ECRONICON OPEN ACCESS

EC PAEDIATRICS
Case Report

Congenital Factor II Deficiency: A Case Report and Review of the Literature

Sara Al Maimouni[1]*, Ismail Belhaouz[2], Nouha Al Maimouni[3] and Abilkassem Rachid[1]

[1]*Department of Pediatrics, Military Hospital of Instruction Mohamed V, Rabat, Morocco*

[2]*Department of Gynecology and Obstetrics, Souissi Maternity Hospital, Chu Ibn Sina, Rabat, Morocco*

[3]*Department of Gastro-Enterology and Hepatology, CHU Mohammed VI Tanger, Morocco*

***Corresponding Author:** Sara Al Maimouni, Department of Pediatrics, Military Hospital of Instruction Mohamed V, Rabat, Morocco.

Received: August 20, 2024; **Published:** September 11, 2024

Abstract

Factor II is a liver-synthesized glycoprotein, a zymogen of a serine protease, and one of the vitamin K-dependent coagulation factors. Factor II deficiency is a rare inherited disorder transmitted in an autosomal recessive manner.

We present the case of a 6-and-a-half-year-old child hospitalized for cutaneous hemorrhagic syndrome. The family history revealed first-degree consanguinity and bleeding disorders in the siblings. The clinical examination showed bruises of various sizes on the extremities. Biological tests indicated a normal blood count, a low prothrombin rate of 30%, and a prolonged activated partial thromboplastin time of 60 seconds. Coagulation factor assays revealed severe factor II deficiency at 3%, with normal levels of factors V, VII, and X, and negative anti-factor II antibodies. Liver and immunological tests were negative. A family investigation showed similar abnormalities in the brothers, while the parents had factor II levels of 50%. The child did not receive specific treatment, with transfusions of fresh frozen plasma considered only in case of active bleeding.

Factor II deficiency is extremely rare, with an estimated prevalence of homozygous forms at 1 in 2,000,000. Clinical signs include epistaxis, menorrhagia, gingivorrhagia and ecchymosis. Diagnosis is based on prolonged prothrombin and activated partial thromboplastin times, and low factor II coagulant activity. Treatments include prothrombin complex concentrates and fresh frozen plasma. The prognosis is good with early diagnosis and appropriate treatment.

This case report highlights the importance of early detection and appropriate management of factor II deficiency, especially in settings with consanguinity. Close monitoring and personalized management of bleeding episodes are crucial for improving patient prognosis. Genetic counseling and raising clinicians' awareness of rare coagulation disorders are essential to optimize management and prevent serious complications.

Keywords: *Factor II Deficiency; Hemorrhagic Syndrome; Coagulation Disorder; Genetic Counseling*

Introduction

Factor II is a liver-synthesized glycoprotein, zymogen of a serine protease. It is a vitamin-k-dependent coagulation factor, belonging to the factors of the prothrombin complex: II, V, VII, X. FII deficiency is a rare autosomal recessive inherited disorder. There is very little written information available on the subject for people with this deficiency and their relatives [1].

Patient and Observation

We report the case of a 6-and-a-half-year-old child, hospitalized in the pediatrics department of the Mohamed V military hospital, for a cutaneous hemorrhagic syndrome. Her antecedents included persistent bruising following minor trauma and first-degree consanguinity. The 4-year-old brother, operated on for hypospadias, presented with profuse bleeding during surgery, and the 12-year-old brother presented with recurrent epistaxis. On clinical examination, the child was in good general condition, hemodynamically and respiratorily stable, with ecchymotic spots of varying sizes on the extremities. Biological tests showed a normal blood count, a low prothrombin rate (PT) of 30%, and an activated partial thromboplastin time (APTT) prolonged to 60 seconds. Coagulation factor assays revealed severe factor II deficiency at 3%, confirmed on two samples, with normal factors V, VII and X and negative anti-factor II antibodies. Liver and immunological tests (AAN, anti-DNA, Anti SSA, Anti SSB, Anti-Sm, APL) were negative. Family investigation showed that the 12- and 4-year-old brothers had low PT, prolonged aPTT and collapsed factor II, while the parents had normal PT and aPTT with factor II at 50%.

The child was not put on any specific treatment, with transfusions of fresh frozen plasma (FFP) considered only in the event of active bleeding.

Discussion

Factor II deficiency is the rarest coagulation factor deficiency. The prevalence of homozygous forms is estimated at 1/2,000,000. The disease affects both boys and girls. FII deficiency is due to mutations in the F2 gene (11p11-q12) encoding prothrombin [2].

Physiological role

During the coagulation cascade, prothrombin is activated by the prothrombinase complex (FXa, FVa in the presence of phospholipids and calcium) into thrombin, which plays a central role in the coagulation process. It transforms fibrinogen into fibrin, amplifies its own formation and activates the protein C, TAFI and platelet systems.

