

A Case of Congenital Haemolytic Anaemia and Thrombocytopenia

Quiz

A 20-month-old boy came from Bangladesh to Singapore for medical consultation. He presented with progressive pallor, easy bruising, intermittent dark-coloured urine, and failure to thrive since birth. There was a history of moderately severe neonatal jaundice but no exchange transfusion was needed. His parents were consanguineous but they were otherwise healthy. The family medical history was negative. Extensive investigations including haemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency were unrevealing. At the time of consultation, he was febrile, obviously pale, jaundiced and multiply bruised. He was irritable but no abnormalities were found in the neurologic and cardiopulmonary examination. The liver and spleen were palpable 2 cm below the costal margins, respectively. Full blood counts show Hb 4.6 g/dL, MCV 98.3 fL, WBC $7.8 \times 10^9/L$, and platelet $14 \times 10^9/L$. The blood film shows a leukoerythroblastic picture with signs of microangiopathy (Fig. 1 and 2). Serum levels of bilirubin (138 $\mu\text{mol/L}$), aspartate transaminase (81 U/L), and lactate dehydrogenase (1678 U/L) were elevated, with normal levels of creatinine and alanine transaminase. Prothrombin time, partial thromboplastin time, and fibrinogen level were normal. D-dimer level (0.5 mg/L) was slightly raised. Tests for direct Coombs test and anti-nuclear antibody were negative. What is the diagnosis?

- A. Haemolytic uraemic syndrome
- B. Upshaw-Schulman syndrome (congenital thrombotic thrombocytopenic purpura)
- C. Evans syndrome
- D. Autoimmune lymphoproliferative syndrome
- E. Disseminated intravascular coagulation-defibrination syndrome

Answer

The answer is B.

Haemolytic anaemia and thrombocytopenia with normal or elevated white cell count are an unusual combination of haematological findings in children. It may be autoimmune in origin, associated with microangiopathy and platelet consumption, or secondary to hypersplenism. Evans syndrome is the classical disease of a Coombs-positive haemolytic anaemia associated with immune thrombocytopenia. It may be an isolated disease or part of a genetic disorder of lymphocyte apoptosis known as

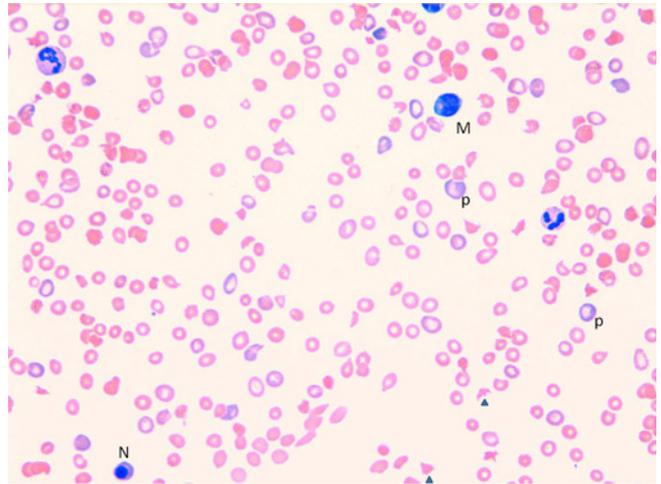


Fig. 1. Blood film ($\times 40$) showing a leukoerythroblastic picture with a circulating myelocyte (M) and a nucleated red cell (N), and red cells with polychromasia (p), schizocytes (\blacktriangle), and fragmentation consistent with microangiopathic haemolysis.

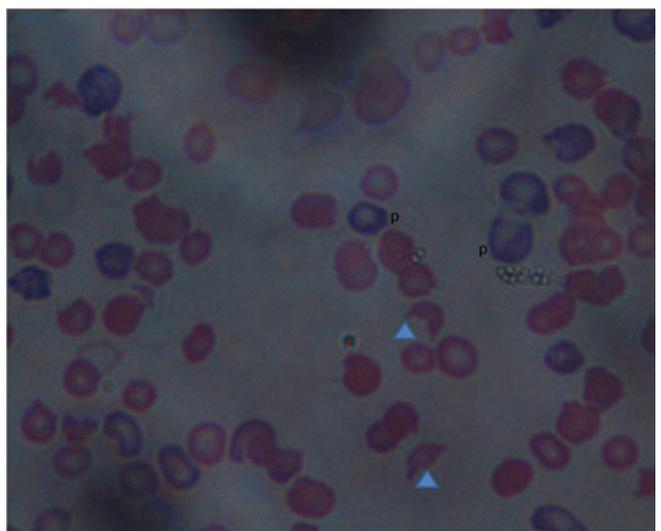


Fig. 2. Blood film ($\times 100$) showing polychromatic red cells (p) and schizocytes (\blacktriangle).

autoimmune lymphoproliferative syndrome.

Microangiopathic haemolytic anaemia (MAHA) is a hallmark of disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP), and haemolytic uraemic syndrome (HUS). DIC or consumptive coagulopathy usually occurs in a sick child with deranged coagulation and thrombocytopenia, but the clotting profile and platelet count can be deceptively normal during the early phase of defibrination secondary to snake envenomation.¹

HUS and TTP are overlapping syndromes with variable combinations of fever, thrombocytopenia, microangiopathic haemolytic anaemia, neurological abnormality, and nephropathy. Classical childhood HUS is almost always secondary to Shiga-toxicogenic *Escherichia coli* or *Shigella dysenteriae* infections, with a prodrome of diarrhoeal illness and a clinical course dominated by renal impairment.

Childhood TTP is a rare disease, now known to be due to the deficiency of a von Willebrand factor (vWF) cleaving protease identified as ADAMTS13 (a disintegrin-like and metalloprotease with thrombospondin type 1 motif 13). The accumulation of ultra-large multimers of vWF is believed to lead to microvascular thrombosis, platelet activation and consumption, and microangiopathic haemolytic anaemia. It may be congenital or acquired in nature. The first case of acquired TTP was reported in an adolescent girl with a rapidly fatal disease in 1924. In acquired TTP, ADAMTS13 deficiency is due to a circulating inhibitor or autoantibody, which may be secondary to systemic lupus erythematosus in childhood cases. It has an abrupt onset, usually after the second decade of life, and carries a high mortality before the advent of plasmapheresis.^{2,3}

Congenital TTP (OMIM No. 274150) is a familial disease with an autosomal recessive inheritance.^{2,3} First reported separately by Schulman and Upshaw, most cases have an early onset during the neonatal or infantile period. Severe neonatal jaundice necessitating exchange transfusion is not unusual. The disease is characterised by a chronically relapsing course of MAHA and thrombocytopenia, which can be effectively aborted by the infusion of fresh frozen plasma. The diagnosis of congenital TTP in the present case is supported by an undetectable level of ADAMTS13 in the absence of an inhibitor (test provided by Blood Center of Wisconsin, Milwaukee). A single infusion of fresh frozen plasma was followed by resolution of fever and amelioration of haemolysis and bleeding. He has since been maintained

on infusions of fresh frozen plasma every 3 to 4 weeks back in his home country.

REFERENCES

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