

Health (NIH) grant number RO1 HL-24173-02, and CNR subprogetto finalizzato 'Malattie Ereditarie dell'Eritrocita (MEE)'.

M FURBETTA, A ANGIUS, A M FALCHI,
T TUVERI, N TANNOIA*, A PIETRA PERTOSA*,
AND A CAO
2nd Pediatric Clinic, University of Cagliari,
Sardinia, and *Department of Medicine,
Policlinico Bari, Italy

References

- 1 Kan YW. Prenatal diagnosis of hemoglobin disorders. In: Brown EB ed. *Progress in Hematology*. Vol 10. New York: Grune and Stratton, 1978:91-104.
- 2 Alter BP, Nathan DG. Antenatal diagnosis of hematological disorders-1978. *Clin Hematol* 1978;7:195-216.
- 3 Cao A, Furbetta M, Angius A, Ximenes A, Angioni G, Caminiti F. Prenatal diagnosis of β -thalassaemia: experience with 133 cases and effect of fetal blood sampling on child development. *Ann NY Acad Sci* 1980;344:165-80.
- 4 Weatherall DJ, Clegg JB. *The thalassaemia syndromes*. 2nd ed. Oxford: Blackwell Scientific Publications, 1972.
- 5 Efreinov GD. Hemoglobins Lepore and anti-Lepore. *Hemoglobin* 1978;2:197-233.
- 6 Marinucci M, Mavilio F, Gabbianelli M, et al. Synthesis of Hb Lepore Boston in peripheral blood. *Hemoglobin* 1979;3:309-26.
- 7 Quattrin N, Bianchi P, Cimino R, De Rosa L, Dini E, Ventruto V. Study of nine families with hemoglobin Lepore in Campania. Hb Lepore trait, heterozygosity for Hb Lepore and thalassaemia, homozygosity for Hb Lepore. *Acta Haematol* 1967;37:266-75.
- 8 Furbetta M, Angius A, Ximenes A, et al. Prenatal diagnosis of β -thalassaemia by fetal red cell enrichment with $\text{NH}_4\text{Cl-NH}_4\text{HCO}_3$ differential lysis of maternal cells. *Br J Haematol* 1980;44:441-50.

Requests for reprints to Professor Antonio Cao, Clinica Pediatrica 2a, Università degli Studi Cagliari, Via Porcell 1, 09100 Cagliari, Sardinia, Italy.

A case of the orocraniodigital (Juberg-Hayward) syndrome

SUMMARY A female with the orocraniodigital (Juberg-Hayward) syndrome is described in whom, in addition to bilateral cleft lip and palate, mild microcephaly, and anomalous thumbs and toes, there was absence of the pituitary fossa and a more widespread skeletal dysplasia.

In 1969, Juberg and Hayward¹ described five children (two brothers and three sisters) in a sibship of six with one or more of a group of associated oral,

Received for publication 21 January 1981

cranial, and digital anomalies. In the two brothers the abnormalities included unilateral or bilateral cleft lip and palate, deformity of the external nares, hypoplasia and distal displacement of the thumbs, bilateral elbow deformities with limited extension, and growth retardation. The three sisters had less severe abnormalities of the same structures. The authors concluded that the spectrum of abnormalities represented a new syndrome, probably resulting from an autosomal recessive gene with variable expression. In this report we describe a female with this rare syndrome.

Case report

The patient, a 7-year-old girl, was born on 27.12.72 to a 21-year-old mother and a 23-year-old father. The parents were unrelated, healthy, and of normal intelligence. She was an only child. The height of the father and mother was 170 and 160 cm, respectively. There was no family history of congenital abnormalities. There had been no antenatal problems. After 40 weeks' gestation, the patient was delivered spontaneously weighing 2160 g. For the first 2 months she was in hospital because of low birth-weight and failure to thrive. The bilateral cleft lip and palate, noted at birth, was repaired when she was 6 months old. Shortly afterwards she was referred to the Medical Genetic Department for assessment.

When seen at the age of 7 years, she was small with a height of 110 cm (less than the 3rd centile), weighing 17.8 kg (between the 3rd and 10th centiles), and of normal intelligence. She had a broad nasal bridge, hypoplastic columella, hypoplastic alar cartilages, and a flat tip to the nose (fig 1). Measurements of the distances between the medial canthi, the outer canthi, and the pupils were 30, 71, and 50 mm,



FIG 1 The patient aged 7 years.

respectively. The upper central incisors were hypoplastic and none of the premolars had erupted. A small postalveolar fistula was present. The skull circumference was 49 cm (less than the 10th centile). The hands were small with bilateral clinodactyly, tapering fingers, and distally placed thumbs (fig 2). There was syndactyly of the second and third toes (fig 3). The elbows had a full range of movements.

On x-ray the skull was normal in size and shape but the pituitary fossa was virtually non-existent with flat anterior and posterior clinoid processes (fig 4). The spine showed moderate flattening of the thoracic vertebral bodies, slight scoliosis, and rotation in the lumbar region. The long bones were normal in shape. The humeral and femoral lengths were on the 50th centile but the length of the forearm and lower leg bones were on the 10th centile for her age. There was no anterior dislocation of the radii. The terminal phalanges of the fingers were short, ranging from 1.5 and 5.0 SD below normal. There was maldevelopment of both fifth middle phalanges and the other

middle phalanges, except for those of the index finger, and the proximal phalanges were all shorter than normal. The metacarpals were of normal length but the proximal half of the first metacarpals was tapered and more slender than normal (fig 5). The development of the carpal bones on the radial side was slightly retarded giving an overall bone age of a 6-year-old girl. The proximal phalanges of both first toes were broad and short and the terminal phalanges were also broad with large epiphyses.

