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Case Report
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Spontaneous Intracranial Hemorrhage as the First Manifestation of Severe Factor X Deficiency in 3-Month-Old SARS-CoV-2 Positive Child: A Case Report

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Abstract

Factor X is a Vitamin K dependent serine protease that serves as the first enzyme in common pathways of the coagulation cascade. The deficiency of Factor X can be inherited or acquired. Clinically it manifests from mild to severe bleeding and the most common symptoms are epitasis and gum bleeding. Intracranial hemorrhages reported in 9% to 26% of all the patients with Factor X deficiency. Here we present a case of a 3-month-old baby girl who presented in the Emergency Department with fever vomiting and lethargy. During the hospital stay, she developed one episode of generalized tonic-clonic seizures and CT-Scan brain showed huge intracranial bleed with tonsillar herniation. Her coagulation profile showed <6% factor X levels and she was SARS-CoV-2 positive. This is a unique case of a 3-month-old SARS-CoV-2 positive child with spontaneous intracranial bleeding as the first manifestation of Factor X deficiency. No guidelines exist as to how to diagnose such patient early so that prompt intervention could be done to save the patient. We suggest prothrombin time and partial thromboplastin to be included as a routine post-natal investigation to pick this disorder early on. We also suggest the use of cranial ultrasonography in early detection of ICH in patients with signs and symptoms of raised intracranial pressures.

Keywords: Factor X deficiency; Bleeding disorder; Intracranial Hemorrhage; SARS-CoV-2; Prothrombin time; Partial thromboplastin time; COVID-19; Coronavirus disease 2019

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Introduction

Factor X deficiency is an extremely rare autosomal recessive inherited coagulation disorder affecting 0.0001% people worldwide [1]. The incidence is higher in developing countries where the rate of consanguineous marriages is high [2]. It has a variable clinical presentation ranging from mild symptoms like epitasis, gum bleeding, and hemarthrosis to life-threatening intracranial bleeding. The frequency of intracranial hemorrhage in Factor X deficiency is reported to be 9% to 26% often without a history of preceding trauma. Raised prothrombin time, partial thromboplastin time and low levels of Factor X levels diagnose the condition. We would like to report such a case with severe intracranial bleeding leading to tonsillar herniation as the first manifestation of factor X deficiency that is a far rare entity.

Case Presentation

A 3-month old baby girl was brought in the pediatric emergency of Aga Khan University Hospital Karachi, Pakistan with the complaints of multiple episodes of non-bilious vomiting followed by lethargy for a few hours and a fever spike three days back. She was a full-term baby born to non-consanguineous parents, delivered through lower segment C-section due to sustained bradycardia. The patient's birth weight was 2.8 kg and her antenatal and post-natal history was normal. She was given Vitamin K at birth. The medical history revealed a prior pediatric emergency visit for yellowish discoloration of skin at the age of eight days. She was diagnosed with neonatal jaundice for which admission advised but the parents opted to leave against medical advice. There was no history of trauma, bruising and bleeding from any site. On arrival to the emergency, the patient was grossly pale but vitally stable with normal GCS, tone and reflexes. There were no bruises, hematoma, or obvious bleeding from any site. An intravenous line was maintained, blood workup was sent and IV fluids were started. Nasal swab for SARS-CoV-2 was sent. After two hours of arrival, the patient developed generalized tonic-clonic seizures. She was given intravenous diazepam and anticonvulsant, after which seizures aborted and she was subsequently intubated secondary to

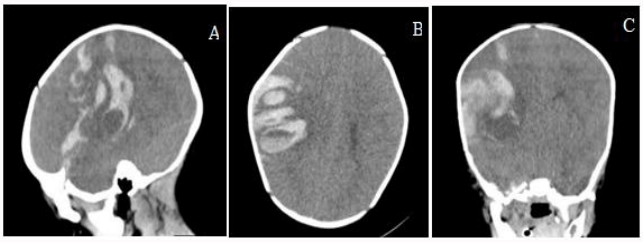

Figure 1: CT-Scan brain without contrast showing massive right front parietal intracerebral hemorrhage with mass effect resulting in contra lateral midline shift with the possibility of impending herniation. A) Sagittal view, B) Axial view, C) Coronal View.

