Primary Hyperparathyroidism Resembling Rickets of Late Onset


Primary hyperparathyroidism is rare in childhood and early adolescence, and may present special difficulties in diagnosis. Delay in treatment is dangerous, since children are prone to develop severe hypercalcaemia (Nolan, Hayles, and Woolner, 1960), and may suffer irreversible mental impairment (Anspach and Clifton, 1939; Harmon, 1956). Moreover, bone disease, if present, may cause rapidly progressive deformity resulting in prolonged or permanent incapacity.

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Important aspects of primary hyperparathyroidism in childhood were encountered in the patient described in this report. The osseous manifestations were of unusual interest, comprising osteitis fibrosa cystica, osteosclerosis, and metaphyseal changes simulating rickets. There was a neurological disturbance resembling chorea.

Case Report
A 14-year-old schoolboy was admitted to Brisbane Hospital on 18 February 1964. He had been well until two years previously, when his scholastic performance began to deteriorate and his cheer-
ful personality changed to one of apathy. In August 1963 he started to grow more rapidly, and his height increased by 5 to 7 cm. in the next six months. During this period he became knock-kneed and complained of weakness in his legs, which prevented him from walking more than ½ mile (1,200 metres) at a time. He had no pain in his legs, and his only other symptoms were occasional sharp pains in the left side of his chest and anaemia in the mornings. There was no excessive thirst or polyuria; nor were there any symptoms referable to the urinary system. He had not taken vitamin-D supplements in any form.

Examination revealed a well-nourished adolescent boy who was apprehensive but co-operative. There was severe knock-knee (intermalleolar distance 23 cm.; Fig. 1), palpable beading of the ribs, but no flaring of the wrists. The lower segment was 16 cm. longer than the upper segment (crown-to-pubis 78 cm.; pubis-to-heels 94 cm.). Apart from a slight thoracic scoliosis, there was no other skeletal deformity. The bones were not tender. The thyroid gland was not enlarged, and no lump was palpable in the neck. There was no corneal calcification. The blood-pressure was normal, and the pulse 80–110 per minute with sinus arrhythmia. The neurological findings comprised mild choreic dysarthria, grimacing, generalized muscular hypotonia, with inactive tendon reflexes, and a mild ataxic tremor in both upper limbs. His gait was laboured, largely because of the severe knock-knee, with, in addition, waddling, high stepping, and circumduction of the feet.

**Investigations**

The results of the principal biochemical investigations are given in the Table. Other results were as follows: haemoglobin 13.2 g./100 ml.; serum amylase 100 Somogyi units/100 ml.; serum creatinine 1.3 mg./100 ml.; serum protein 7.2 g./100 ml. with normal electrophoretic pattern; serum uric acid 9.7 mg./100 ml.; serum protein-bound iodine 6 μg./100 ml.; serum electrolytes: sodium 142, potassium 5.2, chloride 104, CO₂-combining power 21.4 mEq/litre. Microscopical examination of the urine (centrifuge deposit) revealed 20 leucocytes and 10 red cells per high-power field.

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<th>P (mg./100 ml.)</th>
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<th>Blood Urea (mg./100 ml.)</th>
<th>Urine Calcium (mg./day)</th>
<th>Hydroxyproline (Total) (mg./day)</th>
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* Day of operation. † Method of Prockop and Udenfriend (1960).

Radiographs revealed subperiosteal erosions in the fingers, in the proximal metaphyses of the humeri and tibiae, and in the distal metaphyses of the radii. There was a cyst-like lesion in the head of the left fifth metacarpal. The anterior ends of the lower ribs were expanded and cupped (Fig. 2). The epiphysial plates at the shoulders, ankles, and hips were enlarged, irregular, and poorly defined (Fig. 3), but they were normal at the wrists. At the knees the epiphysial plates appeared nearly normal, but in the metaphyses of both femurs, just proximal to the epiphysial plate, a radiolucent zone extended about 2 cm. across the width of the bone (Fig. 4). Bone of increased radiopacity was present in the proximal metaphyses of the tibiae (Fig. 4), and in the upper and lower parts of the bodies of the lower thoracic and lumbar vertebrae (Fig. 5).

