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Wolman disease in twins

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In newborn twins at three hours of age adrenal calcification has been detected. In addition to hepatomegaly, vomiting and diarrhoea, characteristic radiological findings confirmed the diagnosis of the rare heritable lipidosis, Wolman's disease.

Bilateral adrenal calcification may be caused by several pathological conditions [2]. Primary familial xanthomatosis or Wolman's disease [8] has to be considered in the first days of life. The characteristic radiological finding accompanying the clinical symptoms may be the first sign confirming the diagnosis [4]. As a consequence of lacking lysosomal acid esterase [5, 6], cholesteryl ester and triglycerides are stored in the liver, adrenals and bone marrow. The presence of typical foamy histiocytes in the bone marrow is pathognomonic [7].

Case reports

Of the female twins originating from a first cousin marriage of a Libyan Arab couple (Fig 1), the first-born had a birthweight of 2100 g, the second-born member of the pair weighed 1700 g. Both were admitted at three hours of age. Twin A had anaemia with 101 g/l haemoglobin and 0.34 l/l packed cell volume. She was therefore transfused with blood of her own blood group. The twins were monoplacental, monoamnial and monochorial. Their blood groups were identical within the ABO, Rh. Lutheran, Kell and Duffy systems. Physical examination revealed a prominent abdomen with hepatomegaly in both babies. Abdominal X-rays taken at three hours after birth showed bilateral calcification of the adrenal glands of both children (Figs 2 and 3). These changes were even more conspicuous in twin B two weeks later (Fig 4); in the same baby adrenal calcification accompanied by severe hepatomegaly was seen at four months of age (Fig 5). Feeding difficulties appeared as early as three days of age in both newborns, soon joined by profuse vomiting and watery diarrhoea. The patients needed glucose-saline infusions. The condition of twin A was more severe in spite of her higher birthweight. In addition to anaemia the leukocyte count was 3 G/l, platelet count 120 G/l, reticulocytes 1.10^{-3}. In the blood film 35 nucleated erythrocytes per 100 leukocytes were found, the distribution of leukocytes was normal. Twin A also had a congenital heart defect, and septic symptoms appeared accompanied by heart failure. In spite of broad spectrum antibiotics and mechanical ventilation she died at two weeks of age. Necropsy could not be performed, being prohibited by Libyan laws.

Vomiting of twin B ceased during intravenous fluid therapy but her stools continued to be of watery consistence. She failed to thrive in spite of adequate caloric intake. The patient had to be given blood transfusion several times. At three months of age

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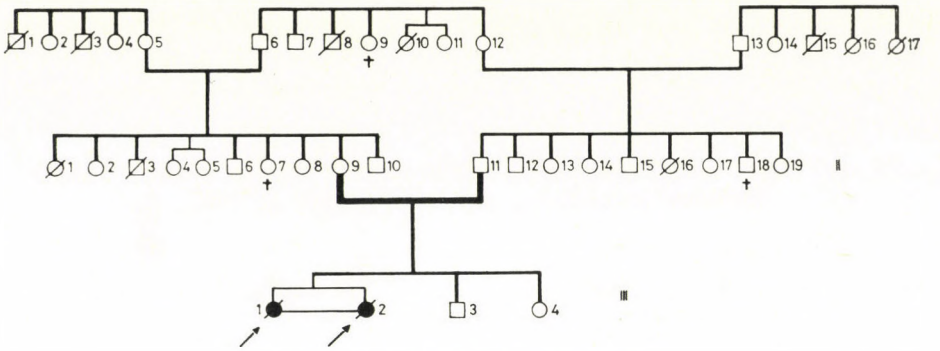


FIG. 1. Pedigree of the patients

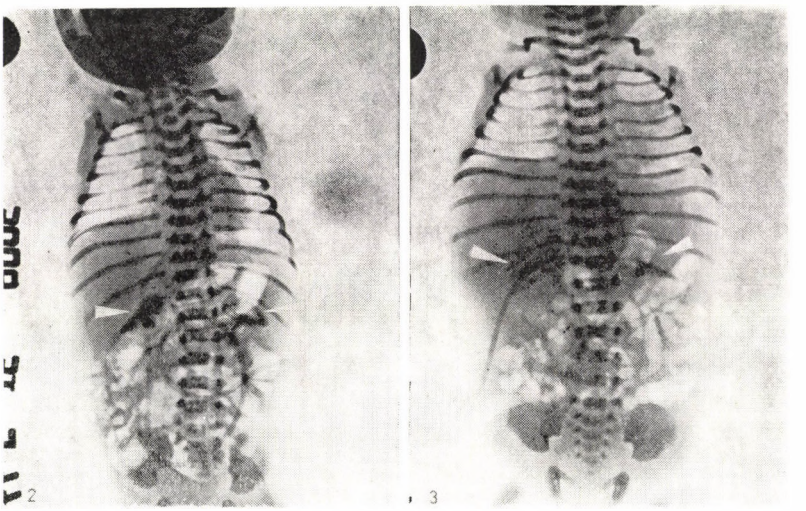
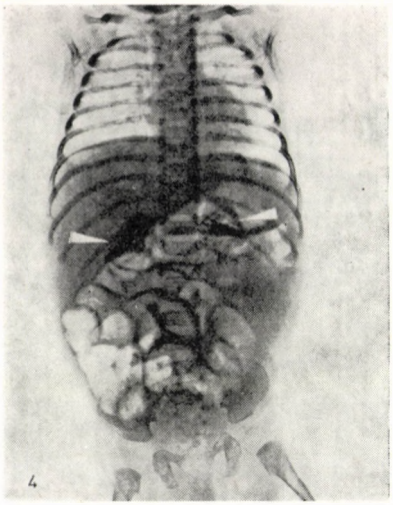


