Published in final edited form as:

Am J Med Genet. 1988 August ; 30(4): 971–980. doi:10.1002/ajmg.1320300416.

Acrodysostosis: Report of a 13-Year-old Boy With Review of Literature and Metacarpophalangeal Pattern Profile Analysis

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Abstract

We report on a 13-yr-old boy with acrodysostosis, a review of 30 cases in the literature, and metacarpophalangeal pattern profile (MCP) analysis. The prominent manifestations (present in >75% of cases) of this condition include nasal and maxillary hypoplasia, peripheral dysostosis, first ray hyperplasia of the foot, acromesomelic brachymelia, decreased interpedicular distance, advanced skeletal maturation and mental retardation. Results of chromosome studies have been normal. An autosomal dominant inheritance pattern was reported in two families. Maternal and paternal ages were 2 and 3 yr, respectively, above the average age of the general parent population, which suggests that advanced parental age may be a factor in the cause of this condition. A characteristically abnormal MCP was found in our patient and in 16 additional cases studied from the literature. A mean MCP was developed for the syndrome. MCP analysis may be useful as a diagnostic tool in patients suspected to have acrodysostosis.

Keywords

acromesomelic brachymelia; first ray hyperplasia of the foot; maxillary hypoplasia; nasal hypoplasia; peripheral dysostosis; skeletal abnormalities

INTRODUCTION

Acrodysostosis is a rare syndrome of peripheral dysostosis, nasal hypoplasia, mental retardation and other skeletal abnormalities [Robinow et al., 1971]. This condition was first delineated in 1968 [Maroteaux and Malamut, 1968; Giedion, 1968a]. Since that time at least 30 cases have been reported [Singleton et al., 1960; Cohen and van Creveld, 1963; Ortolani and Cremonesi, 1963; Steinbach and Young, 1966; Arkless and Graham, 1967; Giedion, 1968b; Garces et al., 1969; Robinow et al., 1971; Ablow et al., 1977; Niikawa et al., 1978; Goodman, 1978; Reiter, 1978; Cerda et al., 1979; Undreiner et al., 1981; Frey et al., 1982]. Here we report on a boy with acrodysostosis, and review the literature and development of the metacarpophalangeal pattern profile (MCP) for the syndrome.

MATERIALS AND METHODS

Clinical Report

C.M. was a 2,185-g infant born at 36 wk of gestation to a 19-yr-old primagravida mother and 20-yr-old father. The pregnancy was complicated by a successfully treated urinary tract infection in the second month, otherwise the pregnancy, labor, and delivery were normal. Consanguinity was denied and the family history was unremarkable. The patient's psychomotor development was delayed: head up at 6 months, smiled at 8 months, sat up at 9 months, walked alone and had a 4–5 word vocabulary at age 2 yr and was toilet trained at 4 yr.

Physical examination at 4⁷/₁₂ yr showed a pleasant child with a height <3rd centile, weight at the 10th centile, and head circumference >97th centile. He had facial abnormalities of frontal bossing, hypertelorism, maxillary hypoplasia, mild exophthalmus, epicanthal folds, broad depressed nasal bridge, short upturned nose with anteverted nares, triangular mouth, gingival hyperplasia and a small penis. All limbs appeared short with stubby fingers and toes with broad hands and wrinkling of the dorsal skin. X-ray studies showed peripheral dysostosis, broad, short metacarpals and phalanges with cone-shaped epiphyses, frontal bossing with premature closure of the sagittal suture and platybasia. Urine for metabolic genetic screen was normal. Routine biochemical and laboratory studies, including calcium and phosphorus levels, were normal.

A Peabody Picture Vocabulary Test showed a receptive ability of 2 to 2³/₁₂ yr and expressive ability of 2 yr at a chronological age of 4⁷/₁₂ yr. A Stanford Binet Intelligence Test performed at age 9 yr produced an intelligence quotient score of 56.

At age 13 yr, hypertelorism and gingival hyperplasia were not present, but scoliosis and first ray hyperplasia of the foot were noted. Results of high resolution chromosome studies were normal. There was no evidence of subcutaneous mineralization. The other anomalies noted at 4⁷/₁₂ yr were again observed (Figs. 1, 2). The dermatoglyphic analysis showed three ulnar loops (digits one, three, and five), one radial loop (digit two) and one whorl (digit four) of the right hand while three whorls (digits three, four, and five) and two ulnar loops (digits one and two) were seen on the left hand. The maximal *atd* angle [reflection of degree of distal displacement of the palmar (*t*) axial triradius] was 53° on the left and 58° on the right hand. There were no abnormal hypothenar or thenar patterns, although a simian crease was noted on the left hand.

