CASE REPORT

Ovarian haemorrhage: a rare presentation and diagnostic dilemma in Factor XIII deficiency

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Abstract

Factor XIII (FXIII) deficiency is a rare (autosomal recessive) genetic disorder which is associated with delayed bleeding symptoms that occur hour or days after trauma. Spontaneous rupture of visceral organs due to FXIII deficiency is a rare cause of abdominal pain with grave consequences and can be easily confused with other abdominal pathologies because of normal standard coagulation profile in these patients. We report a 15-year-old girl with spontaneous ovarian haemorrhage and splenic haematoma with FXIII deficiency. She had normal coagulation screen along with normal FXIII screen initially on the 5M urea testing which lead to delay in her diagnosis.

Keywords: Factor XIII deficiency, Bleeding disorder, Ovarian haemorrhage, Splenic haematoma.

Introduction

Factor XIII (FXIII) deficiency is a rare inherited (autosomal recessive) bleeding disorder usually associated with a severe bleeding diathesis. The incidence is about 1 case per 2-5 million populations.[1] It is more commonly associated with intra-cranial haemorrhage.[2] Spontaneous rupture of abdominal viscera due to FXIII deficiency is rare. The diagnosis of FXIII deficiency is challenging as the initial coagulation screen is normal.[3] The clot urea solubility test (5 M urea), as it detects only the most severe form of FXIII deficiency, is no longer considered to be a reliable screening tool. The quantitative screening tests for FXIII activity assay are usually not available, most routine laboratories still use clot solubility test as an initial test.[4] We report the case of a young Pakistani girl who presented with two episodes of life threatening intra-abdominal bleeding with normal coagulation workup and normal initial screening for FXIII deficiency based on 5M urea. Later, quantitative testing confirmed FXIII deficiency.

Case Report

A 15-year old girl with a possible family history of bleeding tendency presented to emergency department (ED) with severe abdominal pain. There was no history of trauma.She was vitally stable. Abdominal examination revealed distension and tenderness. CT scan of the abdomen (Figure-1) showed retroperitoneal haematoma representing right ovarian haemorrhage. Initial laboratory workup showed Hb 6.1g/dl: Platelet count, prothrombin time (PT), partial thromboplastin time (PTT) were in normal range. Her AFP, beta-HCG level along with vWF and ristocetinco-factor assay was normal. FXIII screen on 5Murea not deficient. She was managed conservatively with fresh frozen plasma (FFP) and packed cell. Her hospital course was uncomplicated. Follow up CT scan after one month showed resolution of previously noticed haematoma.

Approximately 3 months later, she presented again to ED with abdominal pain. Her repeat haematosis workup, including FXIII screen, was again normal. An urgent CT scan revealed a

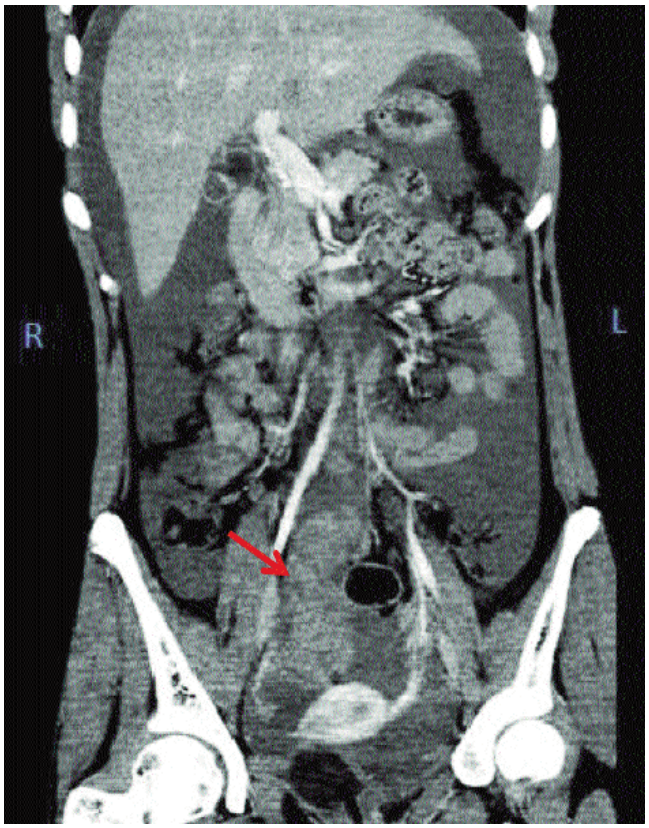

Figure-1: Right Ovarian Haemorrhage.