FIG. 2. Plain abdominal X-ray of twin B at three hours of age. The cap-shaped calcifications in both adrenal regions are indicated by arrows

FIG. 3. Plain abdominal X-ray of twin A. Adrenal calcification of the right side is partly covered by the umbilical catheter, intestinal gases cover the calcification on the left, the lesions are less pronounced than in twin B

she weighed 2420 g; at this time her parents took her home. At discharge from hospital her liver was palpable 2 cm below the costal margin, the spleen could not be felt.

One month later the infant was readmitted because of fever and diarrhoea. At that time she weighed 2850 g. An enlarged, soft liver was palpated 3 cm below the costal margin, only the tip of the spleen could be felt. There were no demonstrable neurological signs. Her laboratory findings were: haemoglobin: 82 g/l, PCV: 0.36 l/l, leukocyte count: 5.3 G/l, platelets: 80 G/l, differential leukocyte count: striking vacuolisation of lymphocytes. Bone marrow: diminished erythropoiesis, foamy histiocytes. Liver function tests: direct bilirubin: 3.4 μmol/l, indirect bilirubin: 6.8 μmol/l, SGOT: 17 IU/l, SGPT: 10 IU/l, LDH: 416 IU/l, alpha-HBDH: 292 IU/l, gamma-GT: 61 IU/l, alkaline phosphatase: 254 IU/l, ESR: 28 mm/hour. Urine analysis revealed no abnormality. Stool bacteriology and parasitology: negative. BUN: 3.0 μmol/l, serum sodium: 136 mmol/l, potassium: 3.1 mmol/l, chloride: 102 mmol/l. In view of the vomitings, diarrhoea and the underlying disease, glucose, saline, amino-



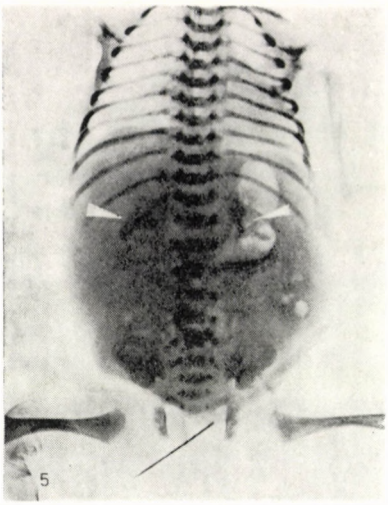


FIG. 4. Plain abdominal X-ray of twin B at two weeks of age. Pronounced calcification in the right adrenal region, on the left side it is covered by intestinal shadows. Hepatomegaly and bronchopneumonia can be observed

FIG. 5. Plain abdominal X-ray of twin B at four months of age. Adrenal calcification unchanged, marked hepatomegaly

acid solutions and protein were given. The patient died of apnoea and cardiac arrest 10 days after admission.

DISCUSSION

In type I of Wolman's disease the characteristic features are hepatosplenomegaly, diarrhoea, adrenal calcification, vacuolized lymphocytes in the blood smear, foamy histiocytes in the bone marrow and neurological symptoms like clonus, hyperreflexia and opisthotonus [1]. In the second type, neurological signs are missing. Our cases appeared to belong to type II although the patients died at an early age.

Wolman disease as a lipid storage disturbance has to be differentiated from Gaucher disease and Niemann—Pick disease. Adrenal calcification may occur in neuroblastoma when the abnormality is unilateral. In case of adrenal haemorrhage the changes may be bilateral but the adrenals usually decrease in size in such cases [3]. Demonstration of lacking or markedly depressed activity of lysosomal acid esterase in liver biopsy material or leukocytes confirms the diagnosis.

The enzyme deficiency can be diagnosed at 3 or 4 months gestational age from fibroblast cultures obtained by amniocentesis. In our cases the clinical features, the radiological findings and demonstration of foamy histiocytes in the bone marrow have confirmed the diagnosis of Wolman disease.

Therapeutic attempts with cholestyramine, d-thyroxine, clofibrate or a medium chain triglyceride diet con-

taining much protein and rich in calories have hitherto failed. Corticosteroid treatment may be attempted.

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