**Fig. 1.—The patient, showing severe knock-knee.**

**Fig. 2.—Expanded, cupped anterior ends of lower ribs.**
months of operation. The ankle metaphyses were nearly normal within one month, but at the hip healing was less rapid. The osteosclerotic changes and beading of the ribs were no longer present six months after operation. He continued to grow in height, with some improvement in the degree of knock-knee, but bilateral femoral osteotomies were thought to be necessary. At the first osteotomy on 9 June bone from the lower end of the femur showed less fibrosis than the previous biopsy specimen of the iliac crest, few inactive osteoclasts, and decreased osteoblastic activity, now only slightly above normal for his age. Since his parathyroidectomy the patient had noticed limitation of forward and lateral flexion of his neck. Radiographs revealed a slight anterior displacement of the fifth on the sixth cervical vertebra, which may have been caused by extension of the neck during the operation.

An electroencephalogram on the tenth day after operation showed that the alpha rhythm frequency had increased to 10 c.p.s., and, while there was still excessive bilateral temporal theta activity, its mean frequency had increased from 4-5 c.p.s. to 5-6 c.p.s. A further electroencephalogram seven months after operation showed bilaterally symmetrical alpha rhythm at 9½-10 c.p.s., with much less bilateral temporal activity at 5-6 c.p.s. than previously.

The serum alkaline phosphatase reached 101 King-Armstrong units/100 ml. 10 days after parathyroidectomy, and had fallen to 43 units four weeks later. Urinary hydroxyproline excretion fell post-operatively (see Table) and then increased to 385 m/m/day one month after operation, remaining thereafter at similar levels at estimations up to four months later. The serum uric acid level was 6.3 mg./100 ml. six months after parathyroidectomy.

**Discussion**

In children primary hyperparathyroidism appears to cause bone disease in a greater proportion of cases than in adults. In a recent review of the literature Nolan, Hayles, and Woolner (1960) noted that 18 out of 22 reported cases showed radiological evidence of bone disease. Renal calculi were present in only six cases, and five of these showed evidence of bone disease as well. Osteitis fibrosa cystica without abnormality of the epiphyseal plate is the predominant type of bone disease in children, but rachitic changes have been described (Ducken, 1928; Brailsford, 1953; Wood, George, and Robinson, 1958) and "condensation" of bone or osteosclerosis has also been reported (Dresser, 1933; Mimpriess and Butler, 1933-4; Albright, Baird, Cope, and Bloomberg, 1934; Shallow and Fry, 1948; Adam and Ritchie, 1954). The patient described by Ducken (1928) was remarkably similar to ours in that knock-knee, beading of the ribs, metaphyseal changes resembling rickets, osteosclerosis in the proximal tibial metaphyses, and subperiosteal erosions were all present. Renal function was normal and a diagnosis of primary hyperparathyroidism is acceptable, although parathyroidectomy was not performed. In our patient the occurrence of various types of

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**Fig. 3.**—Enlarged, irregular, poorly defined epiphysial plates at the ankle.

**Fig. 4.**—Radiolucent zone in femoral metaphysis; osteosclerosis in tibial metaphysis.

**Fig. 5.**—Osteosclerosis in upper and lower parts of vertebral bodies.
Osteosclerotic lesions, including vertebral osteosclerosis, raised the question of associated renal-gonadal osteodystrophy, but renal function was only slightly impaired, and, on the evidence of the blood urea, recovered quickly after removal of the parathyroid adenoma. That all the components of the bone disease had resulted from primary hyperparathyroidism is suggested by their healing after the operation.

The occurrence of osteosclerosis in primary hyperparathyroidism has been discussed elsewhere (Aitken, Kerr, and Lloyd, 1964). In the vertebræ it may take the form of "subchondral condensation" (Jaffe, 1933), or it may resemble the osteosclerosis of renal glomerular osteodystrophy, in which case the patients reported have had either associated chronic renal failure (Beveridge, Vaughan, and Walters, 1959; Willard, Richardson, and Paul, 1961) or steatorrhoea (Davies, Dent, and Willcox, 1956). Two children whose cases have been reported may resemble our patient in having primary hyperparathyroidism and vertebral osteosclerosis without chronic renal failure, but data on their renal function are incomplete (Dresser, 1933; Albright, Baird, Cope, and Bloomberg, 1934). Osteosclerosis in the proximal tibial metaphyses has been described in children with primary hyperparathyroidism (Mimpiss and Butler, 1933-4; Adam and Ritchie, 1954), and appears to be a manifestation of the disease occurring during growth.