MCPP Analysis

Seventeen patients with acrodysostosis were included in this study. This group included 16 patients from the literature (six males and ten females with average age of 8.8 yr and range of 0.6 to 37 yr) for which acceptable hand radiographs were available and our patient (Table II).

Metacarpophalangeal bone lengths were measured to the nearest millimeter with a vernier caliper from photographs of the hand roentgenograms of each patient. Bone length determination was made in accord with the method proposed by Poznanski et al. [1972] and

Kaler et al. [1981] for applying MCP analysis to photographs of hand roentgenograms. By comparing the bone lengths to normal mean lengths, Z scores for the individual bones were calculated. For a given bone, a Z score is computed by taking the difference between the observed length and the mean length specific for age and sex and dividing by the standard deviation associated with the mean length. The normal standards were published by Garn et al. [1972] (white Americans, age 2 yr to adulthood) and Poznanski [1974] (Gefferth Hungarian sample, from birth to age 15 months). The Z score of the first metacarpal was made equal to zero in analyzing the photographs and the MCP was derived for each patient based on the Z scores of the remaining 18 bone lengths. A mean pattern profile was derived based on the 17 patients by calculating the average Z score of each of the 18 bones and plotting the Z scores on a graph. For hand pattern comparisons in this study, a correlation program was employed to produce a Pearsonian r value between each patient's hand profile and the mean profile derived from the 17 patients.

RESULTS AND DISCUSSION

Acrodysostosis is characterized by short hands with peripheral dysostosis, nasal hypoplasia, skeletal abnormalities of the skull, mandible and spine and mental deficiency. We present an additional patient with this rare disorder, review 30 previously reported cases (Table I) and derive the MCP of our patient and for the syndrome (Fig. 3).

The average age at diagnosis for all cases was 11.7 yr for 19 females and 12 males, including our patient. The average age at the time of birth was 27 yr for 15 mothers and 31 yr for 13 fathers. The maternal and paternal ages were 2 and 3 yr, respectively, above the average age for the general parent population [Van Dyke et al., 1983] and suggests that advanced parental age may be a factor in the condition.

The pregnancy history was generally normal. The average birth weight was 2.47 kg with a range of 1.8–3.2 kg based on 21 cases. The average birth length was 46.5 cm with a range of 43–49 cm based on 14 cases. An autosomal dominant inheritance pattern was reported in four individuals from two families or about 14% of reported cases, while the remaining 24 cases had no significant family history [Niikawa et al., 1978; Frey et al., 1982].

In 24 of 31 cases (77%) mental deficiency was reported. The average intelligence quotient and standard deviation in 20 individuals was 61+20 with a range of 24–85.

Several craniofacial abnormalities including maxillary hypoplasia (100%); nasal hypoplasia (97%); and increased mandibular angle (68%) were observed in this syndrome. Hearing abnormalities were reported in 67% of the cases. Less frequent findings include epicanthal folds (35%), hypertelorism (35%) and delayed tooth eruption (23%). At least seven individuals, including our patient, have been reported with cranial hyperostosis.

Skeletal abnormalities were frequently identified in this syndrome. The most common bone changes were peripheral dysostosis (100%); first ray hyperplasia of the foot (100%); and advanced skeletal maturation in all individuals with bone age information reported in the literature. Approximately 75% of the patients had acromesomelic brachymelia and vertebral

anomalies, the most common of which was decreased interpedicular distance. Short stature (< -2 SD) was observed at the time of evaluation in 55% of the cases.

Because of the peripheral dysostosis and short hands, the MCPD was generated from our patient and 16 patients from the literature (Fig. 3) and compared to that from syndromes with similar manifestations. The hand profiles of published acrodysostosis patients as well as our patient were uniformly abnormal with four prominent peaks (1st and 5th proximal, 5th middle and 2nd distal phalanges, Fig. 3). The hand profile in acrodysostosis also appears to be relatively homogeneous with 15 of 17 patients having significant positive correlations (Table II).

