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A Case of Congenital Thrombotic Thrombocytopenic Purpura (Upshaw-Schulman Syndrome) with the History of Three Deceased Siblings

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Abstract

Upschaw-Schulman Syndrome is the recessively inherited form of Thrombotic Thrombocytopenic Purpura (TTP). This report presented a child with congenital TTP or Upshaw-Schulman syndrome with the history of three deceased siblings. Congenital TTP may result in multiple losses in the same family. Clinicians should aware the disease to early diagnosis.

Introduction

Congenital Thrombotic Thrombocytopenic Purpura is first described by Upschaw and Schulman as an inherited autosomal recessive form of TTP [1]. The pathophysiology of TTP has been mysterious until recently. Congenital TTP is associated with a deficiency in a plasma metalloprotease that cleaves a specific peptide bond in the von Willebrand factor (VWF) subunit [2]. Infections or vaccinations may precipitate the disease as repeated thrombotic thrombocytopenic angiopatic episodes [3]. Here, we report a child with congenital TTP or Upshaw-Schulman syndrome with history of three siblings death.

Case Presentation

An three year old girl born of a first degree consanguineous marriage presented to us with generalized petechias, vomitting, pallor and jaundice. She was stuporous. There was no evidence of meningeal irritation in the patient. Patient who developed respiratory arrest was entubated and was followed on mechanical ventilator.

Referring to the history, we learned that she was born as healthy baby from the 7th gestation of healthy 38 years old mother as non-identical twins. Her mother and father had first-degree consanguineous marriages. Family history revealed that her 3 siblings died before diagnosis made. First one was girl gender and died the at 9 months years old after a febrile seizure without any other findings or knowledge of families. Also other two siblings died at 18 months years old after a hospitalization in consequence of febrile seizure and severe vomiting. Interestingly, all cases had a hematoma history after intramuscular injection. Fever and mucosal hemorrhage was common findings with all deceased siblings. Three girl siblings including the patient's twin and a male sibling are healthy.

At the clinical follow up of the patient, her glasgow coma scale was 3 and pupillary bilateral fix dilated. System examinations were normal as cardiac, respiratory and abdominal evaluations. Laboratory evaluations revealed leukopenia and thrombocytopenia with normal renal and hepatic functions with coagulopathy with all day at hospitalization (Table 1). Peripheral blood smear evaluation showed intravascular hemolysis findings like schistocytes, helmet cells and thrombocytopenia like microangiopathic haemolytic anemia. Her immunoglobulin levels were normal. Subarachnoid hemorrhage was detected on Cerebral Tomography.

As a treatment; laboratory hematologic findings and intravascular hemolysis on peripheral blood smear reminded us sepsis and dissemine intravascular coagulation. Seftriaxone and vancomycine were given as an antibiotherapy beside replacement therapy with platelet infusion, fresh frozen plasma and blood transfusion. She was unresponsive to treatment and her cytopenia were refractory to the all transfusion. Because of history of consanguinity between parents and her lost siblings with hemorrhage an inherited defects were suspected related to DIC clinic. After ADAMST13 activity assay revealed 1% activity, with the absence of antibody against ADAMTS13; congenital TTP diagnosis was made. Unfortunately the patient was lost after brain death 5th day of hospitalization.

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Table 1: Laboratory evaluations revealed leukopenia and thrombocytopenia with normal renal and hepatic functions with coagulopathy with all day at hospitalization.

	WBC(mm^3)	Hb(g/dl)	Plt(10^9/lt)	aPTT(s)	PTZ(s)	INR
Days	2500	13	21	32	11.8	1
First	6800	11.4	7	31.4	11.5	1
Second	8300	11.6	54	33	13	1.13
Third	5400	9.1	74	50.8	17.3	1.5
Fifth	5100	10.3	17	53.2	25.2	1.89

Abbreviations: WBC: White Blood Cell; Hb: Hemoglobin (g/dl); PT: Prothrombin Time; INR: İnternational Normalized Ratio; APTT: Activated Partial Thromboplastin Time

Her family was informed about the disease by genetical counseling.

Discussion

The classical description of TTP consists of the pentad of microangiopathic haemolytic anemia, thrombocytopenia, fever, renal and neurological dysfunction. However, this pentad is present in only 40% of cases [4]. Congenital TTP is usually seen in the newborn or during childhood but acquired TTP is almost always seen in young adults. TTP attacks generally seeen after infection trigger in some patients while it is typically present with neonatal jaundice and thrombocytopenia [3].

Patients with congenital TTP are deficient in a plasma metalloprotease (ADAMTS 13) which belongs to the ADAMTS (an acronym for a disintegrin and metalloprotease with thrombospondin-1–like domains) and it is due to several genetic defects on chromosome 9q34. Severe deficiency of ADAMTS13 activity seen the majority of patients that is a like a scissors cleaving large multimers of von willebrand protein to smaller and less active ones. In the absence of this protein large multimers cannot be cleaved and active smaller ones cause "spontaneous" platelet adhesion and aggregation [5]. The clinical picture gives some non spesific complaints as fever, nausea, vomiting, and while progression of the disease neurologic findings and renal failure may be seen. Hematological evaluations revels pallor, purpura and jaundice while laboratory findings are more valuable with thrombocytopenia, unconjugeted hyperbilirubinemia, increased LDH levels and the peripheral smear posses diagnostic findings intravascular hemolysis like spherocytes, fragmented erythrocytes, erythroblasts and polychromasia with basophilic cytoplasms [4].

The treatment of TTP is depends on restoring the ADAMST13 function or getting away the highly active von willebrant proteins by exchange plasmaphresis or fresh frozen plasma infusions. While some other treatment options are started to use at older and immune based disease as Anti CD20 or immunosupressive treatments [6].

Our case which was initially misdiagnosed with sepsis then the clinic came to light with his presentation with MAHA and thrombocytopenia. TTP should be considered in any condition with MAHA and thrombocytopenia with or without renal or neurological dysfunction, without any other obvious cause [3]. This unusual case of congenital TTP with subarachnoid hemorrhage and thrombocytopenia without renal, neurological or any other systemic involvement has been brought out to emphasize the expanding phenotype of hereditary TTP. With the understanding of the role of ADAMTS 13 protease, the disease is being diagnosed more often. It is hoped that plasma or recombinant purified ADAMTS 13 will be available in the future.

As a result, it is important to emphasize, for newborn and infant period; if any clinic combination of MAHA is present without complementary sepsis or DIC table, althoughit is rare, congenital TTP diagnosis should be considered. In these cases, genetic counseling, early diagnosis and timely consideration of TTP treatment modalities can be lifesaving and brings further benefits for the patients.

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