Original Research Paper

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Pediatrics

A CASE REPORT OF COMBINED FACTOR V AND FACTOR VIII DEFICIENCY

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ABSTRACT Combined deficiency of factor V (FV) and factor VIII (FVIII) (F5F8D, or FV+FVIII) is a autosomal recessive bleeding disorder which is caused by mutations in genes encoding two components of the endoplasmic reticulum (ER)-Golgi intermediate compartment (ERGIC-53), that is, lectin mannose binding protein (LMAN1) and multiple coagulation factor deficiency 2 (MCFD2), involved in the FV and FVIII intracellular transport rather than by DNA defects in the genes that encode the corresponding coagulation factors. F5F8D is estimated to be extremely rare (1:1,000,000) in the general population, but an increased frequency is observed in regions where consanguineous marriages are practiced. F5F8D is characterized by concomitantly low levels (usually between 5% and 20%) of both FV and FVIII and is associated with a mild to moderate bleeding tendency(1). We described a case of 8 months old male child who presented with prolonged bleeding with minor trauma, and echymotic patches. On evaluation there is increased clotting time, PT, APTT, INR with normal platelet counts and LFTs and decreased levels of both factor V and VIII. Child was given factor VIII concentrate and FFP which normalizes coagulation profile and symptomatic improvement.

KEYWORDS : Factor V deficiency, Factor VIII deficiency, bleeding time, PT, APTT, INR, ER)-Golgi intermediate compartment (ERGIC-53).

Introduction

In 1954, Oeri et al. first described combined factor V and factor VIII deficiency, which is a rae autosomal recessive disorder. History of consanguinity present. It is likely to be due to a single gene defect (located on long arm of chromosome 18), leading to deficiency of a transport protein, rather than due to coinheritance of separate defects of factor V and factor VIII genes.

Affected individuals have reduced plasma levels of both factor V and factor VIII[2].

Shetty et al. from India reported nine patients from five unrelated families of combined factor V and factor VIII deficiency, youngest being an 8 year old girl[3].

Clinical features are mild bleeding symptoms, such as easy bruising and epistaxis. The most common manifestations observed were prolonged bleeding from cuts, easy bruisability, bleeding gums and post dental extraction bleeding. Following a dental extraction or surgery, bleeding is a common phenomena. In affected women menorrhagia and post partum hemorrhage is seen.

Case report

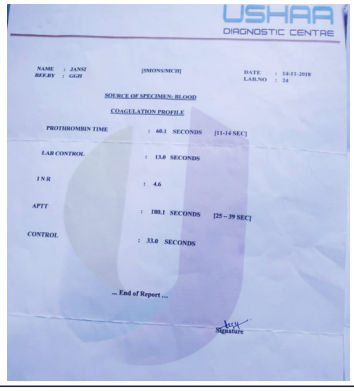
8 months old male child presented with echymotic patches over chest. Past history was significant with prolonged bleeding from minor trauma and hematomas at the injection site. But there was no h/o hemarthroses. On evaluation PT was 60.1 seconds with INR 4.6 and APTT was 180.1 seconds. Platelet counts and functional assay of platelets were within normal limit. Coagulation factor assays and von willebrand panel were obtained which showed factor V activity was 3 % and factor VIII activity was 5 % in the setting of normal VWF panel, a diagnosis of combined factor V and factor VIII deficiency was made. Liver function tests were normal. Molecular testing could not be done in present case. And pedigree analysis- baby was first order born to second degree consanguinous parents. Baby was managed with factor VIII concentrate and FFP transfusions. And baby's clinical and coagulation profile was subsequently improved. And baby was discharged with proper parental counseling regarding the disease.

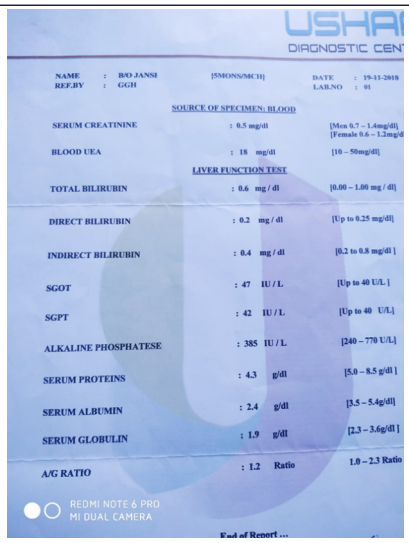
Investigations	
Hb	10 gm%
Platelet count	280000
Platelet functional analysis	Normal
PT	60.1
INR	4.6
APTT	180.1
Factor VIII levels	<5%
Factor IX levels	40%
Factor V functional assay	<3%

