THE TREATMENT AND PROPHYLAXİS WİTH CRYOPRECİPİTATE OF SPONTANEOUS İNTRACRANİAL BLEEDİNG İN A PATİENT WİTH MİLD INHERİTED FACTOR XIII DEFİCİENCY

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Aim

Inherited factor XIII (FXIII) deficiency is a linked autosomal recessive rare bleeding disorder and that can be present with umblical cord bleeding during the neonatal period, delayed soft tissue bruising, mucosal bleeding. and life-theratening intracranial hemorrhage. Although there is a lifelong risk of bleeding, the prognosis is excellent when current prophylactic treatment is available using cryoprecipitate or plasma derived FXIII concentrate. Plasma levels between 5% and 30 % have been shown to be sufficient in preventing spontaneous bleeding. We report a patient with intracerebral hemorrhage (ICH) because of mild congenital FXIII deficiency, who was succesfully treated using cryoprecipitate.

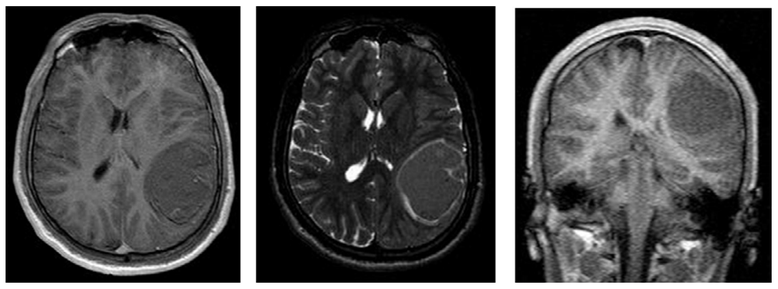
Case report

A 21 years-old young man suffered from severe headache for two days before he was admitted to the hospital and neuroimaging tests (Figure 1) revealed hemorrhage on left temporo-parieto-occipital area. His body weight was 80 kg. He was given 14 bags of cryoprecipitate and FXIII level in plasma was 53.8 % before neurosurgical operation. During the following 15 days after operation, he was given in doses of 4 bags of cryoprecipitate every other day. He received prophlactic cryoprecipitate treatment in doses of 1 bag per 20 kg every 2 weeks fort he next 3 months. During this time period, we did not observe any reccurrent hemorrhage. His medical history revealed that he was born after a first degree consanguineous marriage and diagnosed with mild congenital FXIII deficiency when he was 2 years old (FXIII level in plasma: 7.62%). His elder brother (27 years-old) and one of his sisters (17 years-old) had mild FXIII deficiency.

Discussion

FXIII, the last enzyme in the clotting cascade, catalyses the covalent cross linking of fibrin molecules. It converts the loose fibrin polymer into an organised crosslinked structure with increased tensile strength and makes it relatively resistant to fibrinolysis. FXIII deficiency occurs at a frequency of approximately 1 in 1–5 millions (1). Like other rare bleeding disorders, FXIII deficiency is often prevalent in regions with a high rate of consanguineous marriages. Inherited FXIII deficiency can be a result of FXIIIA or FXIIIB deficiency. FXIIIA deficiency can be due to a reduction in FXIIIA synthesis (Type I) or decreased FXIIIA function (Type II). FXIIIB deficiency is much less common and tends to be associated with milder bleeding symptoms(2). The clinical manifestations of congenital FXIII deficiency include a lifelong bleeding diathesis, in particular subcutaneous bleeding (57%), delayed umbilical cord bleeding (56%), muscle haematoma (49%), haemorrhage after surgery (40%), intracerebral bleeding (34%), and a high risk of miscarriage. Delayed bleeding (i.e., 12-36 hours) after trauma or surgery is pathognomonic of FXIII deficiency(3). The main cause of death or disability in these patients is ICH which may occur spontaneously or after minor trauma. Standard coagulation tests (prothrombin time, partial thromboplastin time) are usually normal for age. Specialized testing, including a clot solubility and FXIII activity assay, are required to make an accurate diagnosis(4). Early diagnosis and treatment of F XIII deficiency is crucial because of the risks associated with ICH. In addition, it is important to start the prophylactic program regimen in the patients with F XIII deficiency as soon as the diagnosis is made(5). Three forms of replacement therapy are variably available for treatment of patients with FXIII deficiency: cryoprecipitate, FFP, and FXIII concentrates. A pasteurized plasma-derived FXIII concentrate (Fibrogammin P) is currently only available in 12 countries worldwide, as many of the developing countries lack the resources to develop fractionated plasma products. A synthetic recombinant FXIII (rFXIII) was developed in and is currently licensed in a few countries (Switzerland, Canada and European Union) (2). The FXIII concentrates don't have available in Turkey. Therefore, we use cryoprecipitate for the treatment of patient. As the half-life of endogenous factor XIII is long, ranging from 5–11 days, prophylactic therapy with fresh frozen plasma in doses of 10 ml/kg can be given every 4–6 weeks. Cryoprecipitate can be administered at 1 bag per every 10–20 kg every 3–4 weeks (6). Fibrogammin P can be given in doses of 10-35 U/kg to prevent bleeding for prophylxis at 4-6 week intervals (7).

Figure 1. MRI scan head showing intraparenchymal bleed in left temporo-parieto-occipital region



Conclusion

Although the patients have mild FXIII deficiency, they can have severe spontaneous bleeding such as intracranial hemorrhage. If F XIII concentrate can not be produced in developing countries, such as Turkey, then cryoprecipitate can be used for treatment and prophylxis of inherited factor XIII deficiency.

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