

## CASE REPORTS

- Clin North Am 2000; 47: 1253-1274.
- Stephan JL, Vlekova V, Le Deist F, Blanche S, Donadieu J, De Saint-Basile G *et al.* Severe combined immunodeficiency: a retrospective single-center study of clinical presentation and outcome in 117 cases. *J Pediatr* 1993; 123:564-572.
  - Altare F, Lammas D, Revy P, Jouanguy E, Doffinger R, Lamhamedi S, *et al.* Inherited interleukin- 12 deficiency in a child with Bacille Calmette – Guerin and Salmonella enteritidis disseminated infection. *J Clin Invest* 1998;102: 2035-2040.
  - Buckley RH, Schiff RI, Schiff SE, Market L, Williams LW, Harville TO, *et al.* Human severe combined immunodeficiency: genetic, phenotypic and functional diversity in one hundred eight infants. *J Pediatr* 1997; 130: 378-387.
  - Rosen FS. Severe combined immuno-deficiency: A pediatric emergency. *J Pediatr* 1997; 130: 324-325.
  - Macchi P, Villa A, Giliani S, Sacco MG, Frattini A, Porta F, *et al.* Mutations of JAK-3 gene in patients with autosomal severe combined immune deficiency SCID. *Nature* 1995; 377: 65-68.
  - Glanzmann E, Riniker P. Essentielle lymphocytophthise: Ein neues Krankheitsbild aus der Säuglingspathologie. *Ann Paediatr* 1950; 175: 1-32.
  - Fasano MB. Risks and benefits of intravenous immunoglobulin treatment in children. *Curr Opin Pediatr* 1995; 7: 688-694.
  - Gunn VL, Nechyba C. Immunologic reference values in Harriet Lane Handbook. 6th ed. Mosby, St. Louis, 2002: 313.

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## Acrodysostosis : Autosomal Dominant Transmission

**Sheela S.R.**  
**Ajai Perti\***  
**Grace Thomas**

*We describe a 2½-year-old male child with acrodysostosis, presenting with nasal hypoplasia, peripheral dysostosis (gross shortening of hands and feet), cone-shaped epiphysis, advanced bone age, and mental retardation. He and his mother also had bilateral first ray hyperplasia of the feet thereby expressing the autosomal dominant inheritance pattern.*

**Key words:** *Acrodysostosis, Peripheral dysostosis, First ray hyperplasia of foot.*

Acrodysostosis is a rare skeletal dysplasia, first described by Maroteaux and Malamut in 1968, and since then around 40 cases have

been published in the literature(1). Though most case reports have occurred sporadically, it is believed to be an autosomal dominant condition. In this report we are presenting the first case with autosomal dominant inheritance pattern of acrodysostosis from India.

### Case Report

A 2½-year-old male child with psychomotor delay was referred for evaluation. He was born to a 24-year-old primigravida mother and a 37-year-old father and weighed 2500 g at birth. There was no history of consanguinity.

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*From Departments of Pediatrics and \*Radiology, Indira Gandhi Co-operative Hospital, Kadavanthra, Cochin 682 020, Kerala, India.*

*Correspondence to : Dr. Sheela SR, G-79, Ujjayini, Pahampillay Nagar, Cochin 682 036, Kerala, India.*

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A chromosomal evaluation showed a normal 46-XY pattern. He started to walk by 2 years of age and is presently able to run about and says 4-5 monosyllables. Evaluation by Washington's scale showed a receptive language of 16 months and expressive language of 13 months.

Height of the child was 88cm (<25th centile) and whereas weight (13kg) and head circumference (48.5 cm) were <50th centile. He had a dysmorphic facies with a broad and depressed nasal bridge and an upturned nose with anteverted nostrils. He had hypoplastic maxillae, a tendency to hold the mouth open, gingival hyperplasia, and dental malocclusion due to anterior open bite. Eyes showed bilateral heterochromia of iris and epicanthal folds and hypertelorism with a normal fundus

(Fig. 1). The striking feature was the short stubby fingers with short and broad hands and wrinkling of the skin of the dorsum of the hands, and bilateral simian creases. The toes were also short but in contrast to that he had hypertrophied great toes bilaterally. The nails were broad on all fingers and toes.

A detailed skeletal survey showed broad and short metacarpals and phalanges with cone-shaped epiphyses (Fig. 2). The bone age was significantly advanced, with 7 carpal bones on each side, with a bone age of more than 6 years and he had very large epiphyses of the long bones for his age. He also had significantly hypertrophied first metatarsals and phalanges of the great toes bilaterally confirming a first ray hyperplasia. The metatarsals and phalanges of the other toes



Fig. 1. Typical nasal hypoplasia, anteverted nostrils, heterochromic irides, hypertelorism



Fig. 2. X-ray of the hand showing accelerated bone age, short metacarpals and phalanges with cone-shaped epiphyses.

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were short and stubby. With these clinical and radiological features a diagnosis of acrodysostosis was made.

A skull X-ray showed a very thick calvarium and increased mandibular angle  $147.5^\circ$  ( $129^\circ$  mean value for  $<6$  years) which are some of the less common features of this syndrome. Brain stem auditory evoked response was normal. Ultrasound study of abdomen showed normal kidneys, and MRI study of the brain and spine was within normal limits with no evidence of lumbar canal stenosis. Serum calcium, phosphorous and alkaline phosphatase levels were normal.

