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CONGENITAL LYMPHOBLASTIC LEUKAEMIA IN AN AFRICAN MALE

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On 23 April 1957 one of us (H.F.T.) was asked to see a male African baby who had been born some hours before. The delivery had been uneventful and the period of gestation was normal. The mother appeared to be fit in all respects. She had not been exposed to X-rays as far as was known.[1,2]

Examination of the child showed the presence of small, discrete petechiae on the face, subcutaneous ecchymoses ranging in size from 1-3 mm. in the palms and soles, and subcutaneous haematomata scattered diffusely over the trunk. The visible mucous membranes showed marked pallor, but no icterus and no pingueculae could be discerned. The face was oedematous but there was no sign of oedema elsewhere. No mongolism was noted.[3,4] The umbilical cord did not bleed once it had been ligated. Dyspnoea was marked but there was no associated cyanosis or engorgement of the neck veins. Slight diffuse abdominal distension was present but clinical examination did not reveal any enlargement of the liver or spleen. No free fluid was found in the peritoneal cavity. The mucous membranes were not ulcerated, the superficial lymph glands did not seem to be significantly enlarged, and the remaining systems were not remarkable. No stigmata of congenital syphilis were found. No congenital morphological defects were noted.[5] Blood for haematological investigations was taken from the child's foot. Bleeding was free and could only be controlled by continuous pressure and by raising the foot.

An intra-tibial blood transfusion was started and the child received about 80 c.c. of blood before it died. Other treatment that was given included Konakion, 1 ampoule by mouth, intramuscular crystalline penicillin, 50,000 units 6-hourly, and streptomycin, ·05 g. every 12 hours.

The child lived for about 26 hours after its birth. The following are the results of the special investigations which were carried out:

1. *Blood Grouping:* Group O Rhesus positive. (The mother was also Group O Rhesus positive, and her Kahn test was negative.) A Coombe's test was not done.

2. *Blood Count.* Haemoglobin 6·25 g. (40%). Leucocytes 40,300 per c.mm. [polymorphonuclear leucocytes 15%, metamyelocytes 5%, 'blast cells' (probably lymphoblasts) 63%, lymphocytes 16%, monocytes 1%.] In each count of 100 leucocytes 7 early normoblasts were noted. The red cells appeared microcytic. Marked anisopoikilocytosis and polychromasia was noted. Platelets appeared to be considerably reduced in number.

3. *Bleeding Time* (Duke's method) markedly increased (bleeding persisted for more than 30 minutes).

4. *Clotting Time* (Wright's capillary-tube method) 1 hour.

5. *Prothrombin Index* 23% (control 20 seconds, patient 89 seconds).

In consultation between us a tentative diagnosis of congenital leukaemia was made.

Autopsy was performed about 12 hours after death, when the following relevant findings were made: The previously noted petechiae, ecchymoses and haematomata were more marked and more extensive than before. There was no special superficial lymph-gland hypertrophy. The peritoneal cavity contained a large amount of blood, which had not coagulated. The *liver* was enlarged, weighing 192 g. Its surface was smooth, its consistency softer than usual, and its colour normal. Subcapsular petechiae and ecchymoses were noted. In the right lobe a tear 1 inch in length extended from the right inferior margin along the inferior surface and between the colic and the renal impressions. The same tear also extended onto the right lateral surface for a further 1 inch. In addition a tear of the left lobe extended from the anterior margin backwards for about 1 inch. The *spleen* was enlarged, weighing 23 g. Its colour and consistency were normal. In both *lungs* large multiple ecchymoses could be seen subjacent to the visceral pleura and also diffusely throughout the parenchyma. *Pericardial* petechiae were seen. The heart was otherwise normal. The pericardial sac contained a small amount of straw-coloured fluid. The *brain* was very pale and oedematous and the convolutions were very flat. A few scattered petechiae were noted in the brain substance. The immediate cause of death seemed to be rupture of the liver with resultant severe peritoneal haemorrhage, and it was thought that cerebral oedema might be a contributory cause. It was considered reasonably certain that the rupture of the liver had occurred during the process of birth. It was believed, however, that the primary underlying cause of the whole condition was congenital leukaemia, probably of a lymphoblastic type.

