Hypochondroplasia

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SUMMARY Clinical, radiological, and genetic features are described in 3 patients with hypochondroplasia. Early recognition of this disorder is possible from the abnormal body proportions with short limbs and lumbar lordosis without facial stigmata of achondroplasia. Radiological confirmation is possible provided a full skeletal survey is made. Two of our patients had a large head.

Hypochondroplasia is one of the milder varieties of chondrodystrophy, resembling a mild form of achondroplasia. Affected individuals are slightly short in stature with short arms and legs (Kozlowski, 1965, 1973; Beals, 1969; Dorst, 1969; Hall, 1969; Murdock, 1969; Walker *et al.*, 1971). Although hypochondroplasia appears to be fairly common (Rimoin, 1975) there have been few cases described. We describe the clinical, radiological, and genetic features in 3 patients.

Clinical details

Case 1. A boy born in March 1967 at 36 weeks' gestation, after a normal pregnancy and delivery (birthweight 3.15 kg). The mother and father were then aged 28 and 30 years. The child was thought to have had a large head from birth and at the age of 18 months he was suspected by a paediatrician of having achondroplasia. One year later the skull circumference was 56 cm and the anterior fontanelle was still open. He was not seen again until 8½ years, at which time the limbs, particularly in their proximal portions, were noted to be short (Table 1). The hands were not trident shaped, but were hyper-extensible. Moderate lumbar lordosis was present. The rest of the examination, including intelligence, was normal.

Case 2. A girl born 2 weeks post-term in July 1969, birthweight 3.94 kg. The mother and father were then aged 33 and 40 years. The mother had always considered the child's head to be large. At 17 months the infant was referred to hospital as she was still not walking, although other milestones had been normal. She had a skull circumference of 48.3 cm,

Table 1 Anthropometric data in patients with hypochondroplasia

Anthropometric data	Case 1	Case 2		Case 3
		At 3	At 7	
Age at measurement (years)	8.75	3.0	7.5	9.0
Height (cm)	107.7 (3)	92.7 (50)	113.7 (10)	119.0 (3)
Weight (kg)	21.6 (10)	16.4 (90)	20.0 (10)	35.6 (90)
Skull circumference (cm)	53.7	52.5	56.0	50.5
Arm span (cm)	98.5	70.4	106.6	113.3
Upper (U) body segment (cm)	56.3	53.9	60.0	85.0
Lower (L) body segment (cm)	52.5	27.5	53.7	67.5
Ratio U/L	1.1	2.0	1.11	1.2

Figures in brackets are centiles.

a wide anterior fontanelle (2.5 × 2.5 cm), posterior fontanelle (1 × 1 cm), and a diagnosis of arrested hydrocephalus was considered. Subsequent developmental progress was quite normal.

At 3 years she was seen in the outpatients department because of loose stools, subsequently shown to be due to giardiasis. At this consultation, however, her body proportions aroused attention, in particular, the fact that her legs were short and bowed; the arms were also short (Table 1). There was a marked lumbar lordosis (Fig. 1), but the hands were normal. A clinical suspicion of hypochondroplasia was confirmed radiologically. Anthropometric data at 7.5 years showed a slowing of the rate of growth (Table 1). Intellectual and educational attainment were normal.

Case 3. A boy born in April 1968, birthweight 4.11 kg, was born after a normal pregnancy of 38 weeks. The mother and father were then aged 22 and 30 years. Since the age of 9 months his parents had thought him to be short in length. While in hospital

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Fig. 1 Case 2 aged 3 years. Showing protruberant abdomen, lumbar lordosis, relatively long trunk and short limbs.

at 14 months (after swallowing analgesia tablets) his body habitus was noted. Skeletal x-rays were interpreted however, as suggestive of achondroplasia, and it was not until aged 7 years that review of the original films led to the correct diagnosis.

At 9 years he was a sturdily built boy with relatively short limbs (Table 1) and a moderate lumbar lordosis. The hands were not trident shaped and skull size and facies were normal. Intellectual function was also normal.