Discussion

F5F8D represents approximately 3% of all rare congenital bleeding disorders, with a prevalence of 1:1,000,000 in unselected populations.[4] Approximately 60–80% of F5F8D patients present with prolonged bleeding following injury or surgery. Gingival bleeding occurs in more than 50% of patients. Hemarthroses, typical of hemophilia A and B, occur in less than a third of patients.[4] The majority of patients are of Middle Eastern or Indian descent. The inheritance pattern is autosomal recessive. Two distinct mutations have been discovered: defects in the Lectin Mannose Binding Protein 1 (LMAN1), first identified in 1998; and defects in the Multiple Coagulation Factor Deficiency gene 2 (*MCFD2*), first identified in 2003.[5] The protein products of these genes are involved in trafficking of factors V and VIII from the endoplasmic reticulum to the Golgi apparatus. MCFD2 and LMAN1 normally occur in 1:1 stoichiometry and allow for the folding and transport of both coagulation factors. In the absence of one of these proteins, neither factor can be transported outside the cell and thus are not available to participate in hemostasis.

In the above reported case male baby born to a consanguinous marriage presented with echymotic patches and prolonged bleeding from minor injuries with significant past history of similar complaints, we evaluated for clotting factor deficiencies. On evaluation PT, APTT both were prolonged which implies there was both intrinsic and extrinsic coagulation pathway defects. Coagulation profile analysis showed < 3% of factor V and < 5 % of factor VIII levels which was showing combined factor V and factor VIII deficiency. As a result, in the cases with a suspect of hereditary bleeding disorder who show simultaneous prolongation of PT and aPTT possibility of combined FV and FVIII deficiency should be considered. The cases with factor levels below 5% should be monitored closely, like the patients with severe hemophilia.





USHA
DIAGNOSTIC CEN

NAME : B/O JANSI [5MONS/MCH] DATE : 19-11-2018
REF.BY : GGH LAB.NO : 01

SOURCE OF SPECIMEN: BLOOD

SERUM CREATININE	: 0.5 mg/dl	[Men 0.7 – 1.4mg/dl] [Female 0.6 – 1.2mg/d
BLOOD UEA	: 18 mg/dl	[10 – 50mg/dl]

LIVER FUNCTION TEST

TOTAL BILIRUBIN	: 0.6 mg / dl	[0.00 – 1.00 mg / dl]
DIRECT BILIRUBIN	: 0.2 mg / dl	[Up to 0.25 mg/dl]
INDIRECT BILIRUBIN	: 0.4 mg / dl	[0.2 to 0.8 mg/dl]
SGOT	: 47 IU / L	[Up to 40 U/L]
SGPT	: 42 IU / L	[Up to 40 U/L]
ALKALINE PHOSPHATESE	: 385 IU / L	[240 – 770 U/L]
SERUM PROTEINS	: 4.3 g/dl	[5.0 – 8.5 g/dl]
SERUM ALBUMIN	: 2.4 g/dl	[3.5 – 5.4g/dl]
SERUM GLOBULIN	: 1.9 g/dl	[2.3 – 3.6g/dl]
A/G RATIO	: 1.2 Ratio	1.0 – 2.3 Ratio

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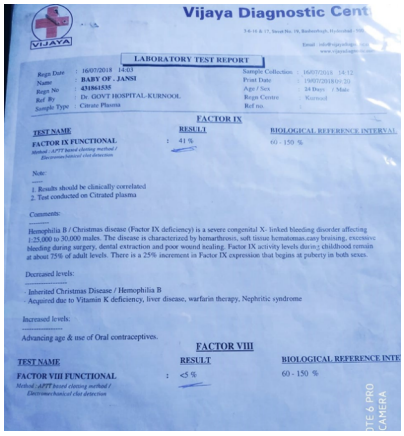

Vijaya Diagnostic Cent

LABORATORY TEST REPORT

Regn Date : 16/07/2018 14:03
Name : BABY OF . JANSI
Regn No : 431861835
Ref By : Dr. GOVT HOSPITAL-KURNOOL
Sample Type : Citrate Plasma
Sample Collection : 16/07/2018 14:12
Print Date : 19/07/2018 01:20
Age / Sex : 24 Days / Male
Regn Centre : Kurnool
Ref no. :

FACTOR IX

TEST NAME	RESULT	BIOLOGICAL REFERENCE INTERVAL
FACTOR IX FUNCTIONAL	: 41 %	60 - 150 %

Method : APTT based clotting method / Electromechanical clot detection

Note:
1. Results should be clinically correlated
2. Test conducted on Citrated plasma

Comments:

Hemophilia B / Christmas disease (Factor IX deficiency) is a severe congenital X- linked bleeding disorder affecting 1:25,000 to 30,000 males. The disease is characterized by hemarthrosis, soft tissue hematomas,easy bruising, excessive bleeding during surgery, dental extraction and poor wound healing. Factor IX activity levels during childhood remain at about 75% of adult levels. There is a 25% increment in Factor IX expression that begins at puberty in both sexes.

