

Hereditary FACTOR VII Deficiency: About Two Cases

Loubna Darfaoui^{a*}, Hajar safour^b, Hicham Yahyaoui^c, Mustapha Ait Ameur^d,
Mohammed Chakour^e

^{a,b,c,d,e} Faculty of Medicine and Pharmacy of Marrakech, Cadi Aayad University, Marrakech , Morocco

^{a,b,c,d,e} Hematology Department of Avicenna Military Hospital of Marrakech, Marrakech , Morocco

Loubna DARFAOUI, Medical Biologist

^aHematology Department of Avicenna Military Hospital Of Marrakech, Marrakech, Morocco

Mobile: +212 658253940

^aEmail: Loubnadarfaoui@gmail.com, ^bEmail: isalmaamrani@gmail.com, ^cEmail:

hichamyahyaoui@gmail.com

Abstract

Coagulation factor VII or proconvertin is a vitamin K dependent glycoprotein synthesized by the liver. This factor initiates the coagulation cascade by binding to tissue factor after a vascular breach. A qualitative or quantitative deficiency in this factor can cause hemorrhagic manifestations of varying severity. Hereditary factor VII deficiency is a rare disease. The clinical symptomatology is very variable and not correlated to the deficiency in this factor. It can be fatal with a severe hemorrhagic syndrome. An isolated prolongation of the prothrombin time is the first assessment that points to this diagnosis and a low level of plasma factor VII activity confirms it. The Treatment is very complex, hence the importance of collaboration between clinicians and biologists.

Keywords: Coagulation factor VII; Hereditary deficiency; hemorrhagic manifestations.

1. Introduction

Coagulation factor VII or proconvertin is a vitamin K dependent glycoprotein synthesized by the liver. This factor is present as low plasma concentration in the active state and initiates the coagulation cascade by binding to tissue factor after a vascular breach. Its normal plasma concentration is in the order of 0.35 to 0.60mg/L (i.e. an activity between 70 and 140%). A qualitative or quantitative deficiency in this factor can cause hemorrhagic manifestations of varying severity. This deficiency may be constitutional or acquired. The congenital origin is very rare, it is estimated at about 1/500000 individuals, but it increases considerably in countries where marriages are consanguineous [1]. We report in our work two cases of inherited factor VII deficiency.

* Corresponding author.

2. Observations

2-1. Observation 1

A 13-year-old girl issued from first-degree consanguineous marriage with no family history of hemorrhagic syndrome. She presents since the age of 1 year with frequent spontaneous epistaxis, especially during the summer, which improves with symptomatic treatment (EXACYL). The quick time (QT) was prolonged to 33.9 sec, the partial thromboplastin time (APTT) was normal. We completed the assessment by measuring the activity of factor VII which was very low (0.9%) controlled twice on two different samples (using a human thromboplastin at SYSMEX CS-2400/2500).

The same assessment was realized for the two parents who did not present any hemorrhagic signs with a prothrombin time (PT) normal and the activity of factor VII at 67% for the father and 57.7% for the mother. A genetic study was proposed for the family but was not done due to limited resources.

2-2. Observation 2

A 5 year old male child, the eldest of two brothers, from a consanguineous marriage. The child never presented any hemorrhagic signs. The diagnosis of congenital factor VII deficiency was made fortuitously during a preoperative workup (circumcision) in front of a low prothrombin level (51%) and a normal partial thromboplastin time (APTT). The functional dosage of factor VII, controlled on two different samples was low: 7%. The same tests were repeated for both parents and the brother, who came back normal.

3. Discussion

Hereditary factor VII deficiency is a rare disorder that can be quantitative or qualitative. It is autosomal recessive and due to mutations in the F7 gene (13q34) coding for F VII. Only homozygous or composite heterozygous patients can present a hemorrhagic syndrome, heterozygous subjects are generally asymptomatic. Nearly 250 different mutations of the FVII gene are listed in the literature. Rare large gene rearrangements have also been identified resulting in a total or partial deletion of the F7 gene.

The clinical expression of this disease is very variable and the severity of the hemorrhagic syndrome is not correlated to the residual levels of FVII activity. The clinical presentation can be very severe with the early occurrence of intracerebral hemorrhages and recurrent hemarthroses, or on the contrary moderate with cutaneous-mucosal hemorrhages. Finally, there are many subjects who are totally asymptomatic despite a very low FVII level [3].

Concerning the biological diagnosis, the respect of the pre-analytical phase is essential and conditions the quality of the results. Factor VII deficiency must be suspected when there is a prolonged quick time (TQ) and a normal partial thromboplastin time (PTT).

Positive diagnosis is based on the determination of Factor VII coagulant activity by chronometric technique

(FVII:C) (reference values between 70 and 140%). Generally, only FVII: C levels <30% are symptomatic [4].

To differentiate between qualitative and quantitative deficiency, antigenic assay of factor VII (FVII: Ag) is realized by enzyme-linked immunosorbent assay or immunoturbometric assay using a monoclonal antibody specific for FVII. Quantitative deficiency is characterized by a concomitant decrease in factor VII activity and antigen levels, whereas in qualitative deficiency there is a discordance between low activity and normal antigen levels.

The genetic study by molecular biology is important to specify the homozygous, composite heterozygous or heterozygous profile and consequently propose a genetic advice to the family. The disease is transmitted according to the autosomal recessive mode. Genetic counseling should be offered to individuals with a disease-causing mutation, informing them that there is a 25% risk of transmitting the disease to descendants if each parent is heterozygous.

For treatment, the approach is to administer recombinant FVII, FVII plasmatic or, as a last resort, fresh frozen plasma. However, the indications remain difficult to establish given the absence of correlation between the bleeding manifestations and the level of factor VII activity. Substitution treatment preoperatively or during a hemorrhagic episode is a real challenge.

4. Conclusion

Hereditary factor VII deficiency is a rare disease. The clinical symptomatology is very variable and not correlated to the deficiency in this factor. It can be fatal with a severe hemorrhagic syndrome. An isolated prolongation of the prothrombin time is the first assessment that points to this diagnosis and a low level of plasma factor VII activity confirms it. The Treatment is very complex, hence the importance of collaboration between clinicians and biologists.

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