Hand profiles of patients with pseudo- or pseudopseudohypoparathyroidism, which may represent a milder form of acrodysostosis [Poznanski et al., 1973], acromesomelic dysplasia [Langer et al., 1977] and Robinow syndrome [Butler et al., 1987] were compared with the profile from our patient because of the similar clinical manifestations found in these syndromes. The up and down deviation pattern in our patient is similar to that of acrodysostosis with a correlation value of 0.69 ($P < .005$). The correlation values of our patient with the mean profiles of pseudo- or pseudopseudohypoparathyroidism [Poznanski et al., 1973], acromesomelic dysplasia [Langer et al., 1977] and Robinow syndromes [Butler et al., 1987] were 0.51 ($P < .05$), 0.42 ($P < .05$), and 0.14 ($P > .05$), respectively. Therefore, MCPD of our patient was more similar with a higher correlation value with acrodysostosis than in pseudo- or pseudopseudohypoparathyroidism, acromesomelic dysplasia, or Robinow syndromes. The MCPD analysis of our patient was useful in ruling out other syndromes with similar clinical characteristics. Therefore, we propose that MCPD analysis is a useful tool for diagnosis in this syndrome similar to the analysis employed with several other conditions such as Prader-Willi and Sotos syndromes [Butler and Meaney, 1985; Butler et al., 1986; Butler et al., 1988].

ACKNOWLEDGMENTS

The authors are grateful to American Academy of Pediatrics Memorial Endowment Fund For Children for support in this research.

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Fig. 1.
a, b, c. Our patient at age 13 yr.

Fig. 2.
a, b, c. Roentgenograms of the hands and photographs of the hands and feet from our patient at age 13 yr. Bone age was 16⁶/₁₂ yr.

Fig. 3. Mean MCP for 17 individuals with acrodysostosis established from published cases (**top**) and MCP from our patient (**bottom**).

TABLE I.

Summary of Manifestations in Acrodysostosis

Trait	C.M.	Literature	Total	%
Gestation and family history				
Normal pregnancy	–	13/17	13/18	72
Birth weight (<2.5 kg)	+	13/21	14/22	64
Birth length (<46 cm)	?	9/19	9/19	47
Family history	–	4/27	4/28	14
Craniofacial				
Maxillary hypoplasia	+	22/22	23/23	100
Nasal hypoplasia	+	27/28	28/29	97
Increased mandibular angle	+	12/18	13/19	68
Epicanthal folds	+	11/30	12/31	39
Hypertelorism	+	10/30	11/31	35
Dental abnormalities				
Delayed tooth eruption	+	6/30	7/31	23
Hypodontia	–	1/30	1/31	3
Musculoskeletal				
Peripheral dysostosis	+	30/30	31/31	100
Foot, first ray hyperplasia	+	23/23	24/24	100
Advanced skeletal maturation	+	17/17	18/18	100
Acromesomelic brachymelia	+	15/19	16/20	80
Decreased interpedicular distance	+	17/23	18/24	75
Short stature (< –2SD)	+	15/28	16/29	55
Urogenital				
Cryptorchidism	–	2/6	2/7	29
Hypoplastic genitalia	+	4/17	5/17	29
Irregular menses	n/a	2/11	2/11	18
Renal abnormalities	–	1/30	1/31	3
Other				
Mental retardation	+	23/30	24/31	77
Hearing abnormalities	–	10/14	10/15	67

TABLE II.

Correlations Between Acrodysostosis Individual's MCPD With Group Mean MCPD

Individual case	Age (years)	Sex	Correlation
C.M.	13	M	0.69 ^b
Cerda et al. [1979]	8	M	0.50 ^a
Cohen and van Creveld [1963]	5	M	0.40 ^a
Reiter [1978]	4 ¹ / ₂	M	0.40 ^a
Singleton et al. [1960]	8	M	0.80 ^b
Niikawa et al. [1978]	7 ⁷ / ₁₂	M	0.10
Robinow et al. [1971]	5	M	0.69 ^b
Garces et al. [1969]	5	F	0.89 ^b
Arkless and Graham [1967]	37	F	0.81 ^b
Maroteaux and Malamut [1968]	15	F	0.79 ^b
Poznanski [1984]	2	F	0.10
Poznanski [1984]	14	F	0.85 ^b
Robinow et al. [1971]	8 ¹ / ₆	F	0.84 ^b
Giedion [1973]	10	F	0.83 ^b
Poznanski et al. [1973]	4	F	0.78 ^b
Smith [1982]	5	F	0.75 ^b
Singleton et al. [1960]	9	F	0.86 ^b

^a*P* < .05 for one tailed test.^b*P* < .005 for one tailed test.