Family data

Consanguinity was not present in any of the families. Each of the parents was of local Ulster stock, with the exception of the father of Case 1 who was born in north-eastern Spain. None of the parents or other relatives resembled the index patient and all x-rays of the parents were normal. The parents except the father of Case 1 (157.5 cm) were of normal stature. Each patient had siblings: Case 1 had two healthy younger sisters, Case 2 had two older brothers and an elder sister, and Case 3 was the second of four children, being the only boy. The youngest sister of Case 3 had a right hare lip and cleft palate.

Radiological findings

Radiological examinations were made on the patients at ages ranging from 15 months to 9 years.

Spine. The main feature was narrowing of the spinal canal with tapering of the interpedicular distance in the lumbar region (Fig. 2). In Case 3, this was only apparent at 9 years, as at 15 months only a lack of widening was seen. In Case 2 there was spina bifida occulta of S1 and S2. In all patients the articulation of the sacrum on the iliac bones was low, and the lumbar lordosis was slightly exaggerated in patients who were weight-bearing.

Pelvis. The iliac and pubic bones were slightly smaller than normal. The sacrosciatic notches were rather small and the pelvic brim appeared to be flattened in the A-P diameter (Fig. 3).

Long bones. In all patients the long bones were short and broad with metaphyseal flaring (Table 2; Fig. 3). In Case 1 in infancy there was an inverted V-notch

Fig. 2 Case 2 aged 3 years. There is slight narrowing of the interpedicular distance in the lower lumbar spine, and spina bifida occulta of upper sacrum.

in the lower femora, and in Case 2 at age 3 there was medial beaking of the upper tibial metaphyses. The lower end of the fibula appeared longer than normal in Cases 2 and 3. The femoral necks were short in each patient.

The hands showed relatively short metacarpals and short terminal phalanges giving short and stubby

Fig. 3 Case 1 aged 18 months. The femora and tibiae are short and thick with metaphyseal flaring. Pelvis shows small sacrosciatic notches and a short A-P diameter of the brim.

Table 2 Radiographic lengths (cm) of limb bones

<i>Ages (years)</i>	<i>Humerus</i>	<i>Radius</i>	<i>Ulna</i>	<i>Femur</i>	<i>Tibia</i>	<i>Fibula</i>
Case 1 1·5	9·0 (11·0)	7·2 (8·4)	8·0 (9·4)	12·3 (14·5)	9·7 (11·5)	10·0 (11·3)
Case 1 8·6	15·6 (20·6)	12·5 (15·5)	13·3 (17·0)	23·0 (30·4)	17·3 (24·1)	17·6 (23·9)
Case 2 3	12·2 (13·2)	9·2 (9·9)	10·3 (11·0)	16·7 (17·8)	12·6 (14·0)	13·2 (14·1)
Case 3 1·25	—	—	—	11·4 (12·8)	8·9 (9·9)	9·0 (9·6)
Case 3 9	18·5 (21·2)	12·8 (15·8)	14·5 (17·5)	25·2 (31·3)	18·8 (24·6)	19·5 (24·6)

Figures in brackets are lower limit of normal (Maresh, 1955).

fingers. In Case 2 there was maldevelopment of the metacarpals of the 5th fingers with cone-shaped epiphyses and slight clinodactyly. In Case 3 at age 9 the lower ends of the ulnae sloped obliquely inwards (Fig. 4).

Skull. In Case 3 the skull was normal. In Case 1 at age 18 months the A-P diameter of the skull was increased with frontal prominence (Fig. 5). In Case 2 at 17 months the skull vault was of abnormally large capacity and increased height, with a wide open anterior fontanelle. At age 3 years the anterior fontanelle had closed and the sutures were normal, but the shape of the skull was unchanged.

Fig. 4 Case 3 aged 9 years. The lower ulna is short with an oblique articular surface.

Fig. 5 Case 1 aged 18 months. There is frontal bossing and the A-P diameter is long.

Chest. No abnormality was seen in the heart or lungs. In Cases 2 and 3 there was slight tapering of the posterior ends of the lower ribs and the clavicles appeared narrow and straight.

Family studies. Skeletal x-rays were obtained of both parents in each family. The father of Case 1 showed a lack of widening of the interpedicular distance in the lumbar spine, but no actual tapering. He showed no other changes suggestive of hypochondroplasia and his tubular bones were of normal proportion. X-rays of the other parents were entirely normal.

