deficiency of 5-α-reductase is described, the elder of two affected male siblings. These patients, who come from Pakistan, are the first to be described outside America.

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References


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Congenital dyserythropoietic anaemia type I in two brothers presenting with neonatal jaundice

Congenital dyserythropoietic anaemia (CDA) is a name given to a group of hereditary refractory anaemias which show ineffective erythropoiesis, characteristic morphological abnormalities of the erythroblasts, an inappropriately low reticulocyte response, mild hyperbilirubinaemia, splenomegaly, and secondary haemochromatosis. From their morphological and serological features these anaemias have been classified into 3 groups although there is some overlap between them (Heimpel and Wendt, 1968). Type I is characterised by macrocytosis and internuclear chromatin bridges, type II shows binucleated and multinucleated normoblasts and positive acidified serum lysis, and type III has giant multinucleated erythroblasts. CDA type I, first described by Heimpel et al., in 1968, appears to be the least common of this rare group of anaemias with 21 cases reported—including three pairs of siblings (Heimpel, 1976). This report describes 2 brothers with CDA type I, both of whom presented with neonatal jaundice.

Case reports

Case 1. A 3·5 kg baby boy was admitted to this hospital at 2 days following vacuum extraction at 38 weeks after spontaneous onset of labour. The liquor was noted to be deep orange. Apgar scores were 4 at 1 minute and 9 at 10 minutes. Cord blood serum bilirubin was 60 µmol/l (3·5 mg/100 ml) and the direct antiglobulin test was negative. Before being transferred to this hospital a cyanotic episode had occurred, slight jaundice was clinically evident, and treatment with antibiotics was begun because of suspected neonatal sepsis. The patient was the first child of unrelated parents and there was no family history of any haematological disorder. Examination revealed a slightly jaundiced, term infant with 2 cm hepatomegaly and 3 cm splenomegaly. Blood count showed Hb 14·5 g/dl, WCC 25·0 × 10³/l; 25 000/mm³ (neutrophils 15·5 × 10³/l, lymphocytes 8·0 × 10³/l; 15 500/mm³, 8000/mm³), nucleated RBC 5·4 × 10⁹/l (5400/mm³), and platelet count 50 × 10⁹/l (50 000/mm³). Red cells showed anisopoikilocytosis, macrocytosis, fragmented cells, and a few stipple cells. Serum bilirubin was 67 µmol/l (3·9 mg/100 ml). Direct antiglobulin test was negative and blood groups of both mother and baby were A-positive. Bacterial cultures and search for prenatal infective agents were negative and antibiotics were stopped on the 7th day. When discharged at 19 days he was well with 1 cm hepatosplenomegaly, Hb 10·5 g/dl, WCC 15·0 × 10³/l (15 000/mm³) platelets 400 × 10³/l (400 000/mm³), and the nucleated red blood cells had disappeared. At 8 weeks he was readmitted with Hb 6·3 g/dl and transfused with packed red cells. The abnormal red cell morphology was unchanged and the provisional diagnosis was infantile pyknotycyosis.

During the subsequent 2 years he remained well but had persistent hepatosplenomegaly of 1 cm. Hb varied between 8·5 and 10·5 g/dl, reticulocytes between 1·0 and 2·5%, serum bilirubin was 19 µmol/l (1·1 mg/100 ml), and haptoglobins were absent. The blood film showed persistent abnormal red cell morphology characterised by anisopoikilocytosis, macrocytosis, fragmented cells, and stipple cells. Blood counts and red cell morphology of both
parents were normal. The following investigations showed no abnormalities: direct antiglobulin test, glucose-6-phosphate dehydrogenase, pyruvate kinase, autohaemolysis, Hb electrophoresis, Hb H, acidified serum lysis, serum and red cell folate, serum B12. The serum iron was raised to 47.8 µmol/l (267 µg/100 ml), the iron binding capacity was 50.7 µmol/l (283 µg/100 ml) and saturation 94%. Bone marrow aspiration at 26 months showed morphological abnormalities of the erythroblasts consistent with CDA type I.