The following are the results of the investigations carried out by the South African Institute for Medical Research:

On 9 May Dr. H. I. Lurie reported as follows:

Sections of the specimens from the *liver*, *spleen*, *kidney*, and *bone marrow* all show the presence of diffuse infiltration by immature cells, the histological features of which suggest lymphoblasts. Section of the specimen of the *thymus* shows no significant

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pathological changes. Section of the specimen from the *lung* shows that the bronchioles and alveolar spaces are filled with blood. The histological features are those of a *neonatal lymphoblastic leukaemia.*

On 18 May Dr. H. B. W. Greig reported as follows:

Peripheral Blood Smear: The red cells show moderate anisocytosis and poikilocytosis. There is severe hypochromasia. Platelets are reduced in numbers (estimated count 50,000 per c.mm.) and are bizarre in morphology. There is a marked leucocytosis, with many abnormal cells present, mostly of the lymphocyte series. Most of the lymphocytes are immature and many are frank 'blasts'. Bizarre monocytoid forms and primitive reticulum cells are present. There are many normoblasts present.

Bone Marrow. This marrow sample shows almost complete replacement of the normal marrow elements by primitive lymphoid cells. There are round cells with deeply basophilic rather scanty cytoplasm, often vacuolated, and a reticular nucleus usually containing 2-3 nucleoli.

This marrow picture, taken in conjunction with the peripheral blood picture, indicates a diagnosis of acute leukaemia, almost certainly lymphoblastic in type.

DISCUSSION

We considered that the patient had congenital leukaemia for the following reasons. He showed widely spread cutaneous haemorrhagic lesions at birth and died about 26 hours later. The peripheral blood showed the presence of large numbers of lymphoblasts. A high percentage of lymphoblasts was also found in the sternal bone marrow. Although normoblasts were found in the peripheral blood, the picture was not that of an erythroblastosis foetalis. Moreover there was no incompatibility in the bloods of the child and its mother. A marked thrombocytopenia was present and both the bleeding and coagulation times were considerably prolonged. The liver, spleen, kidney and bone marrow were invaded by primitive cells which were considered to be lymphoblasts.

Certain critera have been laid down for the diagnosis of congenital leukaemia,[5,6] as follows: Symptoms should be present at birth or develop very shortly thereafter. The liver, spleen and lymph nodes should be enlarged. The leucocyte count should be high and primitive white cells should predominate. There should be nothing in the history suggestive of syphilis, erythroblastosis foetalis or icterus gravis. There should be tissue infiltration by primitive white cells into non-haemopoeitic organs as well as the liver, spleen and lymph nodes. Primitive white cells should be seen in both the peripheral blood and the bone marrow. The possibility that the blood changes may be due to syphilis or to erythroblastosis foetalis should be excluded.

Certain features about our case were unusual. The patient was an African; we have been unable to trace any reference in the literature to congenital leukaemia in Africans. The leukaemia was lymphoblastic in type; the literature stresses the predominance of the myelocytic forms in this rare disease.[5-8] Several reports have appeared in the literature relating to the coexistence of congenital leukaemia and mongolism;[3,4] no signs of associated congenital disease were found of the type described in the cases of Bernhard *et al.*[5] There was no history of any exposure of the patient or his mother to X-ray therapy; such exposure may be important in the production of congenital leukaemia and this possible aetiological factor is receiving increasing attention in medical literature.[1,2]

SUMMARY

A case is described of congenital lymphoblastic leukaemia in an African male. The criteria for making a diagnosis of congenital leukaemia are discussed. The rarity of the lymphoblastic form of congenital leukaemia is stressed.

We wish to thank the medical staff of the South African Institute for Medical Research for their help in the investigation of this patient. A special word of thanks is due to Prof. J. F. Murray and to Drs. H. I. Lurie and H. B. W. Greig.

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