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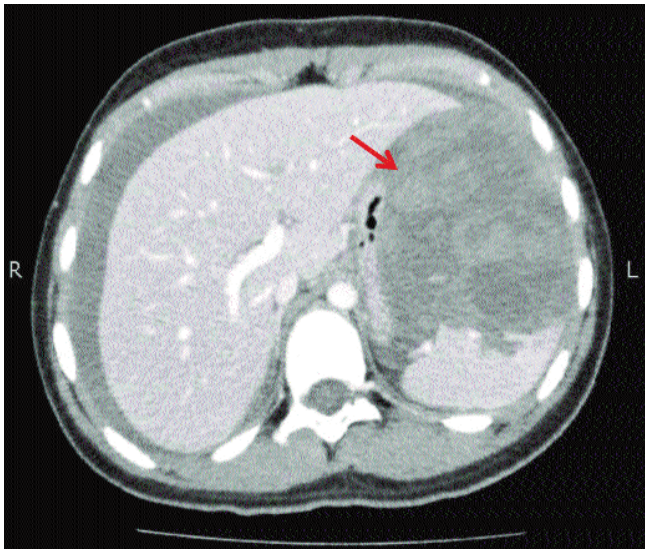

Figure-2: Splenic Haematoma.

large splenic haematoma measuring 10.5 x 8.0 cm associated with complete laceration of the spleen (Figure-2). Splenic angiogram was done to rule out any vascular abnormality. It was unremarkable. She was managed conservatively with packed cell and FFP transfusion. Her rheumatologic work-up (ANA, dsDNA, ASMA, AMA, anticardiolipin and antiphospholipid antibodies) was also unremarkable.

Her follow up scans showed resolution of haemorrhage.Once available, FXIII assay done by quantitative test via ammonia release assays confirmed low FXIII activity (3.5%; normal range 70-140%). She is now on regular cryoprecipitate transfusion, doing well without significant bleeding problems.

Discussion

Factor XIII is a plasma transglutaminase that catalyzes the final step in the coagulation cascade.[5] The incidence is approximately 1in 2-5 million population worldwide with no gender predilection.[1,6] It hasa higher prevalence in families with FXIII Dand consanguinity.[6] Patients with FXIII deficiency usually present at early neonatal period with prolonged umbilical stump or post circumcision bleeding and easy bruises.[3] Recurrent spontaneous abortions and menorrhagia have also been reported.[3,8] The most devastating complication with high mortality in these patients is intracranial bleeding.[2,6] Although congenital deficiency is common, acquired FXIII deficiency has also been reported in some systemic disorders.[7] Ovarian haemorrhage is very rarely reported with FXIII deficiency but there have been three reported cases of spontaneous rupture of spleen.[8]

The prompt recognition is vital. Early diagnosis and placement on primary prophylactic therapy is the key to lower the risk of spontaneous life-threatening bleeding.[9] A simple management plan that is life-saving makes prophylaxis feasible. FXIII deficiency is difficult to diagnose since the initial coagulation screen is normal hence a high suspicion is required. The long half-life of FXIII should also be kept in mind as assay done after transfusion of blood products may lead to a falsely elevated level of FXIII.

The clot solubility test is a qualitative test and is only positive if FXIII activity is zero or close to zero. Thus, the screening test, which establishes the diagnosis, should be a FXIII activity assay with amine incorporation or ammonia release assays or ELISA.[4,10]

Conclusion

We present an unusual but life threatening manifestation of FXIII deficiency in a young girl whose diagnosis was delayed because of the misleading normal initial coagulation screen and FXIII assay. FXIII deficiency should be considered in individuals with otherwise unexplained life threatening haemorrhage. Early diagnosis and placement on primary prophylactic therapy is essential to prevent life-threatening bleeding.

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