

## A Still Rare Case of Congenital Afibrinogenemia

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### Summary

*Congenital afibrinogenemia is characterized by the decrease or the absence of fibrinogen synthesis. It is a rare pathology that is transmitted autosomal recessive mode, with variable clinical demonstrations. The biological diagnosis consists in the presence of traces or absence of fibrogen with blood incoagulability. The coverage of this disease bases itself on the preventive treatment and replacement therapy based on fresh frozen plasma or fibrinogen concentrate. Through this case, we recall the various aspects of these rare condition clinical, biological, genetical as well as therapeutic plans.*

**Keywords:** Afibrinogenemia, Heredity, Bleeding, Diagnosis, Management.

### Introduction

Congenital afibrinogenemia is one of the rare disorders of coagulation, because since its first description in 1920 to our days, only 150 cases have been reported [1]. Prevalence is increased in areas with consanguineous marriages and of this fact the family history is important. The clinical presentation of afibrinogenemias is often characterized by bleeding at the time of umbilical cord drop, then by frequent and repeated bleeding, which could be fatal [2].

### Observation

It is about a 23-month-old, female infant, stemming from a first-degree consanguineous marriage, at last one of siblings of 4, admitted for the recurrent hemorrhagic syndrome. She presents in her personal antecedents a notion of hemorrhaged of the umbilical cord in the neonatal period and bruising at the least trauma, and in her family history two brothers died by a hemorrhagic syndrome. In her admission, the patient is in rather good general state, hemodynamically stable and respiratory, afebrile with cutaneous-mucous pallor. The belly is flexible, without tangible mass, without splenomegaly or hepatomegaly. The cardiopulmonary auscultation is normal. The rest of the clinical examination is without peculiarity. The biological balance assessment revealed an anemia with 8 g / dl, hypergolic microcytic alternative with a low ferritinemia to 7 ng / ml, rate of white blood cells count at 7300 elements / mm<sup>3</sup> and a rate of platelet count at 240 000 elements / mm<sup>3</sup>. The hemostasis assessment showed an activated partial thromboplastin time (APTT) in 60 seconds regard to the control (33 seconds) as well as an elongated Quick time with a rate of prothrombin (RP) level at 45%. Fibrinogen is undetectable, and fibrin degradation products (FDP) are absent in the assay. At the same time, coagulation factors II, VII, VIII, IX and X are normal. The diagnosis of congenital afibrinogenemia was held, and the family was made sensitive. The

evolution was marked by the arisen of a post-traumatic extra-dural hematoma for which the infant was operated as well as the arisen of a haemoperitoneum. The child received from some freshly frozen plasma (FFP) and fibrinogen. Since then, the child is in good shape without intercurrent hemorrhagic incident.

### Discussion

Congenital afibrinogenemia is a rare disease whose prevalence is currently estimated at 1/1 million, due to a constitutional deficit in fibrinogen [3]. In Morocco, its incidence remains underestimated because of the difficulty of access to healthcare for certain populations. The transmission is made according to an autosomal recessive mode and consanguinity is found in 50% of the families, parents being asymptomatic. The sex ratio is 1 (H / F). Two studies were conducted in Morocco and the subjects studied were female [4, 5].

Fibrinogen is a complex glycoprotein made up of three polypeptide chains ( $\alpha$ ,  $\beta$ ,  $\gamma$  chains). These are synthesized mainly by the hepatocyte and assembled inside the cell. We distinguish three forms of inherited deficiency of fibrinogen: dysfibrinogenemias, which are qualitative abnormalities due to the presence of an abnormal fibrinogen, hypofibrinogenemias characterized by partial deficit of fibrinogen and hypodysfibrinogenemias defined by a reduced concentration of abnormal fibrinogen. Afibrinogenemia is the most extreme form of fibrinogen deficiency. It is due to an abnormality of the genes encoding fibrinogen and not to an excessive degradation of fibrinogen or in a defect in the regulation common to the expression of the three genes. Despite the crucial role of fibrinogen in various processes (hemostasis, angiogenesis, tissular repair), the disease is life-compatible and is of the same degree of severity as the hemophilia A or B. The diagnosis can be evoked from the anamnesis: notion of umbilical bleeding or episode of bleeding identical to that of the patient among ascendants or siblings [6]. This suits perfectly to the case of our patient. In the congenital afibrinogenemia, the

