Case Report

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Factor XIII deficiency leading to a life-threatening intracranial hemorrhage in a young female: a case report

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Introduction and importance: Factor XIII (FXIII) deficiency, a rare coagulation disorder resulting from F13A1 gene mutations, can lead to severe bleeding episodes, especially in infants. The authors' case study featuring a 16-year-old female with a history of this deficiency revealed intracranial hemorrhage necessitating immediate medical intervention. The text emphasizes the importance of understanding the epidemiology and genetics of FXIII deficiency, as well as the challenges in diagnosis and management.

Case presentation: A 16-year-old female with FXIII deficiency presented to the Emergency Department (ER) after a fall, experiencing weakness on her right side, headache, seizures, and altered consciousness. Neurological examination showed weakness and increased tone on the right side of the body. Computed tomography (CT) scan revealed an intracranial subdural hemorrhage overlying the superior parietal lobe. Treatment included IV fluids, sodium valproate, antibiotics, fresh frozen plasma, and mannitol. Serial neurological assessments were normal, and the patient remained stable. MRI later confirmed hemorrhage. Upon discharge, she was prescribed medication and physiotherapy, leading to significant improvement at the 6-month follow-up.

Clinical discussion: The prevalence of FXIII deficiency, a rare disorder, is higher in populations with consanguineous marriages, particularly in regions like Pakistan, India, Tunisia, Finland, and Iran due to specific genetic mutations. Diagnosis involves thorough evaluation and specific lab tests, with varied clinical symptoms including prolonged bleeding, especially in newborns. FXIII deficiency can also develop in association with conditions like hepatic failure and leukemia, complicating diagnosis. Treatment options include blood products and recombinant FXIII, with management of intracranial bleeding requiring a multidisciplinary approach.

Conclusion: The case underscores the critical need for early identification and specialized care for individuals with FXIII deficiency to mitigate life-threatening complications like intracranial hemorrhage, promoting tailored treatment approaches and improved patient outcomes.

Keywords: factor XIII deficiency, intracranial hemorrhage

Introduction

Factor XIII deficiency (FXIII) is a rare coagulation disorder usually resulting from mutations in the F13A1 gene[1]. This genetic condition might lead to severe and life-threatening bleeding episodes in homozygous individuals during infancy. Diagnosis can be done early based on symptoms such as prolonged bleeding early in life but sometimes, initial diagnosis might be possible following a grave complication such as intracranial hemorrhage and stroke. Hemorrhagic stroke disproportionately affects individuals aged 15–45 years, with studies reporting a prevalence of 26% within this demographic[2]. Our case study featuring a 16-year-old female with a history of factor XIII deficiency revealed intracranial hemorrhage necessitating immediate medical intervention.

HIGHLIGHTS

- Factor XIII (FXIII) deficiency can lead to intracranial hemorrhage in young patients, emphasizing the urgency of diagnosis and management.
- Despite normal coagulation parameters, accurate diagnosis requires specific tests for FXIII deficiency, highlighting diagnostic challenges.
- Multidisciplinary management is essential, encompassing immediate intervention, imaging, surgery, and tailored treatment for optimal outcomes.

Presentation of case

A 16-year-old female patient arrived at our Emergency Department (ER) reporting weakness on the right side of her body for one day, following a fall. She also complained of a headache, seizures, and a period of altered consciousness. Further inquiry revealed she had a history of delayed hemostasis and had

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been diagnosed with factor XIII deficiency since childhood, which was confirmed with blood investigations.

Upon arrival at the ER, IV access was secured, and a comprehensive evaluation was conducted at the same time. Vitals were within normal limits. She appeared pale and fatigued. Neurologically, she had a score of 15/15 on the Glasgow Coma Scale (GCS), was alert and conscious. However, there was increased tone (3+) on the right side of her body, decreased power (⅕) on the right side, and exaggerated reflexes on the right side. Her right plantar reflex was upward. On the opposite side, tone, power, reflexes, and plantar response were normal. Cardiovascular examination showed regular rhythm, palpable pulses, and normal perfusion. The rest of the physical examination was normal. ECG was done and revealed no abnormal findings. Initial blood investigations revealed a decreased red blood cell count of 3.6×10^{12}/l and normal white blood cell count of 5.7×10^{9}/l. Platelet count was normal at 166×10^{9}/l. Prothrombin time (PT) of 12, international normalized ratio (INR) of 1.1 and activated partial thromboplastic time (aPTT) of 29.8 sec, were all within normal limits. However, Factor XIII activity was significantly decreased.

