Jpn J Human Genet **38**, 433–436, 1993

Case Report

THE COSTELLO SYNDROME: REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Summary A 5-year-old girl with the Costello syndrome is reported. Her clinical manifestations included growth and developmental delay, a distinct facial appearance with sparse and curly hair, nasal papillomata, and dark loose skin of the hands and feet. These manifestations, especially nasal papilloma, an age-dependent anomaly, are distinct in the Costello syndrome.

Key Words Costello syndrome, papillomata, facio-cutaneous-skeletal (FCS) syndrome

INTRODUTION

The Costello syndrome is a MR/MCA (mental retardation/multiple congenital abnormalities) syndrome with mental and developmental retardation, characteristic facial appearance with sparse and curly hair, broad forehead, hypertelorism, depressed nasal bridge, nasal papillomata, thick lips, and dark, loose skin of the hands and feet. Since Costello described two cases in 1977, we are aware of 10 cases of the syndrome reported in the literature (Costello, 1977; Der Kaloustian *et al.*, 1991; Martin and Jones, 1991; Say *et al.*, 1993; Teebi and Shaabani, 1993; Philip and Mancini, 1993; Zampino *et al.*, 1993; Izumikawa *et al.*, 1993).

We report here a 5-year-old girl with the Costello syndrome.

CASE REPORT

A 5-year-old girl was referred to us for genetic counseling. She was born to a 33-year-old, mother after a pregnancy complicated by hydroamnios at 37 weeks.

Received August 13, 1993; Revised version received and accepted September 28, 1993.
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Her father was 34 years old at her birth. The parents were healthy unrelated Japanese. They had an older son and two daughters all healthy. There was no family history of congenital anomalies or mental retardation.

Her birth weight was 4,400 g, length 50.8 cm and OFC (head circumference) 38.0 cm. She had a broad forehead, hypertelorism, depressed nasal bridge, thick lips, large ears, a short neck, and dark skin of the hands and feet. She had feeding difficulties in early infancy: Her weight at 4 weeks was 4,380 g and that at 3 months was 5,040 g. She had a ventricular septal defect which later closed spontaneously. She was moderately hypotonic and her developmental milestones were markedly delayed. She sat without support at age 2 years and stood at 4 years.

At age 5 years, her weight was 11 kg (−3.0 S.D.), length 80 cm (−6.7 S.D.), and OFC 50 cm. She walked alone and understood verbal commands. She talked simple sentences and sang songs. She was friendly and good-natured.

Her facial appearance was characteristic: She had sparse and curly hair, a broad prominent forehead, hypertelorism, a right epicanthal fold, strabismus, a depressed nasal bridge, unteverted nostrils, thick lips, and large ear lobes (Fig. 1). Papillomata were present in the lateral anterior nares and on ear lobes (Fig. 1). Her skin of the hand and feet was dark, loose, and thick, and her nails were hypoplastic (Fig. 2). She had a short neck and a barrel chest.

Normal laboratory tests included: cytogenetic analysis (46,XX), endoclinological studies including growth hormone and bone age. Her I.Q. was 60 at age 5 years.

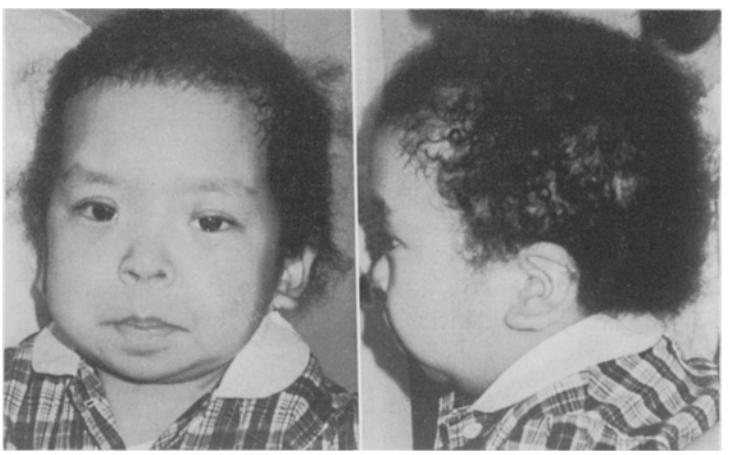

Fig. 1. The patient at age 5 years. Sparse and curly hair, right epicanthal fold, depressed nasal bridge, thick lips, and papillomata in nasal alares and ear lobes.

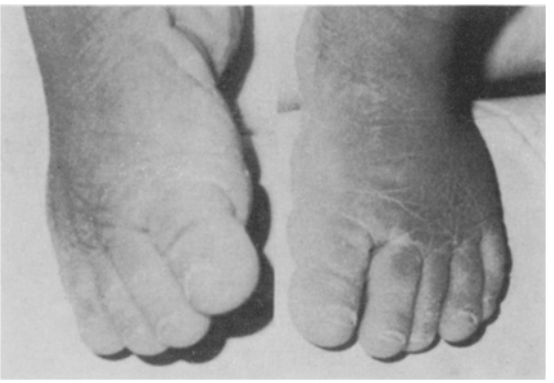

Fig. 2. Dark, loose skin on the feet.

DISCUSSION

Costello (1977) described a syndrome in 2 unrelated, mentally retarded children. Their major clinical findings comprised growth and developmental delay, macrocephaly, sparse and curly hair, depressed nasal bridge, thick lips, and dark loose skin of the neck, palms, soles, and fingers. Nasal papillomata in these patients were a distinguishing trait. Der Kaloustian *et al.* (1991) and Martin and Jones (1991) later reported an additional case with similar clinical findings respectively. All four patients with the Costello syndrome were born unrelated parents and there was no family history of mental retardation. However, characteristic facial appearance was noted in the maternal great-grand mother of patient 2 reported by Costello (1977). The clinical manifestations of our patient, including nasal papillomata, are in complete agreement with the Costello syndrome.

Borochowitz *et al.* (1992) reported 5 patients with multiple congenital anomalies named facio-cutaneous-skeletal (FCS) syndrome. Their clinical manifestations included mental retardation, coarse facies, sparse and curly hair, generalized excessive skin, postnatal growth failure, and skeletal anomalies. These findings closely resemble those in the Costello syndrome. However, papillomata were not observed in these patients. Consanguineous marriage was noted in the parents of the 5 patients, and autosomal recessive inheritance was suggested.

Recently six additional cases with the Costello syndrome were reported (Say *et al.*, 1993; Teebi and Shaabani, 1993; Philip and Mancini, 1993; Zampino *et al.*, 1993; Izumikawa *et al.*, 1993). However, papillomata were not observed in two cases (Teebi and Shaabani, 1993; Zampino *et al.*, 1993). Age of onset of nasal papillomata is variable, then several authors proposed that the Costello syndrome and FCS syndrome should be a single entity (Teebi and Shaabani, 1993; Zampino *et al.*, 1993).

Papillomata around the nasal region, as found at age 5 years in our patients,

are particularly characteristic in the Costello syndrome. In the patients with the syndrome reported in the literature the age of their onset ranged from 2 to 15 years (Costello, 1977; Martin and Jones, 1991). Benign neoplasms of epithelial cell origin—acantosis nigricans, palmar nevi and other—were noted in the oldest reported patient (Martin and Jones, 1991). Therefore, differentiation of the FCS syndrome and Costello syndrome may be very important of patients with these conditions. It remains to be seen whether patients with FCS syndrome represent a portion of the clinical spectrum of the Costello syndrome, or belong to distinct syndrome, the FCS syndrome.

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