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Clinical case report

A Japanese patient with the Costello syndrome

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Abstract. The Costello syndrome is characterized by dwarfism, unique cutaneous lesions, distinct facial gestalt, and mental retardation. We present a Japanese patient with the Costello syndrome. She showed high serum IgM level during the early infantile period. Nissen's fundplication was carried out to treat severe gastroesophageal reflux. Endocrinological investigations revealed a partial deficiency of growth hormone.

Introduction

In 1977, Costello reported two unrelated patients with a new syndrome characterized by short stature, redundant skin of the neck, palms, soles, and fingers, curly hair, relative macrocephaly, depressed nasal bridge, papillomata around the mouth and nares, distinct facial gestalt, hyperextensible joints, and mental retardation (Costello 1977). Additional patients were reported in 1991 (Der Kaloustian et al. 1991; Martin and Jones 1991). We present a Japanese patient with the Costello syndrome and some unique manifestations.

Clinical report

This 7-year-old girl was born to a 27-year-old mother at 38 weeks of gestation after an uneventful pregnancy. Her parents were healthy and non-consanguineous. Her family history is unremarkable. Birth weight was 2850 g, body length was 44 cm, and head circumference was 32 cm. Several days after birth, atrial premature contraction of unknown etiology appeared. Cardiac anomaly was not found. Her serum IgM level was high (329 mg/dl) at the age of 4 months, but she had no other specific manifestations related to the TORCH complex (a group of micro-organisms associated with fetal malformation). Her postnatal growth was poor. She was an irritable infant with feeding difficulties and persistent abdominal distension because of intestinal hypoactivity. At the age of 11 months, Nissen's fundplication was carried out to treat severe gastro-esophageal reflux (GER). She had congenital subluxation of bilateral hip joints.

Her height was 93.9 cm (–4.7 SD), her weight was 15.4 kg (–1.8 SD), and her head circumference was 48 cm (–2.0 SD) at the age of 7 years. She had generalized pigmentation and acanthosis nigricans around the neck and axilla, curly hair, coarse facial appearance, epicanthal folds, low set posteriorly rotated ears, depressed nasal bridge, short and bulbous nose, thick lips, short neck, redundant skin of the neck, palms, soles, and fingers, and deep plantar palmar creases (Figs. 1, 2). She had tight Achilles tendons. She began to walk at the age of 5 years. Her recent developmental quotient was 27.

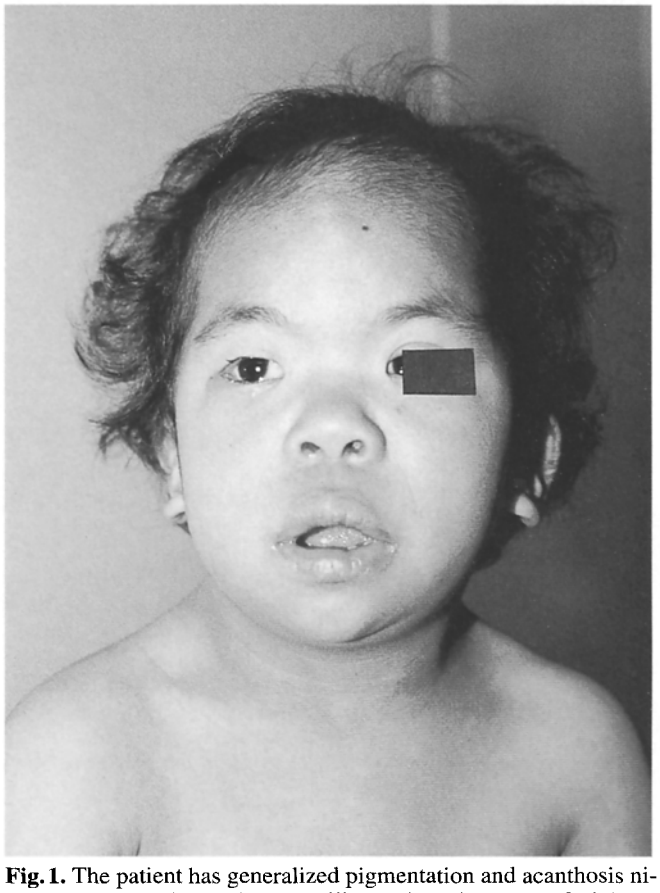

Fig. 1. The patient has generalized pigmentation and acanthosis nigricans around the neck and axilla, curly hair, coarse facial appearance, epicanthal folds, low set posteriorly rotated ears, depressed nasal bridge, short and bulbous nose, thick lips, and short neck

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Fig. 2. Her hands show deep palmar creases and redundant skin of the palms, and fingers

Table 1. Endocrinological evaluations reveal partial deficiency of GH. Most of the plasma GH levels were below 5.0 ng/ml during steep

GH secretory function tests (only the peak values are shown)	
Arginine tolerance test	7.7 ng/ml
Insulin-induced hypoglycemia	5.0 ng/ml
Clonidine test	3.8 ng/ml
Sleep (3 h)	6.0 ng/ml
Insulin-like growth factor-I	0.2 U/ml (0.15–2.3 U/ml)
Tyroid function tests	
Triiodothyronine	109 ng/ml (80–180 ng/ml)
Thyroxine	9.5 μg/ml (5.0–18.7 μg/dl)
Thyroid-stimulating hormone	3.2 μU/ml (0.4–5.0 μU/ml)

Her karyotype was 46,XX and metabolic abnormalities were not found. Endocrinological investigations revealed a partial deficiency of growth hormone (GH) (Table 1). Although she was free from epileptic seizures, electroencephalography revealed sporadic epileptic discharges. Magnetic resonance imaging of the brain showed a normal myelination pattern and no major malformations except for a slight downward deviation of the cerebellar tonsilla.

Discussion

The patient did not have nasal papillomata, although that may appear later (Martin and Jones 1991). Other clinical manifestations were typical of the Costello syndrome. She had several unique manifestations. First, the high IgM level in the early infantile period indicates that some unidentified infectious agents may be associated with her clinical manifestations. Secondly, she had feeding difficulties because of severe GER; this necessitated fundplication. Costello reported a patient with mild GER (Costello 1977). Thirdly, she had GH deficiency. Although GH therapy was continued for several years, it had a limited effect.

She had acanthosis nigricans, which is one of the manifestations of Costello syndrome (Martin and Jones 1991). Acanthosis nigricans is related to endocrinological abnormalities and the development of benign tumors. Martin and Jones (1991) reported a patient with the Costello syndrome and progressive benign neoplasms. GH therapy may enhance the growth of tumors and should be performed under close observation with respect to the Costello syndrome.

The underlying defect of the Costello syndrome is unknown. Familial occurrence and consanguinity have not been reported so far. Whether it is an inherited disorder remains unresolved. Early onset of symptoms and high IgM levels may indicate an association of congenital infections. We suggest that the number of newly diagnosed patients will increase. Further clinical studies should then elucidate the precise nature of the Costello syndrome.

References

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Note added in proof. Recently, additional patients with the Costello syndrome have been reported: Borochowitz Z et al. (1992) Am J Med Genet 43:678–685, Say B et al. (1993) Am J Med Genet 47:163–165, Teebi AS and Shaabani IS (1993) Am J Med Genet 47:166–168, Philip N and Mancini J (1993) Am J Med Genet 47:174–175, Zampino G et al. (1993) Am J Med Genet 47:176–183, Izumikawa Y et al. (1993) Jpn J Human Genet 38: 329–334, Kondo et al. (1993) Jpn J Human Genet 38:433–436, Yoshida et al. (1993) Jpn J Human Genet 38:437–444.