A computed tomography (CT) scan of the brain revealed focal hemorrhage in the superior parietal lobe. Initial laboratory tests showed a slightly decreased hemoglobin level (hemoglobin = 9.3 g/dl). Intravenous fluids, Inj Sodium Valproate (500 mg), broad-spectrum antibiotics (ceftriaxone 1 g) and 5 pints of fresh frozen plasma (FFPs) were administered. IV mannitol was given at the dose of 0.5 mg/kg every 6 h as indicated for ICH.

After stabilizing her in the ER, she was transferred to the ward. Throughout her stay, serial neurological assessments were done for any features of raised intracranial pressure (ICP) and were normal. She remained conscious and stable. MRI with contrast was recommended and revealed hemorrhage in the superior left parietal lobe. (Fig. 1)

Upon Discharge, patient was advised oral Sodium Valproate (200 mg OD), Tab Paracetamol (500 mg sos), Capsule Omeprazole (20 mg before breakfast), physiotherapy and was advised follow-up in outpatient department after a month. On 6-month follow-up, there was significantly improved power in the right side of the body owing to regular physiotherapy and good compliance to medications.

Discussion

FXIII deficiency, though rare, follows an autosomal recessive inheritance pattern, with an estimated occurrence of one case per 2–3 million live births. Prevalence is higher in populations with prevalent consanguineous marriages, and specific genetic mutations are associated with founder effects in regions such as Pakistan, India, Tunisia, Finland, and Iran[3,4].

Diagnosing FXIII deficiency involves comprehensive evaluation, including history, physical examination, and specific laboratory tests. Followed by traditional coagulation tests, specific assays such as FXIII activity and antigen assays are necessary for accurate diagnosis. Clinical manifestations vary widely, with ~80% of cases exhibiting prolonged bleeding, notably from the umbilical cord in neonates[5–8].

FXIII deficiency can present in acquired forms associated with conditions such as hepatic failure, inflammatory bowel disease, and myeloid leukemia. Key clinical indicators include delayed bleeding despite normal coagulation profiles, necessitating a strong clinical suspicion for accurate diagnosis. Differential diagnosis is challenging due to normal coagulation parameters[9]. Intracranial hemorrhage is one of the most severe and life-threatening complications of Factor XIII deficiency.

In individuals with congenital FXIII deficiency, the occurrence of intracranial hemorrhage is notably higher, ranging from 25 to 30%, surpassing the frequencies observed in hemophilia A or B. This type of hemorrhage stands as a primary contributor to mortality or long-term impairment in these patients. Although clot formation might initially proceed without issue, the weak cross-linking of fibrin strands characteristic of FXIII deficiency often leads to clot destabilization within 24–48 h, resulting in recurrent bleeding episodes[16]. A case reported in BMJ Case Reports described a 15-year-old patient with FXIII deficiency presenting with intracerebral bleeding, managed with intravenous mannitol and fresh frozen plasma[10]. Management of intracranial bleeding requires a multidisciplinary approach, including immediate medical attention, imaging studies, surgical intervention, monitoring, supportive care, and factor replacement therapy[11]. Treatment options for FXIII deficiency include various blood products and recombinant FXIII. Prophylactic and replacement therapies are tailored to individual needs, with considerations for pregnancy-related bleeding, surgeries, and trauma. Limitations of recombinant FXIII, such as the lack of the B subunit, may impact effectiveness in patients with B subunit deficiencies[12–14]. The conventional treatment for FXIII deficiency typically involves the administration of cryoprecipitate and fresh frozen plasma. Given the prolonged half-life of endogenous FXIII, which can range from 5 to 11 days, prophylactic therapy with fresh frozen plasma is often prescribed at doses of 10 ml per kg every 4–6 weeks. Alternatively, cryoprecipitate can be administered at doses of 1 bag per 10–20 kg every 3–4 weeks. Prophylactic therapy is generally advised for patients with a previous history of intracranial hemorrhage[16].

Methods: This case report has been prepared in line with the SCARE 2023 Criteria[15].