The nature of the radiolucent metaphyseal lesions in our patient was unfortunately not established by histological examination. Bone from the iliac crest revealed changes of hyperparathyroidism, and among these the considerable increase in osteoblastic activity suggests that a true rachitic process might possibly have developed. However, it is of particular interest that the radiolucent zones in the distal femoral metaphyses were just proximal to the epiphysial plates, which did not appear to be enlarged. The radiolucent metaphyseal lesions here and elsewhere may represent fibrous replacement of the bone as part of the process of osteitis fibrosa. Experiments described by Shelling (1935) indicate that rachitic bone in young animals is especially sensitive to the effects of parathyroid hormone. Using different experimental procedures, Shelling was able to produce various changes in the metaphyses of young rats, including lesions grossly resembling rickets but histologically characterized by fibrosis and osteoclastic proliferation in the subcartilaginous zone. In other experiments metaphyseal osteosclerosis resulted. In an infant of 4 months with primary hyperparathyroidism Phillips (1948) found fibrosis of the distal femoral metaphysis, increased numbers of osteoblasts, and, at the epiphysial line, irregularity of the cartilaginous cap and uneven calcification. The evidence suggests, therefore, that in our patient the lesions simulating rickets consisted of osteitis fibrosa occurring in young metaphyseal bone.

Increased hydroxyproline excretion is found in primary hyperparathyroidism with overt bone disease (Klein, Albertsen, and Curtiss, 1962; Dull and Henneman, 1963; Lee and Lloyd, 1964). Growing children excrete larger quantities than adults (Ziff, Kibrick, Dresser, and Gribetz, 1956), and during growth in adolescence excretion may range from 100 to 700 mg./day (Jones, Bergman, Kittner, and Pigman, 1964). Hence, in our patient rapid growth as well as bone disease probably accounted for the level of urinary hydroxyproline. The high rate of metabolic processes in bone in children as evidenced by urinary hydroxyproline excretion may have a bearing on the greater relative incidence of bone disease in children with primary hyperparathyroidism than in adults. Immature bone undergoing increased turnover of its collagen and other constituents may be more susceptible to the effects of increased parathyroid secretion than mature bone.

Nolan et al. (1960) drew attention to the high levels of serum calcium in children with primary hyperparathyroidism. Our patient survived, without apparent ill effects, a serum calcium of 19.2 mg./100 ml. just before his operation, a rise of 3.5 mg./100 ml. from the day before. Routine restriction of fluid intake pre-operatively may have precipitated this rise. Gordan (1961-2) has emphasized the risks of restricting fluid intake for the performance of urine-concentration tests in hypercalcicaemic patients.

Neuropsychiatric disorders in primary hyperparathyroidism were the subject of a review by Karp and Frame (1964). Whereas muscle weakness and hypotonicity are well-recognized features of the disease, choreic movements are not mentioned by these authors. There are very few reports of electroencephalographic studies in primary hyperparathyroidism. Slowing of electrical activity (Edwards and Daum, 1959) and right temporal dysrhythmia (Harmon, 1956) have been described. The tracings in our patient indicated a non-specific dysfunction of the upper brain stem which returned progressively to normal after operation.

Apart from the persisting limitation of flexion of the neck, the patient has made an excellent recovery with no evidence of permanent neurological or renal damage. The results of osteotomy of the left femur have been satisfactory. The deformity of the right lower limb is improving spontaneously, and further osteotomy may not be necessary. Considerable though slow improvement in severe knock-knee from primary hyperparathyroidism occurred without orthopaedic surgery in a patient reported by McClure and Lam (1945).

Summary

A case of primary hyperparathyroidism in a boy of 14 years is reported. The principal clinical features were knock-knee, mental apathy, and a neurological disturbance resembling chorea. Radiographs revealed osteitis fibrosa cystica, osteosclerosis, and metaphyseal lesions resembling rickets.

We are indebted to Dr. J. Gallagher for the orthopaedic management of the patient, to Dr. M. J. Edie for advice on the neurological aspects, and to Dr. N. G. Johnston for histological reports.

References