

Congenital Thrombotic Thrombocytopenic Purpura: An Unusual Case of Microangiopathic Haemolytic Anaemia in a Newborn.

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Received: March 2016

Accepted: April 2016

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ABSTRACT

We present an extremely rare case of hyperbilirubinemia with rapid progression leading to bilirubin encephalopathy in term neonate. Despite early recognition and intervention, death occurred as a total serum bilirubin reached 25 mg/dl. It was a case of Coomb's negative microangiopathic haemolytic anaemia in a newborn period which is autosomal recessive inheritance i.e. Upshaw-Schulman Syndrome. (Congenital thrombotic thrombocytopenic purpura) characterised by numerous schistocytes on peripheral blood smear, thrombocytopenia, increased reticulocyte count, increased bilirubin and LDH level. This rare disease is often misdiagnosed especially in newborn baby. So we present this case not only for its variety but also for to create more awareness among pathologist and paediatrician as treatment protocol entirely differ.

Keywords: Congenital, Schistocytes, TTP.

INTRODUCTION

Congenital thrombotic thrombocytopenic purpura is an autosomal recessive disorder. It is one of the type of microangiopathic haemolytic anaemia characterised by profound peripheral thrombocytopenia, microangiopathic haemolytic anaemia and single or multiple organ failure of variable severity.^[1]

Congenital TTP is much less common than acquired form of the disease, accounting for up to only 5% all TTP cases, around 100 cases have been reported worldwide and annual incidence is estimated at less than 1 per 1000000.^[1]

We present this unusual case of congenital TTP in a newborn male child presented with severe hyperbilirubinemia on the first day of life to laid down more emphasis on the diagnosis as well as particularly its differential from immune mediated haemolytic anaemia as the treatment protocol entirely differs for this extremely rare subtypes of microangiopathic haemolytic anaemia.

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CASE REPORT

A 38 week gestation, 3.045 kg male infant was born via spontaneous vaginal delivery to a 30 year old gravid 3, para 1 without significant past medical history. Maternal blood group was O+ve and antibody screen was negative. Other maternal prenatal investigations were within normal limits. There was no known history of jaundice, anaemia or haematological disorders in family members. Cry of baby was normal at birth. 3 hrs after birth baby presented with respiratory distress. On clinical examination icterus⁺⁺⁺, pulse feeble, cyanosis⁺, pallor⁺⁺, purpuric rashes on the body. Laboratory investigations revealed Hb- 11.2 gm%, WBC-22700/mm³, platelet count- 25000/cumm, Reticulocyte was 8.5%. Based on these findings provisional diagnosis of haemolytic anaemia was made. Peripheral examination showed numerous schistocytes [Figure 1] admixed many nucleated R.B.C's. Neutrophilic leucocytosis without prominent toxic granules was evident. Serum bilirubin was 25 mg/dl. Indirect bilirubin was 23 mg/dl and direct was 2 mg/dl. Urea was 50 mg/dl, creatinine 0.8 mg/dl, Na⁺ 136 mEq/L, K⁺ 3.2 mEq/L, serum calcium 6.8 mg/dl, serum magnesium 1.8 mg/dl. Coomb's test was negative. LDH level was elevated.

Based on peripheral smear findings i.e. numerous schistocytes, nucleated R.B.C's [Figure 1] and raised bilirubin (Indirect) level, reticulocyte count (8.5%) diagnosis of microangiopathic haemolytic anaemia was made. Since it was a consanguineous marriage of III⁰, second male child also presented with similar complaints, final diagnosis of congenital thrombotic thrombocytopenic purpura was made.

At the end of first day, baby's condition was deteriorated and unfortunately, baby died because of diffuse encephalopathy due to bilirubin toxicity.

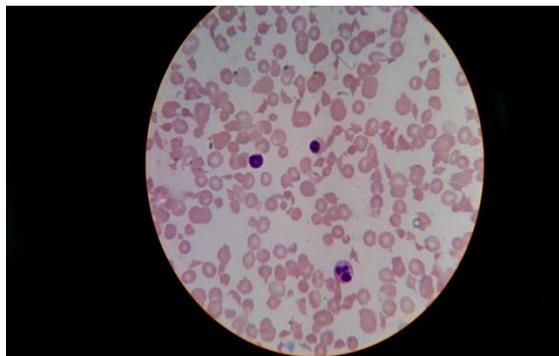


Figure 1: Peripheral smear showing numerous schistocytes and nucleated RBCs.

DISCUSSION

Congenital thrombotic thrombocytopenic purpura often described as the Upshaw-Schulman syndrome.^[1] It was reported by Schulman in 1960 in a 8 year old child who had episode of thrombocytopenia and haemolytic anaemia since birth that responded to plasma infusion.^[2]

Very handful reports are there in literature particularly by Thornton KM et.al^[2], Borgi A et al^[3]. TTP is a disease in which microthrombi are formed in multiple small vessels throughout the body leading to signs and symptoms of organ ischaemia. The normal coagulation process involves von Willebrand factor which is large multimeric protein which binds platelet to areas of intravascular endothelial cell damage. In normal haemostasis the function of ADAMTS13 protease is to cleaved vWF multimers when ADAMTS13 activity is deficient, ultra large vWF multimers accumulate, leading to deformation of platelet rich intravascular microthrombi^[4]. These microthrombi in turn cause damage to circulating red blood cells that is characteristically seen as 'schistocytes' in peripheral blood smear.

Acquired TTP is more common and which is usually because of development of autoimmune antibody directed against ADAMTS13 protein.^[3] The most common thrombotic microangiopathy in child is typical post diarrheal haemolytic uraemic syndrome (HUS). In HUS characteristically

schistocytes appear in peripheral smear it is always a closest differential diagnosis to TTP. Neurological symptoms are more common in TTP while renal symptoms (raised urea and creatinine) are more common in HUS. But congenital form of HUS doesn't exist so it can be very easily ruled out in our case as our patient was newborn infant.

Initially in our case diagnosis of pathological jaundice was made and we thought of Rh incompatibility but as mothers blood group was O^{+ve} it was ruled out and a rare possibility of ABO incompatibility is also ruled out by negative Coomb's test. Peripheral smear showed numerous schistocytes, raised indirect bilirubin, reticulocyte cell count 10%, elevated LDH level, normal urea and creatinine level and most importantly consanguinity of marriage in parents. Diagnosis of hereditary microangiopathic haemolytic anaemia was made. As the second male child of mother was also presented in a similar manner and died, it was finally concluded that this case was of congenital thrombotic thrombocytopenic purpura. The classic symptoms were bilirubin encephalopathy, respiratory distress, purpuric rashes on external body parts, pulmonary haemorrhage. Baby died because of bilirubin toxicity rather than micro ischaemic events, which was confirmed by brain MRI findings. Because of economical constraints, ADAMTS13 activity was not estimated. But genetic counselling was offered to the parents.

CONCLUSION

Thus to conclude, though congenital TTP is rare disease but should be considered in any case presented with hyperbilirubinemia in association with thrombocytopenia and haemolytic anaemia and characteristic schistocytes in peripheral blood smear.

So we want to put more weight on obtaining a peripheral blood smear which characteristically shows fragmented red blood cells i.e. schistocytes and thrombocytopenia.

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How to cite this article: Mane A, Kumbhar SS, Wader JV, Sonawane R, Kale P. Congenital Thrombotic Thrombocytopenic Purpura: An Unusual Case of Microangiopathic Haemolytic Anaemia in a Newborn. Ann. Int. Med. Den. Res. 2016;2(4):12-4.

Source of Support: Nil, **Conflict of Interest:** None declared