

Congenital Factor V Deficiency of Coagulation in a Moroccan Family

Ikhlas Mouayche*, Rayhane Bahri, Siham Khayati, Mohammed Chakour, Mustapha Ait Ameer

Laboratory of Hematology, Military Hospital Avicenna of Marrakech, Morocco

DOI: [10.36347/sjmcr.2019.v07i08.020](https://doi.org/10.36347/sjmcr.2019.v07i08.020)

Received: 20.07.2019 | Accepted: 27.07.2019 | Published: 30.08.2019

*Corresponding author: Mouayche Ikhlas

Abstract

Case Report

Congenital factor V deficiency is a rare hereditary abnormality of autosomal recessive coagulation. Factor V is an essential cofactor in the conversion of prothrombin to thrombin by activated factor X. In the absence of this factor, thrombin generation is slowed down and fibrin formation is delayed. This results in a tendency to bleeding. We report a case of factor V deficiency in a Moroccan family following the discovery of an index case. Our work aims to shed light on this rarely diagnosed pathology.

Key-words : Congenital Factor V Deficiency, Hemorrhagic Syndrome, Familial, Coagulation.

Copyright @ 2019: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

Factor V coagulant (VF) also known as proaccelerin is the plasma cofactor of prothrombinase which converts prothrombin to thrombin [1]. It also participates in physiological anticoagulation by deactivating activated factor VIII (FVIII) [1, 2].

Congenital factor V deficiency (DFV) is a rare affection, corresponding to a coagulation disorder reported for the first time in 1947 by OWREN, under the term para-haemophilia [3]. autosomal recessive and generally symptomatic in the homozygous state [4]. It can be manifested at any age by a haemorrhagic syndrome of variable intensity [3].

We report a family case of a constitutional deficiency isolated in FV, diagnosed in the Hematology laboratory of the Military Hospital Avicenna of Marrakech. In order to sensitize general practitioners and specialists on the importance of determining coagulation factors in case of anomaly of the balance of hemostasis.

CASE REPORT

This is a male child (index case № 1), 12 years old, 2nd child of 5 siblings (3 boys and 2 girls), originally from Marrakech, from a non-consanguineous marriage, having as antecedents haemorrhagic manifestations such as epistaxis and spontaneous ecchymoses with severe bleeding episodes especially post-traumatic requiring sometimes hospitalization for blood transfusion. It was sent to the Hematology laboratory of the Military Hospital Avicenna in

Marrakech for exploration of the bleeding syndrome following a tooth extraction.

The first initial assessment showed a TP at 69% and a TCA always elongated with a ratio of 1.30 corrected by mixing with a normal plasma. This assessment was recontrolled on a second sample with TP at 70% and TCA with a Ratio of 1.45. The Rosner index was <12 in favor of a deficit in coagulation factors whose dosage showed a factor V rate of 45%. Subsequent tests performed at 2-month intervals showed factor V levels of 59%, 43% and 36%, respectively. Levels of other factors (II, VII, VIII, IX, X, XI), fibrinogen, and liver function were normal. The isolated factor V deficiency has therefore been confirmed. The family survey of parents and siblings of 5 children was done based on biological tests (TP, TCA and Fibrinogen) to identify two other cases (the father and elder brother).

The brother (case № 2) is 14 years old, the eldest of 5 siblings, having as antecedent spontaneous haemorrhagic manifestations such as bruising and epistaxis with severe hemorrhagic episodes especially post-traumatic requiring sometimes the blood transfusion and in whom the brother's family screening found a TQ at 15 sec corresponds to a 65% TP with a TCA at 39 sec with a ratio of 1.35 and fibrinogen at 3g / l. The diagnosis of factor V deficiency of coagulation was retained at a rate of 38%.

The father (case № 3) is 50 years old from a non-consanguineous marriage, not known to have an autoimmune or neoplastic pathology, having as

antecedent episodes of medium to large epistaxis having caused once hemorrhagic shock.

The hemostasis assessment in this patient showed a time of Quick at the limit of the normal: TQ at 13 sec which corresponds to a TP at 70% with a

prolongation of TCA which was at 37.6 sec with a ratio to 1.25 (Table 1). Both sisters and mother had no hemorrhagic signs, hemostasis (TQ, TCA and fibrinogen) and coagulation factor V were normal.

