case is present in letterature: Balci S, et all, Genet Couns, 2010;21(3):317–312.[8]

Clinical bleeding can widely vary and does not always correlate with the level of FVII coagulant activity measured in plasma. Mortality is related to severe bleeding, most often resulting from CNS hemorrhage. Most severe cases of FVII deficiency are diagnosed during childhood, often during the first 6 months of life. In infancy, the most common bleeds occur in the gastrointestinal tract or CNS, accounting for 60–70% of bleeds in this age grou.[9,10]

The PT is prolonged in FVII deficiency and the INR is elevated. The aPTT is within the reference range in isolated FVII deficiency as seen in the index case. FVII assays are performed by using thromboplastin-dependent one-stage clotting assay. The more sensitive thromboplastins, usually recombinant human thromboplastin, are preferred for measuring FVII activity in the very low range.

Conclusion

Congenital Factor VII deficiency is a rare cause of bleeding disorder, which should be suspected in a bleeding child presenting in infancy when platelets and aPTT are normal with abnormal PT. Congenital Factor VII deficiency association with 46, XX, del (13q32– 13q33) syndrome is very rare disorder and further cases should be reported to know the outcome and the risk of complication in such a cases.

Conflicts of interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report.

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Addendum

All authors contributed to data collection, literature review and writing the paper.

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