A 3-MONTH-OLD infant, the second child of nonconsanguinous parents, was born by spontaneous vaginal delivery at 37 weeks' gestation weighing 3350 g (75th percentile). Maternal exposure to drugs or alcohol during pregnancy was denied. Polyhydramnios was noted at 20 weeks' gestation. The infant had feeding difficulties and became emaciated. By 3 months, her weight had fallen to 3070 g and her head circumference was 36.6 cm, both less than the third percentile. The infant had a dysmorphic appearance with coarse features, including depressed nasal bridge, full lips, and posteriorly rotated and thickened auricles (Figure 1). Her scalp hair was sparse and curly. A flame nevus was present on the glabella, and the skin of the forehead was wrinkled. Macroglossia was present. Her cry was coarse. Loose skin was noted over the neck, in the axillae, and on the arms (Figure 2). The nipples were hyperplastic. A grade 3/6 blowing systolic murmur was heard on cardiac examination. The palms and soles had deep skin creases (Figure 3).

Echocardiographic study demonstrated a perimembranous ventricular septal defect. Markedly prolonged gastric emptying time was demonstrated by radionuclide study. A study of the esophagus showed no abnormalities. Plasma amino acids, blood glucose levels, and thyroid function test results were normal. The karyotype was 46,XX. A FISH (fluorescent in situ hybridization) study with the elastin probe for Williams syndrome was negative.

From the Department of Pediatrics, National Taiwan University Hospital, Taipei (Dr Hou), and the American Board of Pediatrics, Chapel Hill, NC (Dr Tunnessen).
Denouement and Discussion

Costello Syndrome

Figure 1. Coarse facial features suggestive of a storage disease are apparent.

Figure 2. The skin over the upper arm appears loose.

Figure 3. Deep creases are present in both the palmar and plantar surfaces.

In 1971 and again in 1977, Costello described a syndrome with characteristic cutaneous findings, dysmorphic features, and multisystem involvement. Prenatal polyhydramnios occurs in almost half of affected pregnancies, probably the result of poor fetal swallowing. Although almost all affected infants have birth weights greater than the 50th percentile, all manifest feeding difficulties and poor growth after birth.

CLINICAL FEATURES

The facial features are coarse, suggesting a storage disorder. The nasal bridge is flat; the lips, thick; the mouth and tongue, large; and the ears, low set. Epicanthal folds and down-slanting palpebral fissures are present in most infants. Characteristic cutaneous findings include sparse, curly hair, loose skin, hyperpigmentation, and deep creases of the palms and soles. Later in life, many children with this syndrome develop papillomata around the nares, mouth, or anus. Acanthosis nigricans may appear on the neck and axillae. Musculoskeletal findings in most infants include a short neck, increased anteroposterior diameter of the chest, hyperextensible fingers, wide phalanges, abnormal position of the feet, and tight Achilles tendons.

Cardiovascular problems are common in children with this syndrome. Congenital heart defects include atrial or ventricular septal defects, pulmonary stenosis, bicuspid aortic valve, patent ductus arteriosus, and mitral valve prolapse. Hypertrophic cardiomyopathy and dysrhythmias have been described in more than half of the reported cases but have resulted in minor problems in most patients.

All patients described with this syndrome have had severe mental and developmental delay; however, an outgoing personality has been described in more than 90% of 37 patients reported. Less commonly reported features include hepatosplenomegaly, cataracts, heat intolerance, increased sweating, and graying hair. Abnormal laboratory findings have included delayed bone age, osteoporosis, fasting hypoglycemia, and postprandial hyperglycemia.

DIFFERENTIAL DIAGNOSIS

Patients with this syndrome have been considered to have other disorders, including cutis laxa, Noonan syndrome, Donahue syndrome (leprechaunism), Williams syndrome, and lipodystrophy. Careful attention to the constellation of findings, particularly the unusual skin findings in Costello syndrome, should help in differentiation.

PATHOGENESIS

The cause of Costello syndrome has not been determined. Most cases reported have been sporadic, although siblings have been described on 2 occasions. An association with advanced parental age has been noted, which has been described in conditions with germline mutations. A single case with a chromosomal translocation of 1q and 22q may provide clues to localization of a genetic defect. In addition, defects of elastic fibers, possibly relating to alternative splicing in the elastin gene or to defects in elastin microfibrils, has been observed in patients with this syndrome. The varied manifestations, particularly physical features suggestive of a storage disease, the growth disturbances, hypertrophic cardiomyopathy, and occasional hepatosplenomegaly, suggest a metabolic disorder.

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Reprints: Jia-Woei Hou, MD, Department of Pediatrics, Chang Gung Children’s Hospital, 5 Fu-Shing St, Kwei-Shan, Troyuan, Taiwan.

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