A CASE OF HYPOTHYROIDISM WITH NEPHROCALCINOSIS

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Hypothyroidism is the commonest of all endocrine disorders in childhood. Its association with extensive nephrocalcinosis, however, must be very rare, and so the following case is of interest.

Case Report

A girl aged 4½ years was admitted to the Paediatric Unit, Clatterbridge Hospital, Bebington, Cheshire, on February 8, 1954. She had been taken to her family doctor for treatment of a furuncle below the right eye and he had referred her as a case of cretinism.

The child weighed 7½ lb. at birth and was born in West Kirby, Wirral. She was breast fed for one month and then the family moved to Scotland. She is the second child in a family of three. The siblings, a sister aged 6 years and a brother aged 2 years, are normal and healthy. The parents are well and there is no family history of goitre.

At the age of 3 months the mother noticed that the child had little interest in her surroundings and that she had a large tongue and a squint. At 9 months she started to hold up her head, and began to sit with support when 3½ years old. Her first tooth erupted at that time. She had always been constipated. Normal amounts of vitamin D in the form of cod liver oil and ‘minadex’ had been given.

When 10 months old, the patient was seen at another hospital and a diagnosis of mongolism was made. No treatment was advised and the parents accepted this opinion.

On admission to Clatterbridge Hospital she presented the typical appearance of hypothyroidism. She had dry, scanty hair, a dull expression, and a large protruding tongue. The abdomen was protuberant, the extremities blue and cold, the skin greyish, mottled, coarse and dry, and there was non-pitting oedema and myxoedematous firmness of the tissues. She was grossly stunted (height 26 in., weight 18½ lb., skull circumference 16½ in., abdominal girth 19½ in.) and the limbs were short. One upper and one lower incisor were erupting. She could smile and hold up her head and just sit with support. However, she was not interested in her surroundings, could not stand even with support and could not talk. Feeding was difficult and mainly from the bottle and she was very constipated (Fig. 1).

A radiograph (Fig. 2) showed retarded ossification of the skull bones. The anterior and posterior fontanelles remained open. Several Wormian bones were present and the bones at the base of the skull were thickened and the base was short. A radiograph of the lower limbs (Fig. 3) showed retarded ossification of all the epiphysial centres with sclerotic lines at the ends of the long bones. The ossification centres showed epiphysial dysgenesis. A radiograph of the wrist also showed delay in ossification and dense lines at the lower ends of the radial and ulnar shafts. Radiographs of abdomen and hips (Fig. 4) showed extensive calcinosis in both renal areas and delay in ossification of the femoral heads. A radiograph of the spine (Fig. 5) showed that maturation of the vertebrae was retarded and that there was deformity of some vertebral bodies. An intramuscular pyelogram showed impaired renal function. A radiograph of the chest and an electrocardiograph were within normal limits.
A blood count gave haemoglobin 60%, red cells 2,660,000 per c.mm., white cells 14,200 per c.mm. (81% neutrophils, 19% lymphocytes). The blood cholesterol level was 458 mg. %, serum alkaline phosphatase 16·5 units, serum inorganic phosphates 6·6 mg. %, serum calcium 12·2 mg. %, serum calcium ions 6·1 mg. per 100 ml., blood urea 148 mg. %. The serum proteins were 5·8 g. % and the CO₂-combining power of the blood was 46 vol. %.

A trace of protein was found in the urine, numerous pus cells, and an occasional red blood cell and granular cast. The pH was 5·0 and the CO₂-combining power was 0 vol. %. Chromatography of the urine showed no abnormal amino-aciduria; glycine, alanine and cystine were detectable in small amounts.

Treatment was begun on February 12 with thyroid, grain 1/2 daily, increased to grain 1 daily on March 6, and to grain 1 1/2 daily on March 29, in divided doses. Frequent enemas were necessary.

While in hospital the child's progress was rather disappointing. Her general appearance improved. The skin became smoother, the tongue smaller and the abdomen less protuberant. The extremities became pink and warm. The blood cholesterol level fell from 458 to 265 mg. %, There was, however, no change in

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**Fig. 2.**—Radiograph of the skull, showing open anterior and posterior fontanelles; short base with thickened bones.

**Fig. 3.**—Radiograph of the lower limbs, showing retardation of ossification, sclerotic lines at the ends of long bones, and epiphysial dysgenesis of ossification centres.

**Fig. 4.**—Radiograph of the abdomen and hips, showing nephrocalcinosis and delay in ossification of femoral heads.

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her feeding, and she continued to behave like a 6-month-old baby in this respect; she seemed drowsier at times and was not smiling so much. On admission she could just support herself in the sitting position, but gradually she was unable to do this. She remained constipated and lost a little weight. We thought that this regression was in part due to being in hospital and lack of maternal care and so she was discharged on March 29.