Conclusion

Although rare, factor XIII can manifest in young patients with grave complications like intracranial hemorrhage as discussed in our case. Early diagnosis with comprehensive history and investigations such as FXIII activity assay, FXIII antigen assay, inhibitor assay, and molecular diagnosis. Following early diagnosis, intracranial hemorrhage should be treated with the aim to reduce intracranial pressure when raised and maintain normal vitals, with special caution to detect features of raised intracranial pressure and serial neurological examination.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient's parents/legal guardian for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

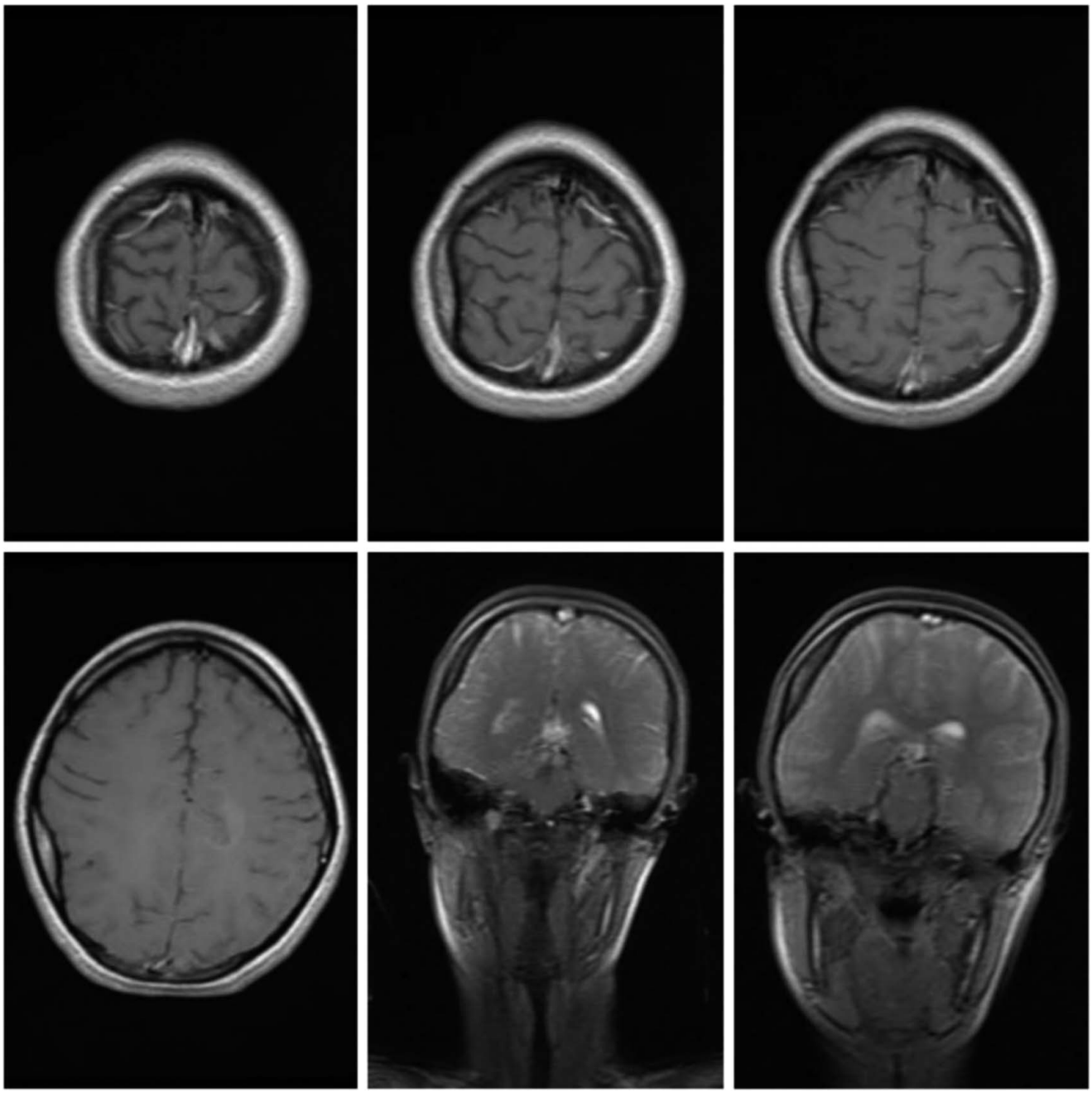

Figure 1. MRI with contrast shows an abnormal signal hyperintensity area is noted in the left top parietal region with no significant post contrast enhancement suggestive of contusion/hemorrhage in the left parietal lobe.

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Author contribution

H.N.U.F., FNU P. and S.A. were involved in the study concept, data collection, and writing of the manuscript. H.S. and S.A. were involved in the treatment and reviewing of the manuscript. All the authors were involved in the final review of the manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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