Transfusion-dependent Microcytic Anaemia in a 10-year-old Girl

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Quiz

A 10-year-girl from Bangladesh presented with a moderately severe anaemia (lowest recorded haemoglobin level of 5.6 g/dL) and a mild jaundice (latest serum bilirubin, 31 µmol/L) 3 years ago (Figs. 1 and 2). Test for haemoglobin electrophoresis on agarose gel did not reveal any abnormal bands. Both parents were asymptomatic, not anaemic, with red cell indices within normal ranges, but the father was incidentally found to be a haemoglobin S carrier. The child has since been receiving erythrocyte transfusions at bimonthly intervals. She was once treated with hydroxyurea 500 mg daily, but the treatment was subsequently withdrawn. What is the diagnosis?

a. Thalassaemia intermedia
b. Iron deficiency anaemia
c. Congenital sideroblastic anaemia
d. Lead poisoning
e. Pearson syndrome

(answer below)

Discussion

This 10-year-old girl is suffering from a sporadic form of congenital sideroblastic anaemia, with ineffective erythropoiesis characterised by microcytosis, anisopoikilocytosis, lack of reticulocytosis and mild hyperbilirubinaemia, and the characteristic ring sideroblasts in the bone marrow on Prussian blue staining.

Congenital sideroblastic anaemia is a rare form of childhood anaemia. The most common form occurs as an X-linked recessive disorder and is associated with molecular defects of the erythroid-specific 5-aminolevulinate synthase isoenzyme (ALAS2), which is the first and rate-limiting step of heme biosynthesis. Congenital sideroblastic anaemia occurring in families compatible with autosomal dominant or recessive inheritance has been described. About 20 cases of sporadic congenital sideroblastic anaemia have been reported in which no other family members are affected.[1]

Children suffering from congenital sideroblastic anaemia may respond to treatment with pyridoxine in pharmacological doses. Pyridoxine is the precursor of 5'-pyridoxal phosphate, the essential cofactor of 5-aminolevulinate synthase, and response to pyridoxine is usually seen in patients with mutations close to the pyridoxal binding site of the ALAS2. Patients who do not respond to pyridoxine have to be supported by erythrocyte transfusion, and strategies to ameliorate or treat iron overload are necessary. Allogeneic haematopoietic stem cell transplantation has been attempted in congenital sideroblastic anaemia. Five successful transplants and a case of treatment-associated mortality have been reported.[2]

The differential diagnoses of childhood microcytic anaemia include thalassaemic syndromes and various disorders associated with iron utilization, and the morphologies of the red cells in the peripheral blood can be deceivingly similar. Abnormal haemoglobins can usually be detected on electrophoresis in thalassaemias and transfusion requirement may be ameliorated or eliminated in some thalassaemic patients after hydroxyurea treatment. Iron deficiency anaemia is usually characterised by an elevated total iron binding capacity or hypoferritinaemia. An absence of stainable iron in the marrow smear is virtually diagnostic. Basophilic stippling of the peripheral red cells is typically seen in children with lead poisoning, and the diagnosis can be made with an elevated plasma lead level. Pearson syndrome is a unique form of mitochondrial cytopathy characterised by infantile sideroblastic anaemia and vacuolated normoblasts associated with multisystemic manifestations. The finding of a characteristic 4977-kb deletion in the mitochondrial DNA is diagnostic, and most patients die during early childhood from non-haematological complications.[3]

REFERENCES

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answer: c

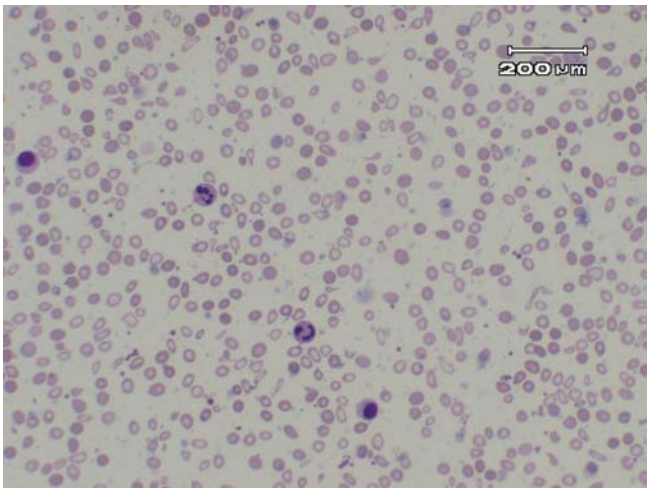

Fig. 1. Peripheral blood film showing microcytosis, hypochromia, anisopoikilocytosis with elongated cells, tear drop cells and target cells. Polychromasia is not obvious and basophilic stippling is not seen. The morphology of the white cells and platelets is normal. The automated cell counts show haemoglobin 7.1 g/dL, mean corpuscular volume 63.2 fL, red cell distribution width 27.5%, and reticulocytes 1.8%.

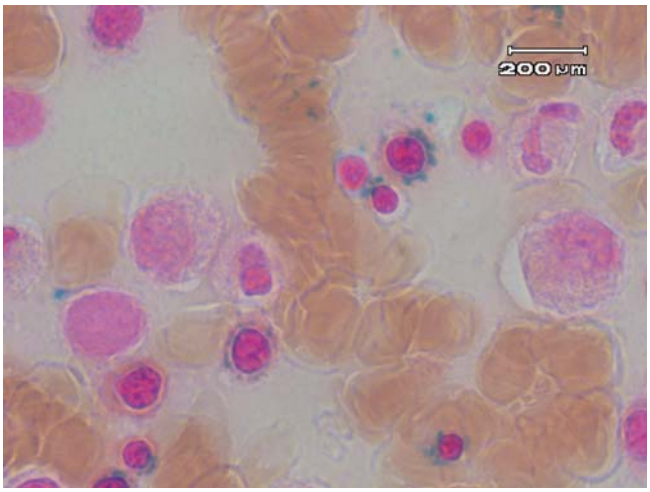

Fig. 2. Prussian blue staining of the bone marrow smear showing numerous ring sideroblasts. The iron stores are increased and the erythropoiesis is active and normoblastic (not shown).