



## CASE REPORT

# A Rare Case of Co-Inheritance of Beta Thalassemia Intermedia and Coagulation FVII Deficiency

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### ABSTRACT

We present a 34-year-old man with combination of beta thalassemia intermedia and coagulation factor VII deficiency who was presented with pallor and irregular nose bleeding episodes. On physical examination, he had splenomegaly and yellow sclera. Pallor and splenomegaly could be reminder of thalassemic syndromes or hemoglobinopathies including thalassemia intermedia. Association with unusual bleeding tendency such as prolonged and repeated episodes of epistaxis without any evidence of liver failure in hemoglobinopathies suggest the possibility of coinheritance of a bleeding disorder. As a result, coagulation assay for proper diagnosis, management and prevention of probable life-threatening bleeding episodes is suggested.

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### Introduction

Beta thalassemias are a group of inherited disorders caused by decreased or absence synthesis of beta chain of hemoglobin molecule. Frequency of beta thalassemia major is estimated to be 1 in 1000,000.<sup>1</sup> Beta thalassemia is consisted of different types: Thalassemia major (TM), Thalassemia intermedia (TI) and Thalassemia minor. TM is known by severe anemia during the first year of life which can be fatal unless transfusion in combination with adequate iron chelating therapy has been started. TI generally has been known as milder anemia and better chance of survival.<sup>1,2</sup>

FVII is one of the vitamin k-dependent coagulation factors synthesized by liver and has a variety of activities in different physiological states.<sup>3</sup> Factor VII deficiency is an autosomal recessive disorder with a frequency of

approximately 1 in 500,000 individuals,<sup>4</sup> characterized by various clinical presentations.<sup>3,5</sup>

Based on our best knowledge, there is not any report of combined deficiency of coagulation FVII and beta TI. In this case report, we are supposed to emphasize about factor VII activity and its effect on beta thalassemia.

### Case Report

A 34-year-old man was presented with recurrent epistaxis and pallor. On physical examination, sclera was icteric and spleen was 4 cm below costal margin. Hematological data showed Hb: 9.6 gr/dl, hematocrit: 31.5%, MCV: 63.38 fl, MCH: 18.51 pg. Biochemistry results showed total bilirubin: 2.8 mg/dl, direct Bilirubin 0.4 mg/dl, SGOT 22 U/L, SGPT 6 U/L. Hemoglobin electrophoresis showed: Hb A: 2.1% and Hb F: 97.9%. Abdominal ultrasound

confirmed the presence of splenomegaly. Genetic study and mutation analysis showed homozygosity for IVS II-I.

The patient was scheduled to be examined by ENT specialist because of repeated epistaxis, but no abnormal finding was found. He had received only 1-2 times blood transfusions annually and had not have any bleeding history until the age of 9. The coagulation assay was done for the patient which showed prolonged PT (43.8 sec with control 12.8 sec), normal aPTT 33.6 sec (control 30.0 sec) and normal bleeding timing (Ivy method, 3 minutes). Factor FVII activity was assessed (IL ACL 9000 Coagulation Analyzer, USA) that showed less than 1% activity.

Two sisters of our case were known to be beta thalassemia minor which one of them also had positive history of severe episodes of menorrhagia and epistaxis that confirmed to be a severe case of FVII deficiency (<1% activity). Their parents (second-degree relative) were carrier for both beta thalassemia and Factor VII deficiency. Serum ferritin level was 790 ng/ml, so deferasirox (Exjade) 15 mg/kg/day was started for the patient.

Recombinant FVII, 30 µg/Kg as well as tranexamic acid (local and systemic) was started for episodes of recurrent epistaxis with good responses. The patient is under regular follow-up without any complication. Written informed consent was obtained from a patient.

### Discussion

FVII deficiency and beta thalassemia are two genetic autosomal recessive disorders and as a result, their prevalence is higher in traditional populations that consanguineous marriage is common such as Iran.

Inherited FVII deficiency is a rare bleeding disorder with bleeding manifestations ranging from mild including: epistaxis, easy bruising, menorrhagia, hematuria, and gum bleeding to severe conditions such as hemarthrosis, hematoma and central nervous system bleeding may also occur.<sup>6</sup>

In this case report, we present an Iranian male patient with combination of these two genetic disorders; thalassemia intermedia and coagulation FVII deficiency. According to our knowledge, this is the first report of this combination.

The patient was diagnosed as thalassemia intermedia when he was 3 years old. He was non-transfusion dependent except for a few occasions due to recurrent epistaxis and subsequent anemia. Coagulation assay was performed following repeated prolonged nose bleeding with no evidence of liver disease or local anatomical problem.

Previous studies have stated that hypercoagulable state in thalassemia can mask the bleeding diathesis and symptoms of coagulation factor deficiency. Roshan Colah et al. reported a case with combination of hemophilia A and beta thalassemia major in an Indian patient.

They concluded that the presentation of hemophilia A with mild symptoms may be due to masking effect of hypercoagulable state of thalassemia major.<sup>7</sup> However, diagnosis of FVII deficiency was delayed in our patient which indicated that severity of the symptoms was not correlated with the level of activity of factor VII.

One can hypothesize that bleeding tendency in thalassemia major patients may be due to iron overload in the liver and some degree of hepatic failure in synthesis of coagulation factors. So, iron overload even in non-transfusion dependent patients with beta thalassemia should be considered seriously and monitoring of serum ferritin levels is recommended for prevention of iron overload and its complications. In this case, iron chelating agent (Deferosirox) was started for the patient.

In conclusion, it is recommended that unexplained bleeding episodes in patients with beta thalassemia major or intermedia should be taken into account and coagulation assays be assessed, particularly if liver failure due to severe iron overload is not suggested.

**Conflict of Interest:** None declared.

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