Achondroplasia and Down's Syndrome*

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Down's syndrome in association with various other chromosomal disorders such as Klinefelter's, Turner's, trisomy 15, and triple X (Penrose and Smith, 1966), are well known. Other combinations of Down's syndrome with various metabolic disorders (e.g. hypothyroidism and diabetes mellitus (Daniels and Simon, 1968)) have also been reported.

An unusual patient was recently seen at Columbus Children's Hospital with trisomy 21 in association with achondroplasia. The latter diagnosis was suspected at age 17 months, but Down's syndrome was not considered until the patient was referred to us for evaluation of mental retardation at age 5 years.

Case History

The patient was the product of a full-term pregnancy complicated by excessive weight gain for which the mother had taken 'diet pills' beginning at the fourth month. Labour began spontaneously, and delivery was uncomplicated. Birthweight was 2.86 kg. At birth the patient was noted to have a right undescended testis and webbed toes bilaterally. Icterus, of unknown aetiology, was noted shortly after birth and lasted approximately 1½ weeks. No treatment for the jaundice was required. Breast feeding was attempted but was unsuccessful because of the poor sucking ability of the patient.

During infancy the child was susceptible to frequent upper respiratory tract infections, and his early development was slow. He did not sit unsupported until 10 months of age, and did not walk alone until 27 months. He was thought to be 'double-jointed' as reported by his mother. He was never toilet trained. He had no

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FIG. 1. Patient at age 5 years. Note mongoloid facies and disproportionately shortened limbs.

FIG. 2. Close-up view emphasizing typical facies of Down's syndrome.

intelligible speech but would communicate through the use of gestures.

The family history revealed no consanguinity or other member with either Down's syndrome or achondroplasia. A paternal great uncle and a paternal aunt were of short stature being 1.52 m. and 1.37 m. respectively. Both parents as well as two younger sibs are of normal height. The parental ages at the time of birth of the patient were 17 and 18 years, respectively.

Physical examination. On physical examination (Fig. 1 and 2), the patient presented as a Caucasian male, short in stature for 5 years of age. He had obvious mongoloid facies, appeared to be retarded, and was extremely hyperactive. He weighed 17.25 kg., which is at the 30th percentile for his age. His height was 0.89 m., obviously below the 3rd percentile (Stuart and Meredith, 1946). The head measured 51.2 cm. and appeared shortened in the A-P diameter with a flattened occiput. The ears were low set. His eyes were slanted upward and outward, and epicanthal folds were present. The nasal bridge was short and flattened. The mouth appeared to be somewhat small with a large protruding tongue, a high arched palate, and 'pegged teeth'. The examination of the heart and lungs revealed no abnormality. There was a small umbilical hernia and a diastasis recti. The left testis was palpable in the left inguinal canal, but the right testis could not be felt.

The extremities were shortened disproportionately in relation to the trunk. A simian crease was present on the right hand. There was no clinodactyly of the 5th fingers. Syndactyly was present on the 3rd and 4th toes on the right foot, and partial syndactyly was observed on the 2nd to 5th toes on the left foot.

FIG. 3. Antero-posterior view of pelvis showing deep sciatic notch, small narrow sacrum, coxa valga, and flattened acetabular angle. Narrowing of the interpedicular distance of the lower lumbar vertebrae is also evident.

FIG. 4. Lower extremity view showing widening of the metaphyses.

Neurological examination revealed a mild degree of hypotonia and hyperactivity but no localizing or lateralizing signs.

A complete psychological examination was administered. On the Merrill-Palmer Scale of Mental Tests and the Gesell Developmental Schedule the patient was found to be at the 24-month level for over-all development. Language ability, however, was only at the 8- to 24-week level. An audiological evaluation revealed no hearing impairment.

Studies. The radiographic studies showed characteristic signs of achondroplasia including the following. Films of the pelvis (Fig. 3) showed a deep sciatic notch and a small narrow sacrum. There was evidence of coxa valga, and the acetabular angle was flattened. The tubular bones of the upper and lower extremities (Fig. 4 and 5) were shortened and slightly widened. Most of the widening of the tubular bones was at the metaphyseal area. The ulna was seen to be slightly shorter than the radius and there was early bowing of both radii. Spine films (Fig. 6) showed narrowing of the interpedicular distance of the lower lumbar vertebrae in the antero-posterior view, and lateral x-rays showed a slight reduction in the antero-posterior diameter of the vertebral bodies as well as concave posterior borders of the vertebrae (Langer, Baumann, and Gorlin, 1967). Hand and wrist studies revealed a bone age consistent with a chronological age of 5 years. The skull films (Fig. 7) show a marked shortening of the base of the skull. Other investigations including a complete blood count, urinalysis, blood and urine amino acid chromatograms, and chondroitin sulphate B determinations were within normal limits.

FIG. 5. Foreshortening of the long bones of the upper extremity.

FIG. 6. Lateral view of the spine showing reduction in the anteroposterior diameter of the vertebral bodies as well as concave posterior borders of the vertebrae.

Discussion

Although both Down's syndrome and achondroplasia are distinct clinical entities, they do have some features in common which may explain the delay in the diagnosis in this patient.

The following physical findings may be present in both achondroplasia and Down's syndrome: (1) short stature; (2) unusual shape of head; and (3) flat nasal bridge. However, contrasting features of these two conditions were also present in this patient.

In achondroplasia, one usually expects to find normal mentality, yet this patient was significantly retarded. In addition, he was hypotonic. While hypotonia has been reported in early infancy in achondroplasia, older children with this disorder have good muscle tone (Maroteaux and Lamy, 1964).

Characteristic stigmata of Down's syndrome present in our patient were: slanted eyes, epicanthal folds, a 'large' tongue, 'pegged teeth' (Penrose and Smith, 1966), unilateral Simian crease, a deep furrow between the 1st and 2nd toes, and undescended testis with poorly developed scrotum.

Down's syndrome—trisomy 21—occurs in approximately 1 in 2300 births at a maternal age of 20 years. While genetic evaluation is most important in patients with a translocation, genetic counselling is important in both types of Down's syndrome.

Though there are numerous skeletal disorders, achondroplasia is a well-delineated distinct entity resulting from an inborn error in the growth and

FIG. 7. Lateral view of skull.

Chromosome analysis and dermatoglyphs.

Chromosome analysis revealed a karyotype of 47,XY, trisomy 21, consistent with Down's syndrome.

Dermatoglyphs showed the patient to have whorls on both thumbs and ulnar loops on all fingers. The distal axial triradius was in the r'' range, and third interdigital patterns were present bilaterally. An arch tibial was present on both feet. The log index was +4.25, consistent with Down's syndrome (Walker, 1958).

development of cartilage (Maroteaux and Lamy, 1964). Approximately 85–90% of all cases of achondroplasia occur as a new dominant mutation. Only a few cases are transmitted by autosomal dominant inheritance since effective reproductive fitness is considerably reduced in this disorder (McKusick, 1966 a and b).

This patient probably represents a new mutation since the family history revealed no other members with achondroplasia. Parental age did not appear to play a role since both parents were quite young at the time of the birth of the patient.

Summary

This patient is presented as an unusual combination of two genetic disorders. He was incompletely diagnosed for several years because of some similarities in the clinical picture between Down's syndrome and achondroplasia.

The occurrence of this rare combination of dis-

orders cannot be explained by any definite genetic mechanism but appears rather to have been coincidental.

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