Congenital factor X deficiency of coagulation revealed by epistaxis

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The congenital factor X (FX) is a plasmatic glycoprotein, which plays a crucial role in coagulation. Its deficit is among rare causes of the hemorrhage in child. It could be acquired or congenital. The main hemorrhagic manifestations are epistaxis, hematuria, and menorrhagia in females, sometimes hemarthrosis even craniocerebral hemorrhage. The measurement of the FX rate in the blood allows the diagnosis. The healthcare consists of perfusion using prothrombin complex concentrate (PCC). In North Africa, no FX case was reported. Therefore, our goal is to report a new case of congenital FX of coagulation deficiency. On the light of this case, we suggest discussing recent facts, which are connected to this pathology.

Our Moroccan female patient is 4.5 years old, she is from Amazigh ethnical group; her parents are consanguineous (cousins of first range). No personal or familial antecedents of bleeding or hepatic injury were recorded. She was presented with epistaxis, which was installed one week earlier, the bleeding occurred in a context of apyrexia and maintenance of the general state. No medicamentous treatment carried out with the patient according to the parents. The examination shows pallor without icteric or cutaneous eruption neither other signs of bleedings, nor adenopathy. A stable hemodynamic state without hepatosplenomegaly was noticed. The remaining examination is completely normal. The initial assessment carried out shows a normochromia normocytic anemia at 6.8 g/L, a low prothrombin rate (PR) at 24% without anomaly of the activated cephalin time. The platelets rate is normal. The remaining hepatic assessment is strictly normal. The rate of the fibrinogenemia and coagulation factors II (77%) and V (114%) were all normal at 4.62 g/L. In contrast, the FX is lower than 5% despite the fact that the minimal value for patient age should be at 55%; this was assessed by chronometric assay using deficient plasma in FX. The urgent action to be considered consisted of transfusing the child by red blood cells and frozen fresh plasma, this treatment allowed stopping the hemorrhage and the control of PR was at 54%. In a previous study, FX was also known as the factor of Stuart. It is a very rare coagulation abnormality characterized by an autosomal recessive hereditary attribute. Few authors reported the pathology in terms of isolated case or in terms series of patients.[1] So far, the clinical expressions are not well established due to the rarity of this pathology. The prevalence in the general population is one case per one million.[2] The acquired deficit in FX can be associated to a hepatocellular insufficiency, a malabsorption syndrome, a medicamentous intake,[3] a poison ingestion[1] and amylose.[4] The congenital deficit is characterized by a great heterogeneity in clinical, phenotypic and genotypic aspects. The prevalence of the deficit in FX in the composite resulting form homozygote or heterozygote is approximately one per 0.5 million. Explicitly, the prevalence in the form heterozygote is varying between one per 500 to one per 2000. The responsible gene would be localized at the level of chromosome 13 in 13q34-ter. The severe deficits remain exceptional and are fact of composite heterozygotes (FX San Antonio) or of homozygotes (FX Santo-Domingo).[1] The coagulation factor could be an isolated one such as the case of our observation, or associated to other factors in particular coagulation factor VII[5] or more complex factors FII, VII, IX and X.[1] The importance of the deficit and the severity of the symptoms result from the site of change in the gene. The heterozygotes are generally asymptomatic; hemorrhages are complicating the aggressive surgical acts without hemostasis or serious traumatisms. At the composite heterozygotes and homozygotes, the hemorrhagic manifestations are related to the residual activity of the factor. Occurred and the importance of the hemorrhagic syndrome are correlated with the degree of the deficit of the factor.[1,2] The epistaxis is the most frequent symptom, followed by menorrhagia, gastro-intestinal bleedings, and the hematuria. None exteriorized hemorrhages are principally represented by the hemarthrosis and the hematoma.[1] (**Table 1**) Cerebro-meningeal hemorrhages are described in the severe forms.[2] In addition, a hemorrhage observed at the fall of the umbilical cord might direct towards a deficit in factor XIII, thus could be seen also in a congenital in FX deficit.[1] The diagnosis is evoked when a quick time is lengthened (or rate of prothrombin lowered) associated to lengthened activated cephalin time. It can be also evoked when Stypven time is lengthened (activation of FX by the venom of Russel viper). The thrombin time is normal. Currently, with progress of molecular biology, the FX deficits are better defined. We can measure the rate of the FX: C and the FX: Ag using endogenous and

Table 1 - Prevalence of bleeding symptoms in congenital factor X deficiency (1).