LABORATORY STUDIES

Metabolic screening, including urine analysis, urinary and plasma amino-acid chromatography, and urinary mucopolysaccharides, was normal. Plasma ACTH was 63 ng/l. Thyroid function tests were normal. Chromosome analysis using a variety of banding techniques revealed a normal 46,XX karyotype.

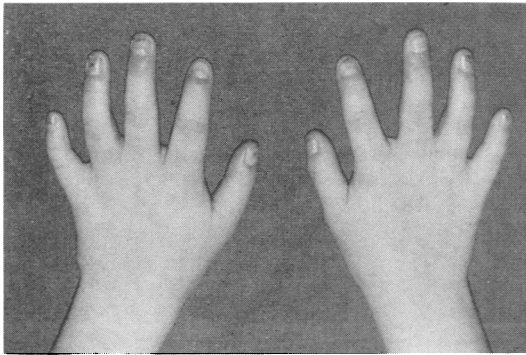


FIG 2 Hands showing bilateral clinodactyly, tapering fingers, and distally placed thumb.

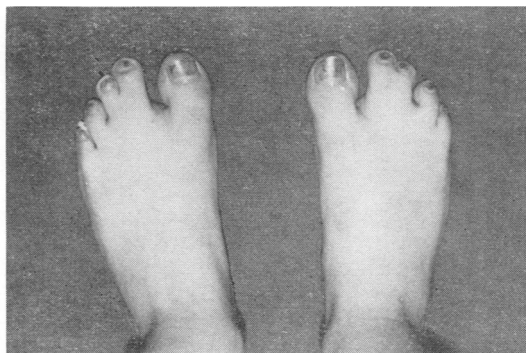


FIG 3 Feet showing syndactyly of the second and third toes.

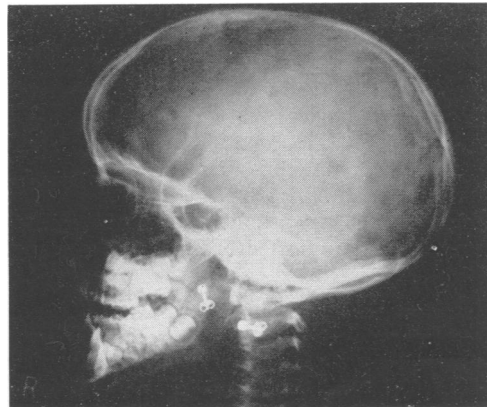


FIG 4 Skull x-ray with absence of the pituitary fossa.

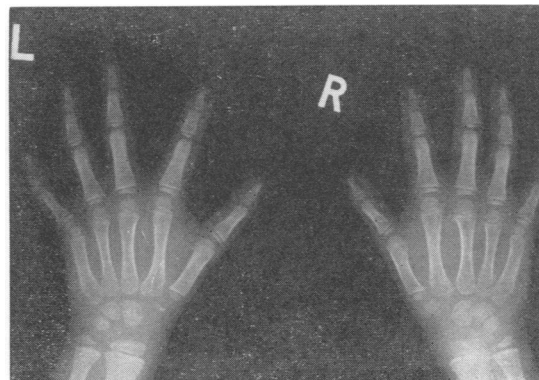


FIG 5 X-ray of hands at age 7 years.

Discussion

The full expression of the orocraniodigital (Juberg-Hayward) syndrome includes cleft lip and palate, microcephaly, hypoplasia of the thumb, dislocated and shortened radii, and mediodorsal curvature of the fourth toes with syndactyly of the second and third toes.¹ Juberg² has suggested that the minimum criteria for diagnosis are bilateral or unilateral cleft lip and palate, microcephaly, and anomalous thumbs and toes. Our patient has sufficient features to indicate she has a similar disorder. In particular, she had mild microcephaly and identical facial abnormalities. However, in addition to the abnormalities of the hands and feet, she had a more widespread skeletal disturbance. The bones of the forearm and lower leg were shortened. In case II.6 of Juberg and Hayward,¹ the forearms appeared shortened and on x-ray the right radius was short at the lower end while the left appeared normal in length. In the original description of the syndrome,¹ two of the five affected subjects had restricted movement at the elbow because of an anterior dislocation of the head of the radius. In our patient there was no abnormality of the elbows. Interestingly, she had an additional radiological feature, namely absence of the pituitary fossa. However, there was no evidence of endocrine dysfunction to account for her short stature.

In the Juberg-Hayward family¹ five of six sibs were affected. The two affected brothers had a complete

manifestation of the syndrome whereas the other three sibs, all girls, had a milder expression of the disorder. The abnormalities in our patient were as severe as those described in the boys in the original description of the syndrome.

Juberg and Hayward¹ suggested that the spectrum of abnormalities was the result of an autosomal recessive gene. Our patient was an only child of non-consanguineous parents and thus does not help to resolve the mode of inheritance. However, as she is as severely affected as the reported males, this would indicate that sex limitation of this disorder is unlikely.

N C NEVIN,* P HENRY,* AND P T S THOMAS†
 *Department of Medical Genetics,
 The Queen's University of Belfast,
 and †Department of Radiology,
 The Royal Belfast Hospital for Sick Children,
 Belfast, Northern Ireland

References

- ¹ Juberg RC, Hayward JR. A new familial syndrome of oral, cranial, and digital anomalies. *J Pediatr* 1969;74:755-62.
- ² Juberg RC. Oro-cranio-digital syndrome. In: Bergsma D, ed. *Birth defects compendium*. 2nd ed. New York: Liss, 1979:828.

Request for reprints to Professor N C Nevin, Department of Medical Genetics, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ, Northern Ireland.