When seen on July 7 (after five months of thyroid therapy) there was a striking improvement (Fig. 6). A considerable amount of new soft hair had grown in and the skin was smooth and had lost its grey, mottled appearance. The child was warm and the extremities were pink. The tongue was small and 15 teeth had
erupted. She had lost the thickened subcutaneous tissues. She was taller, had lost 2 lb. in weight and her infantile proportions. The abdomen was no longer protuberant, the girth being 15 in. The skull circumference remained the same, but the fontanelles were smaller. For about a fortnight she had been attempting to pull herself into the sitting position; she could now sit for a few minutes without support, and had more balance. Her mother thought that she was taking more notice and she preferred a cup to a bottle. She was having a daily bowel action without aperients and the only trouble seemed to be that she was a little cross at nights; in view of this the thyroid was not increased from 1½ grains daily.

The radiograph taken on July 7 showed that the anterior and posterior fontanelles were smaller, but otherwise there was no change. No centres of ossification had appeared in the wrist.

On August 14 the blood urea was 114 mg, serum protein 6·55 g, serum calcium 15·1 mg, serum calcium ions 7·2 mg, serum phosphate 7·0 mg, serum alkaline phosphatase 19 units, and blood cholesterol 195 mg.

Discussion

Wilkins (1950) emphasizes that a diagnosis of hypothyroidism should be made on (1) physiologic evidences of thyroid deficiency—sluggishness, impaired circulation and constipation, and (2) evidences of retarded growth and development—delayed bone age and dental development, infantile facies and skeletal proportions and epiphyseal dysgenesis. All this evidence is present in the case described, which is an extreme example of untreated hypothyroidism. The serum phosphatase estimation, which is a useful confirmatory test of hypothyroidism, was not reduced as is almost constantly so in this endocrine disorder (Gaisford, 1952). The interesting feature in the case is the extensive nephrocalcinosis and the raised level of blood serum calcium.

Aub, Bauer, Ropes and Heath (1927) found that in hypothyroidism calcium and phosphorus are deposited in greater concentration in the bones and eliminated less freely in the urine and stools than they are in the normal person. Robertson (1941) studied the calcium and phosphorus balance in three cases of myxoedema in adults and found that the blood serum level of calcium and phosphorus was normal but the output greatly reduced. Braid (1951) reports a case in which there was clinical evidence of calcium retention in that there was increased density of the bones and a diffuse calcinosis of the soft tissues. This occurred in a child of 2½ years who was a case of untreated hypothyroidism. This child, however, had a normal blood calcium in.
contrast to the case described here where the blood calcium level was raised.

Conditions causing hypercalcaemia have been reviewed by Wilkins (1950). They include vitamin D poisoning, osteoporosis of disuse, hyperparathyroidism, neoplasms and sarcoid. There was no evidence in this case that excessive doses of vitamin D had been given. In vitamin-D intoxication, renal impairment with extensive deposition of calcium in the inter-tubular tissues of the kidney can occur. Nephrocalcinosis has been described in osteoporosis of disuse. In this condition hypercalcaemia may occur, but the serum phosphorus level is usually normal and the phosphatase not increased, in contrast to the case described here, where both the serum phosphorus and phosphatase were raised. This child was immobile, because of mental retardation, for four and a half years, and might well fit into this group. There was no evidence of demineralization of bones as occurs in hyperparathyroidism, but in this condition there may be metastatic calcification including deposits of calcium in the kidneys and urinary tract.

Lightwood (1952) describes cases of idiopathic hypercalcaemia, which clinically are indistinguishable from renal acidosis. Two of his series of 10 showed nephrocalcinosis. The blood chemistry showed a raised blood calcium and urea without concurrent renal acidosis. Payne (1952) describes the blood chemistry in idiopathic hypercalcaemia. There was a raised plasma protein as well as raised blood calcium and urea. The phosphate, phosphatase, chloride and bicarbonate levels were normal. The renal function was depressed in the active phase.

The prognosis is poor in regard to mental development and duration of life; first because of the age at which treatment was begun and secondly because of the poor renal function and raised blood urea. All that can be hoped for is an improvement in the physical condition, which has already taken place. There is a danger in treating this type of case (where thyroid therapy has been withheld until after the most active period of growth of brain and body) of producing a manic type of psychosis and so it is wiser to under-treat and leave the child placid and manageable (Wilkins, 1950).

Summary
A case of hypothyroidism with associated nephrocalcinosis is described. The possible aetiology of the renal calcification and the prognosis are discussed.

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