bleeding may vary from mild to severe. The intervals between episodes of bleeding can be very long. Several types of bleeding have been described: bruising, hemorrhage following circumcision, bleeding gums, epistaxis, gastrointestinal bleeding, genitourinary or intracranial or rupture of the spleen. Approximately 20% of people with afibrinogenemia have hemarthrosis. Because of this particular aspect, the disease can be confused with hemophilia A or B. The hemorrhagic complications which are met in this pathology are most often the result of trauma, sometimes minimal, and which can sometimes go unnoticed. At our patient, the notion of umbilical haemorrhage is noted and repeated ecchymoses dominated the clinical picture. On the other hand, spontaneous bleeding is rare [7]. Although afibrinogenemia is congenital, bleeding may arise only late in the second decade of the life. A case of spontaneous bilateral dissection of the vertebral arteries in a 28-year-old young woman is reported by Garcia-Monco et al [7, 8]. A peculiarity is to be noted at the girl's affected by afibrinogenemia on the impact of this disease on the menstruation and the conception. There is an increased risk of menorrhagia that may require oral contraception and a tendency to spontaneous abortions with post-abortion hemorrhages.

On the biological point plan, the blood is incoagulable and the activated partial thrombin (APTT) and Quick (TQ) and thrombin times are very stretched out [9, 6]. Fibrinogen is undetectable by the conventional, chronometric, weight or immunological measurement methods, although traces may be detected by more sensitive radioimmunoassay or immunoassay methods.

The platelet count is normal. At the level of primary haemostasis, afibrinogenemia leads to a reduction in platelet aggregation translated by an elongated bleeding time. All coagulation factors, except fibrinogen, show normal rates. The fibrin degradation products are negative. The immunoassay can confirm the diagnosis and eliminate the dysfibrinogenemia [2, 6, 10, 11].

It should be noted that very sensitive assaying techniques may reveal the presence of some traces of fibrinogen in the blood of some patients. The family survey is essential to know better the disease. The genes that code for fibrinogen biosynthesis are located on the distal third of chromosome 4 (4q28-q31) [9, 12]. At present, the prenatal diagnosis of this disease is made possible thanks to accurate molecular diagnosis for families at risk, allowing ante-natal identification of the disease. This would have been able to be realized in our context, unfortunately the family as not made sensitive enough especially that there is the notion of consanguine marriage first degree and the death of two children further to bleeding.

The coverage bases on the prevention and administration of fibrinogen, according to the indications of the French Agency for Health Safety of Health Products (FAHSHP). Prevention consists of crowding out sports activities that can lead to even minimal trauma, raising awareness among parents and children, apprenticeship of the first care in case of bleeding, and the need for prompt consultation in the event of severe symptoms. Transfusion of PFC is recommended as a general rule only in the case of association of haemorrhage or haemorrhagic risk with a profound abnormality of haemostasis defined by a fibrinogen level  $<1 \text{ g/L}$ , TP  $<40\%$ , and TCA  $>1.5$  times the control value [13].

## Conclusion

Congenital afibrinogenemia is a very rare dyscrasia whose diagnosis

is based on a bundle of clinical and biological arguments. Despite clinical variability, it is advisable to evoke this diagnosis in the face of recurrent bleeding in children and particularly in the neonatal period. The early diagnosis allows a coverage and care adapted to avoid severe bleeding that may put the child's vital or functional prognosis at risk. Management is based primarily on the prophylaxis and administration of fibrinogen concentrates in the presence of hemorrhagic syndrome.

**Conflict of interest:** None.

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