Table-1: Summary table of our three family cases

Patients	Age	Sex	Circumstances of discovery	Syndrome Hemorrhagic	TQ	TCA	Fibrinogen	Factor V
The case Index (Case № 1)	12 years old	masculin	bleeding syndrome after tooth extraction	yes	13sec	45,4 sec	2,5g/l	45%
His brother (Case № 2)	14 years old	masculin	Family Screening	yes	15sec	39 sec	3g/l	38%
His father (Case № 3)	50 years old	masculin	Family Screening	yes	13sec	37,6sec	2,5g/l	40%

DISCUSSION

Factor V deficiency represents a rare disorder of coagulation with an incidence of one per 10 000 [5]. It can be isolated or associated with congenital factor VIII deficiency. It is due to mutations of the F5 gene (1q23) that controls the production of plasma factor V. Transmission is autosomal recessive. Epidemiologically our three patients were male. And there was no notion of consanguineous marriage.

Clinically, the revelation was symptomatic in the 3 members of the family with minimal spontaneous haemorrhage (bruising and epistaxis) and severe traumatic hemorrhage requiring blood transfusions in the father and elder brother. Clinical manifestations of congenital factor V deficiency are variable and bleeding may be minor or absent [6]. Most often, it is bruising, epistaxis, meno-metrorrhagia in girls and women [7] or haemorrhages after an invasive procedure (circumcision or tooth extraction [8]), post-traumatic or postoperative. Biologically, TQ and TCA were longer in our patient, father and older brother and bleeding time was normal at home.

The factor V rate was asked in all our patients, it was around 40% in the three patients of the same family. The determination of the other coagulation factors was normal in all our patients which allowed to eliminate a combined deficiency including factors V and VIII and vitamin-k dependent factors. The determination of antigenic activity and von Willebrand factor ristocetin cofactor (vWF: Ag and vWF: Rco) were normal in all three patients. Hepatic assessment was requested in all patients and it was normal.

The impact assessment (NFS-PQ is performed at a distance from the bleeding episodes) was normal in all patients. Clinical and biological assessments in all our patients have eliminated any secondary cause of coagulation factor V deficiency. The diagnosis of constitutional deficiency of coagulation Factor V should be suspected in view of the prolongation of Quick >

15sec time associated with an elongated TCA with a ratio > 1.2 in adults > 1.3 in children corrected by the addition of normal plasma (Rosner index <12 in favor of a deficit in coagulation factors) [9]. The level of fibrinogen is normal to eliminate hypo or afibrinogenemia [10]. Bleeding time using the 3-point IVY incision method, platelet count and liver function are normal [10].

The biological diagnosis of certainty of congenital VF coagulation deficiency is based on the demonstration of an isolated decrease in plasma VF in general <70% with the absence of any secondary cause of this deficiency [11]. An FVIII assay is necessary to distinguish an isolated VF deficiency from the combined deficiency of FV and FVIII [10]. Rates of other coagulation factors are normal (especially FVIII and vitamin K-dependent factors) [12]. Molecular analysis is possible but is not necessary for diagnosis. Clinical history is generally useful for distinguishing between congenital and acquired DFV. Inhibitors are most often associated with autoimmune or neoplastic pathologies that secrete anti-FV antibodies.

The published series of patients with DFV are rare and discordant: for some, half of them suffer from bleeding mainly mucocutaneous mucosa, but in other series, the majority of patients would be completely asymptomatic even with a collapsed rate of FV, testifying to the absence of correlation between the level of plasma VF and the clinical expression of this pathology [11]. It has been suggested that platelet VF levels may modulate clinical hemorrhagic expression, which may explain the fact that there is no correlation between VF rate and severity of signs hemorrhagic [11]. Given the unavailability in Morocco of factor V concentrates, PFC remains the only useful treatment [13,14]. Since the half-life of factor V is 12 to 36 hours, an infusion of 15 to 20 ml / kg of PFC is sufficient. If an invasive procedure is planned, this infusion should

be repeated daily to maintain the factor V level greater than 20% [14,15].

To avoid the risk of volume overload, allergic reaction, and infection with PFC infusion, plasma exchange has been used successfully [13,16]. Transfusion of platelet concentrates may also be useful, in addition to PFC in severe haemorrhage [13]. For our patient, his father and his older brother the treatment is on demand and in case of necessity, that is to say preoperatively or before the dental care which must be done under surveillance and with coverage by the PFC.

Overall, the prognosis for most patients with constitutional deficiency in FV coagulation is good. In none of the patients in the North American registry, including those with VF <1%, prophylaxis was required. In the Iranian cohort patients with DFV had a more benign prognosis than patients with hemophilia A and B with activity levels of comparable factors [17].