Interestingly, the mother also showed a similar hypertrophy of the first metatarsals and phalanges of both great toes of her feet, thereby showing the autosomal dominant inheritance pattern with variable expressivity, as she did not have any of the other features of

this syndrome (*Fig. 3*). No other family members had any similar anomalies.

The mother became pregnant a second time, and due to her fear of having a second child with psychomotor delay the fetus was closely monitored by serial 4 dimensional Echo evaluation with comparison of fetuses with similar gestational age and sex as controls for parameters like short fingers, hypoplastic nose and hyperplasia of the first metatarsal. Ultrasound study has its own limitations as nomograms are not available for detection of short fingers and nasal bone hypoplasia in acrodysostosis in fetuses. Fortunately the fetus did not show any of these features and the mother gave birth to a normal male baby.

## Discussion

Acrodysostosis is a rare syndrome characterized by peripheral dysostosis (gross shortening of hands and feet), mental



*Fig. 3. X- ray foot of proband and mother showing classical first ray hyperplasia.*

retardation, nasal hypoplasia (pug nose) and maxillary hypoplasia(2). Mental deficiency is reported in 77% of patients. The characteristic cranio-facial features include brachycephaly, low nasal bridge, anteverted nostrils, hypertelorism, epicanthal folds, tendency to keep the mouth open, prognathism, dental malocclusion, and delayed tooth eruption.

The fingers and toes are abnormally short (peripheral dysostosis), with broad and short hands, with wrinkling of the skin of the dorsum of the hand. The nails on the fingers and toes are broad. Affected children exhibit advanced bone age and have large epiphyses for their age. Short stature and shortened hands and feet are caused by advanced bone age resulting in premature epiphyseal ossification.

The metacarpals and phalanges show typical cone-shaped epiphyses, which fuse prematurely. Cone shaped epiphyses are a rare and distinctive clue to the diagnosis. Acrodysostosis, pseudohypoparathyroidism and acromesomelic dwarfism may present with cone shaped epiphysis. Even though these conditions share some important clinical features, advanced bone age and first ray hyperplasia are two important findings which distinguish acrodysostosis from the other conditions(3). A pointer in neonates with suspected acrodysostosis is the extensive epiphyseal stippling, which almost always disappears by 8 months of age(3).

Vertebral defects include loss of normal caudal widening of the lumbar interpedicular distance, lumbar canal stenosis and scoliosis. Calvarial hyperostosis and increased mandibular angle are features that are less commonly associated with this condition. In our case the child had these two unusual features too. Urogenital anomalies include cryptorchidism, hypoplastic genitalia, irregular menses, hypogonadism and renal anomalies. Hearing

deficit is described in 67% of patients but our patient had normal hearing.

Most of these cases occur sporadically. Autosomal dominant inheritance pattern was seen in only 14% of patients in a review of 30 cases of acrodysostosis(4-6). In our case the mother had only first ray hyperplasia in both feet which is an important feature of this syndrome which suggests an AD inheritance with variable expressivity. Advanced paternal age has been noted in the fathers of some affected individuals(7).

The differential diagnosis includes pseudohypoparathyroidism (Albright's hereditary osteodystrophy) which classically presents with short stature, short metacarpals and metatarsals and mental deficiency but they have low calcium and elevated phosphorus and alkaline phosphatase(8). Acromesomelic dysplasia also presents with extreme short stature, short hands and feet, and mild mental retardation, but our patient did not have mesomelia and was near normal in height. Lower thoracic kyphosis is an important clue to the condition, and is transmitted as an autosomal recessive pattern. Though patients with Robinow syndrome also have short hands and short stature and anteverted nostrils, their typical facies, hypoplastic genitalia and small penis differentiate them from acrodysostosis.

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## REFERENCES

1. Mariteaux P, Malamut GE. L' acrodysostose. *Presse Med* 1968; 76: 2189-92.

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2. Robinow M, Pfeiffer RA, Gorlin RJ, McKusick VA, Renuart AW, Johnson GF, *et al.* Acrodysostosis: A syndrome of peripheral dysostosis, nasal hypoplasia and mental retardation. *Am J Dis Child* 1971; 121: 195-203.
  3. Jones KL. *Smith's Recognizable Patterns of Human Malformation*, 5th edn. Philadelphia, W B Saunders Company, 1997; pp 444-445.
  4. Butler MG, Rames LJ, Wadlington WB. Acrodysostosis: Report of a 13-year-old boy with review of literature and Metacarpophalangeal Pattern Profile Analysis. *Am J Med Genet* 1988; 30: 971-980.
  5. Hernande RM, Miranda A, Kofman- Alfaro S. Acrodysostosis in two generations: An autosomal dominant syndrome. *Clin Genet* 1991; 39: 376-382.
  6. Steiner RD, Pagon RA. Autosomal dominant transmission of acrodysostosis. *Clin Dysmorphol* 1992; 1: 201-206.
  7. Jones KL, Smith DW, Harvey MA, Hall BD, Quan L. Older paternal age and fresh gene mutations: data on additional disorders. *J Pediatr* 1975; 86: 84-88.
  8. Graham JM, Krakow D, Tolo VT, Smith AK, Lachman RS. Radiographic findings and Gs-alpha bioactivity studies and mutation screening in acrodysostosis indicate a different etiology from pseudohypoparathyroidism. *Pediatr Radiol* 2001; 31: 2-9.
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