Case 2. A 3.5 kg baby boy, the younger brother of Case 1, was admitted to this hospital at 18 hours of age after normal delivery at 41 weeks and artificial rupture of the membranes. The liquor was noted to be deep orange. Apgar scores were 8 at 1 minute and 10 at 5 minutes. Cord blood serum bilirubin was 92 µmol/l (5.3 mg/100 ml) and direct antiglobulin test was negative. Blood groups of mother and baby were A-positive. On examination the baby was a healthy, term infant with obvious jaundice and 2 cm hepatosplenomegaly. Serum bilirubin was 240 µmol/l (14 mg/100 ml). Blood count showed Hb 15.4 g/dl, WCC 25.0 × 10⁹/l (25 000/mm³), (neutrophils 13.5 × 10⁹/l; lymphocytes 8.5 × 10⁹/l; 13 500/mm³, 8500/mm³), nucleated RBC 11.0 × 10⁹/l (11 000/mm³) and platelets 120 × 10⁹/l (120 000/mm³). Red cell morphology showed anisopoikilocytosis, macrocytosis, fragmented cells, and an occasional stipple cell; many of the nucleated red cells were bilobed. Bone marrow aspiration on day 3 showed morphological abnormalities of the erythroblasts suggestive of dyserythropoietic anaemia. Glucose-6-phosphate dehydrogenase, pyruvate kinase, osmotic fragility, autohaemolysis, acidified serum lysis, serum B12, serum and red cell folate were all normal. The patient was treated with phototherapy for 48 hours and discharged well on the 5th day with Hb 16.7 g/dl and serum bilirubin 158 µmol/l (9-2 mg/100 ml). At 8 weeks of age Hb had fallen to 6.3 g/dl and he was transfused with packed red cells. During the next 12 months he remained well with persistent hepatosplenomegaly of 1 cm and Hb between 9.6 and 10.8 g/dl, reticulocytes 1.0%, and serum bilirubin 19 µmol/l (1.1 mg/100 ml).

Bone marrow morphology

Light microscopy.

Case 1. Iliac crest aspirate at 26 months of age was hypercellular with erythroid hyperplasia, and a myeloid erythroid ratio 1.5:1. Granulopoiesis was normal and megakaryocytes appeared normal. Morphological abnormalities were confined to the intermediate and late erythroblasts while the pro-erythroblasts and basophilic erythroblasts appeared normal. There was asynchrony of nuclear cytoplasmic maturation and abnormalities of both nuclear chromatin structure and cytoplasm. Some nuclei were pale and poorly demarcated, and others were denser than normal, some with coarse chromatin clumps, others a dense homogenous mass. In many cells the cytoplasm appeared irregularly haemoglobinised with pale areas and vacuolisation. Double nuclei were found in 2.6% of erythroblasts and many were of unequal size and of different chromatin appearance (Fig. 1); a few cells had 3 nuclei. In 2.4% of erythroblasts large cells contained a large nuclear mass partially cleaved into 2 segments. Fine internuclear chromatin bridges joining pairs of cells were seen in 1.4% of erythroblasts (Fig. 2). Iron stores were increased.

Case 2. Marrow was aspirated from the tibia at 3 days. Cellularity was normal and the myeloid erythroid ratio was 1:5:1. Abnormalities were confined to the intermediate and late erythroblasts with asynchrony of nuclear-cytoplasmic maturation, irregularities and vacuolisation of the cytoplasm, and changes in nuclear chromatin structure. Some nuclei were pale and poorly demarcated, others were denser than normal. Bilobed nuclei were seen in 1.5% of erythroblasts and a few cells had 3 nuclei. A large partially cleaved nucleus was present in 3.5% of erythroblasts. No definite internuclear

![Bone marrow smear. A double nucleated erythroblast with two nuclei of unequal size and different chromatin appearance.](image-url)
reticulocyte counts were only 1.0 to 2.0%. Two years later the second sibling presented with deep orange liquor and neonatal jaundice with no sepsis. The peripheral blood picture of numbers of bilobed nucleated red blood cells prompted an early bone marrow examination which proved to be highly suggestive of a congenital dyserythropoietic anaemia, and a bone marrow examination on the elder child showed the typical features of CDA type I as described by Heimpel et al. (1971) and Lewis et al. (1972). However, in both cases these features could have been overlooked on light microscopical examination. The incidence of internuclear chromatin bridges was very low, and on the first bone marrow in Case 2 they were not found despite an intensive search; the more subtle changes in nuclear chromatin structure were also relatively low in incidence.

**Summary**

Two brothers with congenital dyserythropoietic anaemia type I are described. Both presented with neonatal jaundice, required transfusion for anaemia at 8 weeks of age, and have subsequently remained well with only mild anaemia. Peripheral blood findings and bone marrow morphology on light and electron microscopy are discussed.

**References**


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