CONCLUSION

Factor V isolated constitutional deficiency is a rare condition of coagulation. It is characterized by a low level of plasma FV caused by mutations in the gene coding for this factor. Its prevalence is significantly higher in regions with high consanguinity. DFV is clinically heterogeneous, it can manifest itself at any age by hemorrhagic signs especially mucocutaneous as it can remain asymptomatic (even with a very low level of plasma VF) testifying the absence of correlation between the rate of FV and the clinical expression of the pathology.

Morocco is one of the countries concerned by this deficit, hence the need for a national registry to collect data on patients suffering from this deficit and a center specialized in the management of rare deficits in coagulation.

Detailed information on deficits in coagulation factors and especially rare deficits should be given to general practitioners and specialists.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

REFERENCES

- Duga S, Asselta R, Tenchini ML. Coagulation factor V. The international journal of biochemistry & cell biology. 2004 Aug 1;36(8):1393-9.
- Asselta R, Peyvandi F. Factor V deficiency. In Seminars in thrombosis and hemostasis 2009 Jun (Vol. 35, No. 04, pp. 382-389). © Thieme Medical Publishers.
- Chemaou A, Ayachi M, Benjelloun O, Zineddine A. Ménorragies par déficit congénital en facteur V chez une adolescente. Archives de pédiatrie. 2013 Jan 1;20(1):33-6.
- Pavithran K, Sankar S, Thomas M. Late presentation of congenital factor V deficiency--a case report. Indian journal of medical sciences. 2001 May;55(5):271-2.
- Vigue B, Treamey B, Tazarourte K. Hémorragies sous antivitamines K: les freins à la prescription du PPSB, mythes et réalités. JEUR. 2007; 20 (1): 1S1-1S.
- Bouines V, Lagarde F, Battefort F, Ruols E, Frontin P, Ducassé JL. Impact de l'échographie préhospitalière lors de son utilisation en routine. Journal Européen des Urgences. 2008 Mar 1;21:A24.
- Chemaou A, Ayachi M, Benjelloun O, Zineddine A. Ménorragies par déficit congénital en facteur V chez une adolescente. Archives de pédiatrie. 2013 Jan 1;20(1):33-6.
- El Koraïchi A, Mokhtari M, Ghannam M, Mekaoui N, El Haddoury M, Ech-Cherif EK. Deficiency of factor V and circumcision: perioperative management. About a clinical case. In Annales francaises d'anesthésie et de réanimation 2011 Apr (Vol. 30, No. 4, p. 377).
- Sosa IR, Ellery P, Mast A, Neff AT, Gailani D. Acquired factor V deficiency in a patient without evidence of a classical inhibitor. Haemophilia: the official journal of the World Federation of Hemophilia. 2014 Jan;20(1).
- Asselta R, Peyvandi F. Factor V deficiency. In Seminars in thrombosis and hemostasis 2009 Jun (Vol. 35, No. 04, pp. 382-389). © Thieme Medical Publishers.
- Bonhomme F, Schved JF, Giansily-Blaizot M, Samama CM, de Moerloose P. Déficits rares de la coagulation et gestes invasifs. In Annales françaises d'anesthésie et de réanimation 2013 Mar 1 (Vol. 32, No. 3, pp. 198-205). Elsevier Masson.
- Vijapurkar M, Mota L, Shetty S, Ghosh K. Menorrhagia and reproductive health in rare bleeding disorders: a study from the Indian subcontinent. Haemophilia. 2009 Jan;15(1):199-202.
- Huang JN, Koerper MA. Factor V deficiency: a concise review. Haemophilia. 2008 Nov;14(6):1164-9.
- Mannucci PM, Duga S, Peyvandi F. Recessively inherited coagulation disorders. Blood. 2004 Sep 1;104(5):1243-52.
- Lak M, Sharifian R, Peyvandi F, Mannucci PM. Symptoms of inherited factor V deficiency in 35 Iranian patients. British journal of haematology. 1998 Dec;103(4):1067-9.
- Baron BW, Mittendorf R, Baron JM. Presurgical plasma exchange for severe factor V deficiency. Journal of Clinical Apheresis: The Official Journal of the American Society for Apheresis. 2001;16(1):29-30.
- Mann KG, Kalafatis M. Factor v: A combination of dr jekyll and mr hyde. Blood. 2003 Jan 1;101(1):20-30.