Table 1: Laboratory parameters.

Labs	Results
Hemoglobin	8.2 g/dl
White Blood Cells	14
Platelets	613
Prothrombin time	139.2 sec
Partial Thromboplastin time	123.2 sec
Factor X	<6%
Factor V	Normal
Factor VIII	Normal
Factor IX	Normal
Factor XI	Normal
Serum Sodium	132
Serum Bicarbonate	20.2
Serum Calcium	8
Serum Glucose	166 mg/dl
Total Bilirubin	0.6
ALT	34
AST	39
SARS-CoV-2	Positive

low GCS. Initial labs showed low hemoglobin (Hb 8.4 g/dl), normal white blood cells with mild neutrophilia and normal platelets. The CT-Scan brain was done which showed a massive right front parietal intracerebral hemorrhage with mass effect resulting in contra lateral midline shift with the possibility of impending herniation (Figure 1). An intravenous bolus of mannitol and Vitamin K were given. Her prothrombin time and partial thromboplastin time were reported as 139.2 sec and 123.5 sec respectively. After detailed examination, Neurosurgery and Intensive Care Teams counseled the parents regarding the guarded prognosis, subsequently, withdrawal of support was decided and the patient expired. The factor assays were later reported as Factor X having levels of less than 6% with normal Factor V and the Rt-PCR for SARS-CoV-2 came positive (Table 1).

Discussion and Conclusion

Factor X is a Vitamin-K dependent coagulation factor that is produced by the liver [3]. It plays a crucial role in linking the intrinsic and extrinsic pathways of the coagulation cascade. Factor X deficiency can be either acquired or inherited in the autosomal recessive fashion. The causes of acquired Factor X deficiency are usually associated with light-chain amyloidosis, atypical lymphoid leukemia, chronic liver disease, anticoagulation therapy, medications such as phenytoin. The clinical manifestations of Factor X deficiency are highly variable ranging from mild bleeding episodes to severe life-threatening intracranial bleeding and may present at any age. The patients with severe disease are either homozygous or compound heterozygous and usually present within the first six months of life. The severity of the disease is based on clinical presentation and functional factor X levels. It is classified severe when levels are less than 1% [4]. Since 1943, around 150 cases of Factor X deficiency have been reported and the available literature suggests no racial or gender preferences [5]. In Pakistan, consanguineous marriages are common in certain parts so is the incidence of rare inherited diseases. The only study conducted on Factor X deficiency in North Pakistan, published in 2004, revealed that in patients with Factor X deficiency, 60% of the patients were from consanguineous marriage [6]. In our case, the patient was born to non-consanguineous parents and did not have a family history of bleeding diathesis. Due to rarity of the disease, and limited literature the physician's gestalt lags in such cases resulting in poor outcomes. This case report is first of its type to suggest routine PT and a PTT testing in all the newborns to screen such rarer cases of coagulation defects so that early diagnosis can be made and presentations with worst outcomes might be prevented. Moreover, the child was born during the SARS-CoV-2 pandemic and hypothetically acquired SARS-CoV-2 from the community, as there are no cases reported for vertical transmission yet. However, it is yet to establish whether the finding of SARS-CoV-2 in our patient was merely coincidental or it has any association with Factor X deficiency and intracerebral bleeding. This study is first to point a possible association of SARS-CoV-2 with Factor X deficiency and spontaneous intracerebral bleeding in pediatric patients and suggests the need of further studies to see the prevalence, clinical spectrum, and associations of the disease, to improve diagnostic and management approach in such cases. Furthermore, the bedside cranial ultrasound should be utilized in the evaluation of pediatric patients presenting in the ED with signs and symptoms of raised ICP secondary to intracranial bleed, meningitis, and encephalitis and brain tumors, although its operator dependent but positive findings might help in early diagnosis and prompt management of such cases in the ED. The Emergency Physicians should be trained in doing cranial ultrasound in pediatric patients for the evaluation of raised intracranial pressure [7].

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