Symptom	All patients (n = 32)	Factor X: c < 1% (n = 18)	Factor X: c 1-5% (n = 9)	Factor X: c 6-10% (n = 5)
Epistaxis	23/32 (72)	11/18 (61)	8/9 (88)	4/5 (80)
Menorrhagia*	4/8 (50)	3/5	1/1	0/2
Gastro-intestinal bleeding	12/32 (38)	12/18 (66)	0/9	0.5
Hematuria	8/32 (25)	7/18 (39)	1/9	0/5
Hemarthrosis	22/32 (69)	14/18 (77)	7/9 (77)	1/5
Hematoma	21/32 (66)	14/18 (77)	6/9 (66)	1/5
Central nevous system bleeding	3/32 (9)	2/18 (11)	1/9 (11)	0/5
Umbilical cord bleeding	9/32 (28)	7/18 (39)	1/9 (11)	1/5

*Eight women of reproductive age

exogenous methods. The rate of FX: C allows the classification of the deficit, whatever the character of the molecular anomaly. The deficit is severe for rates of FX: C lower than 1%, moderated for rates between 1 and 5% and minor for rate higher than 5%. The congenital deficit has to be distinguished from the isolated deficit in FX observed in primitive amylose, and more rarely the secondary amylose with the vitamin K deficiencies and the hepatic attacks. It should be reminded that new-born baby has factors of FX coagulation, which is qualitatively normal, but in smaller quantity (such as in our observation). The normalization is acquired by the third month. The indication of a substitutive treatment depends on the hemorrhagic risk, which can be estimated by the type of intervention, the severity of hemorrhages and the FX concentration.[1] There are 2 sources of FX, frozen fresh plasma, viro-inactivated solvent/detergent, and the human complex concentrates, which contains the 4 vitamin-K dependent factors (FII = 37 UI/mL, FVII = 25 UI/mL, FIX = 25 UI/mL, and FX = 40 UI/mL). The posology and the duration of the treatment depend on the severity of the deficit, the localization of the bleeding and the type of treatment to be started (preventive or curative) as well as clinical and biological state of the patient. For the constitutional deficits in FX, the rate of recovery of FX is 1.7%. As in indication, usual posology is 20-40 UI/kg.

In conclusion, the congenital deficit in FX of coagulation is a rare affection but of real gravity in the case of significant deficit. A lower rate of prothrombin without other obvious causes of hemorrhage in patients with family antecedents of bleeding would evoke the diagnosis, and dosing the rate of FX. The treatment consists in substituting the deficient factor by the PCC. In the event of non-availability, the perfusion of frozen fresh plasma remains very useful. The surgical acts must be covered by higher dose than those used usually used, this is useful to limit the blood losses.

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References

1. Peyvandi F, Manucci PM, Lak M, Abdoullahi M, Zeinali S, Sharifian R, et al. Congenital factor X deficiency: spectrum of bleeding symptoms in 32 Iranian patients. ***Br J Haematol*** 1998; 102: 626-628.
2. Bahri E, Rahmi O, Ayhan T, Fatih O. Severe congenital factor X deficiency with intracranial bleeding in two siblings. ***Brain Dev*** 2004; 26: 137-138.
3. Hamasaki A, Ishii K, Yamaguchi K, Sunamoto M, Ozaki H, Yanagita M, et al. Steroid hormone-responsive secondary factor X deficiency. ***Thromb Haemost*** 1998; 80: 1032-1033.
4. Choufani EB, Sanchorawala V, Ernst T, Quillen K, Skinner M, Wright DG, et al. Acquired factor X deficiency in patients with amyloid light-chain amyloidosis: incidence, bleeding manifestations, and response to high-dose chemotherapy. ***Blood*** 2001; 97: 1885-1887.
5. Boxus G, Slacmeulder M, Ninane J. Deficit hereditaire combine en facteur VII et X revele par un allongement du temps de Quick. ***Arch Pediatr*** 1997; 4: 44-47.