Clinical description

Congenital FII deficiency can occur at any age, with severe forms manifesting early in life. Common clinical signs include epistaxis, menorrhagia, gingivorrhagia, soft-tissue bleeding, hemarthrosis, ecchymosis and prolonged bleeding after tooth extraction, trauma or surgery. In severe forms, there is an increased risk of intracranial or umbilical haemorrhage. The lower the Factor II level, the more severe the bleeding. Manifestations of thromboembolic disease have been described in dysprothrombinemia.

Diagnosis is based on prolonged prothrombin and activated partial thromboplastin times (APTT, APTT) and low FII coagulant activity measured by an APTT-based test. Molecular tests are available, but are useless for diagnosis [3].

Pathological variations

Constitutional factor Il deficiency

Constitutional factor Il deficiency, which is autosomal recessive, is exceptional. It may be quantitative (reduced antigen and activity) or, more often, qualitative (normal antigen, reduced activity). Seven mutations have been identified in the factor Il gene, located on chromosome 11, which are responsible for this deficiency. Clinically, homozygous or double heterozygous deficiency manifests itself as moderate hemorrhages (ecchymosis, epistaxis, post-traumatic). Heterozygotes are usually asymptomatic. The diagnosis of constitutional deficiency is made only after checking the deficiency on a second sample taken at a distance, and after eliminating the causes of acquired deficiency, which are much more frequent [4,5].

A family investigation is necessary.

Acquired factor Il deficiencies (the most frequent) may be observed during:

- Treatment with antivitamin K,
- Vitamin K deficiency,
- Malabsorption (impaired absorption of vitamin K),
- Hepatocellular insufficiency,
- Fibrinolysis states, disseminated intravascular coagulation (DIC),
- Presence of anti-factor II autoantibodies in the course of anti-phospholipid syndrome (notably with systemic lupus erythematosus), or associated with viral infection in children.

Differential diagnosis

These aim to rule out deficiencies in factors V, VII, X, VIII, IX, XI, XIII or acquired deficiencies in FII (lupus anticoagulant).

Prenatal diagnosis

It is available for the most severe forms.

The mode of transmission is autosomal recessive. Genetic counseling should be offered to at-risk couples (both parents are carriers of a heterozygous pathogenic variant), informing them that the risk of transmitting the disease to the child with each pregnancy is 25%.

Treatment

Two treatments are currently available: the first is a prothrombin complex concentrate containing prothrombin (FII) and factors VII, IX and X; the second is fresh-frozen plasma. Both are blood derivatives and are administered intravenously [6,7]. The following table summarizes the different products used, their suggested doses, contraindications and warnings.

Product	Dose	Contraindication
Prothromplex® TIM 4 or Bebulin®VH: Contains: FII, FVII (very little), FIX, FX, protein, heparin	Intravenous: Dose: Hereditary FII deficiency 1 IU/kg increases blood levels to 1.6% Give at 2 mL/min.	Contraindications: DIC (disseminated intravascular coagulopathy). Precautions: Vaccination against hepatitis A and B. Side effects: Fever Urticaria Nausea Anaphylactic shock Risk of thrombosis.
Fresh frozen plasma: Contains: Plasma proteins, including labile and stable coagulation factors FII: 2 to 4 mg/mL Other coagulation factors: 1 IU/mL	Intravenous: Dose: 10 - 15 mL/kg	Contraindications: Warnings Side effects: Transmission of infectious disease Allergic reactions Plasma volume overload

Table

Prognosis

Good if diagnosed early and treated appropriately.

Conclusion

This case report describes a rare case of factor II deficiency in a 6-and-a-half-year-old child, highlighted by persistent bleeding manifestations and first-degree consanguinity. The diagnosis was confirmed by specific laboratory abnormalities, including low PT, prolonged APTT and severely reduced factor II levels. The absence of specific treatment in this case, with transfusions of fresh frozen plasma considered only in the event of active bleeding, underlines the need for close monitoring and appropriate management of bleeding episodes. This observation highlights the importance of early detection and personalized management to improve the prognosis of patients with this rare disease. Genetic counseling and clinician awareness of rare coagulation disorders are essential to optimize management and prevent serious complications.

Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

All authors contributed to the conduct of this work. All authors also declare that they have read and approved the final version of the manuscript.

Bibliography

1. Bezeaud A., *et al*. "Les déficits constitutionnels en prothrombine et les informations qu'ils peuvent nous apporter sur la structure et les fonctions de la prothrombine". *Hématologie* 11 (2005): 397-407.
2. Lacroix S., *et al*. Canadian Hemophilia Society. Factor VII Deficiency: an Inherited Bleeding Disorder. 29.
3. Canadian Hemophilia Society Other Factor Deficiencies (2001).
4. Samama MM., *et al*. "Hémorragies et thromboses: du diagnostic au traitement". Collection Les abrégés. Paris (2004).
5. Mori K., *et al*. "Clinical and coagulation studies in 3 cases of congenital factor X deficiency and review of reported cases in Japan (author's transl)". *Nihon Ketsueki Gakkai Zasshi* 43.3 (1980): 572-586.

Volume 13 Issue 10 October 2024