Discussion

Hypochondroplasia, a mild form of chondrodys trophy is probably more common than is generally realised, but has been little reported in Britain. It often goes unrecognised in childhood or is mistakenly diagnosed as achondroplasia. Clues to accurate, early diagnosis are the abnormality of body proportions with short limbs and lumbar lordosis, but without the extreme short stature or facial stigmata of achondroplasia. Cases 1 and 2 had large skulls with abnormally wide anterior fontanelles, which may have been clinically confusing.

Early recognition is important as it may prevent unnecessary investigations and help to allay parental anxiety. This is particularly true in terms of differentiation from achondroplasia, as prognosis for ultimate height is more favourable in hypochondroplasia. The height of the father of Case 1 is below the 3rd centile. His son is much shorter than the other two cases because genes determining stature probably modify expression of the gene for hypochondroplasia. A better prognosis can also be given regarding neurological complications which may develop in adults with achondroplasia. Cranial and spinal nerve compression have not been recorded in hypochondroplasia. Intelligence was normal in all 3 patients, but in other series there has been an association with mental retardation. The incidence of this was high (5 out of 11) in the patients of Kozlowski (1973) but Beals (1969) found only 2 of his 16 patients to be affected.

Radiological confirmation of hypochondroplasia is quite simple, provided a full skeletal survey is undertaken (Kozlowski, 1965). The long bones are shorter than the normal range for age (Table 2). They are also broader and slightly bowed with mildly flared metaphyses.

Beals (1969) found that the shortening of the long bones was frequently mesomelic, but in our cases shortening affected the long bones equally. The vertebral changes, which are important, consist of mild tapering of the spinal canal and low articulation

of the sacrum on the iliac bones. The pelvis is small with normal flaring of the iliac wings, but slight flattening of the A-P diameter of the pelvic brim. These changes were present in all our patients.

Other reported abnormalities include slight shortening of the ulna relative to the radius at the wrist, enlargement of the radial aspect of the distal ulnar metaphysis (present in Case 3 at age 9 years), and elongation of the ulnar styloid, which is seen only in older patients in whom the ulnar styloid is developed fully. Obliquity of the lower end of the distal ulna, present in Case 3 at 9 years, has not been described previously. Elongation of the lower fibula was seen in our patients, but the varus deformity with which it may be associated has not yet developed.

The skull in hypochondroplasia is often described as normal. Spranger *et al.* (1974) mentioned that a moderate increase in the size of the neurocranium may occasionally be seen, and Kozlowski (1973) listed several minor skull changes—including bulging of the cranial vault, increased depth of the posterior fossa, shortening of the base, and narrowing of the foramen magnum. Cases 1 and 2 each had a large head with delayed closure of the fontanelles which led to erroneous diagnoses of achondroplasia in Case 1 and arrested hydrocephalus in Case 2. An early diagnosis of hypochondroplasia may be facilitated by recognition that the skull is not always normal.

Differential diagnosis is from achondroplasia, metaphyseal chondrodysplasia (type Schmid), and the normal but heavily built person of short stature. Differentiation is made mainly on radiological findings.

In achondroplasia the skull, hands, and feet are affected and the limb shortening is rhizomelic. The x-ray changes, while qualitatively similar, are much more severe than in hypochondroplasia. In the Schmid form of metaphyseal chondrodysplasia there is metaphyseal flaring and the x-ray appearances of the long bones, particularly at the knees, in both conditions may be similar. Usually in metaphyseal chondrodysplasia there is also widening and irregularity of the growth plates and coxa vara while spinal changes are absent. In the normal person of short stature, no abnormalities are present on skeletal radiography.

Hypochondroplasia is inherited as an autosomal dominant trait (Rimoin, 1975). Many reported cases have been sporadic as were our 3 patients, presumably owing to fresh dominant mutations. Advanced paternal age, initially set forth by Penrose (1955), has been documented as a factor in sporadic fresh mutational cases of several autosomal dominant disorders—such as achondroplasia and Apert's syndrome. In our patients, the fathers' ages were 30,

40, and 30. Hypochondroplasia is distinct from achondroplasia. McKusick *et al.* (1973) described parents, one with achondroplasia and the other with hypochondroplasia, who had a child whose disease was different from heterozygous achondroplasia, homozygous achondroplasia, and heterozygous hypochondroplasia. They postulated that achondroplasia and hypochondroplasia are allelic disorders.

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