Decreased levels:
- Inherited Christmas Disease / Hemophilia B
- Acquired due to Vitamin K deficiency, liver disease, warfarin therapy, Nephritic syndrome

Increased levels:
Advancing age & use of Oral contraceptives.

FACTOR VIII

TEST NAME	RESULT	BIOLOGICAL REFERENCE INTE
FACTOR VIII FUNCTIONAL	: <5 %	60 - 150 %

Method : APTT based clotting method / Electromechanical clot detection

Dr Lal PathLabs

528 - SITHARA DIAGNOSTIC
KURNOOL

Name	: BABY OF JANSI			Collected	: 1/12/2018 11:45:00AM
Lab No.	: 249083276	Age: 6 Months	Gender: Male	Received	: 2/12/2018 1:46:21PM
A/c Status	: P	Ref By : GOVT.HOSPITAL		Reported	: 7/12/2018 5:36:43PM
				Report Status	: Final

Test Name	Results	Units	Bio. Ref. Interval
FACTOR V, FUNCTIONAL @ (Photo Optical Clot Detection)	<3.00	%	70.00 - 120.00

Result Rechecked.
Please Correlate Clinically.

Advised:
Followup and clinical correlation
Note
1. Results should be clinically correlated
2. Test conducted on Citrated plasma

Comments
Factor V / Proaccelerin / Labile factor deficiency is an inherited autosomal recessive disorder which is usually asymptomatic. Homozygous Factor V deficiency is rare, leading to easy bruising & mucosal bleeding in children. Patients with Factor V deficiency should also perform Factor VIII assays to evaluate for combined deficiency. Acquired deficiencies may be seen in liver disease and Disseminated Intravascular Coagulation.

Dr. Anil Arora
MD (Pathology)
HOD Hemat & Imm - NRL

End of report

IMPORTANT INSTRUCTIONS

*Test results released pertain to the specimen submitted.*All test results are dependent on the quality of the sample received by the Laboratory. *Laboratory investigations are only a tool to facilitate in arriving at a diagnosis and should be clinically correlated by the Referring Physician.*Samples repeats are accepted on request of Referring Physician within 7 days post reporting.*Report delivery may be delayed due to unforeseen circumstances. Inconvenience is regretted.*Certain tests may require further testing at additional cost for derivation of exact value. Kindly submit request within 72 hours post reporting.*Test results may show interlaboratory variations.*The Courts/Forum at Delhi shall have exclusive jurisdiction in all disputes/claims concerning the test(s) & or results of test(s).*Test results are not valid for medico legal purposes. *Contact customer care Tel No. +91-11-39885000 for all queries related to test results.

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If test results are alarming or unexpected, client is advised to contact the laboratory immediately for possible remedial action.
@ Tests conducted at National Reference Lab, New Delhi, a CAP (7171001), NABL (MC-2113) and ISO (IS 6241:) accredited laboratory

REFERENCES

1. Spreafico M, Peyvandi F. Combined factor V and factor VIII deficiency. Seminars in Thrombosis and Hemostasis. 2009 Jun;35(4):390-399. https://doi.org/10.1055/s-0029-1225761
2. . Peyvandi F, Tuddenham EG, Akhtari AM, Lak M, Mannucci PM. Bleeding symptoms in 27 Iranian patients with the combined deficiency of factor V and factor VIII. Br J Haematol. 1998;100:773-6.
3. Shetty S, Madkaikar M, Nair S, Pawar A, Baindur S, Pathare A, Ghosh K, Mohanty D. Combined Factor V and VIII deficiency in Indian population. Haemophilia. 2000;6:504-47.
4. Viswabandya A, Baidya S, Nair SC, et al. Clinical manifestations of combined factor V and VIII deficiency: a series of 37 cases from a single center in India. Am J Hematol. 2010;85:538-539.
5. Zhang B, McGee B, Yamaoka JS, et al. Combined deficiency of factor V and factor VIII is due to mutations in either LMAN1 or MCFD2. Blood. 2006;107:1903-1907.
6. Textbook of pediatric hematology and hemato-oncology :MR Lokeswar