Case Report

**A NAGER ACROFACIAL DYSOSTOSIS SYNDROME
PATIENT WITH SEVERE RESPIRATORY
DISTRESS SYNDROME (RDS)**

Tatsuro KONDOH,* Masaki ITO, Akinori ARIYAMA, Takeshi SHITJOH,
Tadashi MATSUMOTO, and Yoshiro TSUJI

*Department of Pediatrics, Nagasaki University School of Medicine,
Nagasaki 852, Japan*

Summary Nager acrofacial dysostosis is characterized by radial defect and the facial manifestations like Treacher-Collins syndrome. There are few reports about this syndrome in Japan. We report a typical Japanese Nager syndrome patient. He was complicated with respiratory distress syndrome.

Key Words Nager syndrome, respiratory distress syndrome, thumb hypoplasia, absence of radius

INTRODUCTION

Nager acrofacial dysostosis (Nager syndrome) was originally described by Nager and de Reynier (1948), and there were only 35 cases of this syndrome in the literature. The main manifestations are as follows. The facial appearance is similar to Treacher-Collins syndrome, *i.e.*, malar hypoplasia, micrognathia, down slant palpebral fissure, lower lid coloboma, hypoplasia of lower eyelash, macrostomia, cleft palate, dysplastic ears, external ear canal defects, and conductive hearing loss. The limb features are thumb hypoplasia or absence, absence of radius, and radioulnar synostosis. This syndrome usually occurs sporadically, but some cases were inherited with autosomal recessive (Chemke *et al.*, 1988) or autosomal dominant trait (Aylsworth *et al.*, 1991). There are few reports about Japanese patient of Nager syndrome. We report a Japanese patient with severe facial involvement and respiratory distress syndrome.

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*To whom correspondence should be addressed.

CASE REPORT

The propositus was a Japanese boy of a gravida 3, para 2, 24-year-old healthy mother. His father was 26 years old, and healthy, too. There were not particular in the family history. At 30 weeks and 5 days of gestation, the mother was hospitalized because of her polyhydramnios. His cleft lip/palate and small stomach (miniature stomach) were pointed out by the ultrasonography at 32 weeks and 2 days of gestation. The chromosomal analysis was performed by using his cord blood, and his karyotype was 46,XY.

He was delivered vaginally at 34 weeks and 2 days of gestation, birth weight was 2,200 g and length was 46 cm. Apgar score of 3 and 4 were recorded at 1 and 5 min, respectively. He had a severe dyspnea and apnea caused by a respiratory distress syndrome (RDS; Bonsel IV). So he was treated with a surfactant to improve his lung condition.

The patient (Figs. 1 and 2) had peculiar facial characteristics like Treacher-Collins syndrome; hypertelorism, down slant palpebrae fissure, deviated bifid nasal tip, cleft lip/palate, remarkable micrognathia, sparse eyebrow, lower lid coloboma, low set and deformed ears, external ear canal defects, and deformed skull. His hearing loss was severe bilaterally, and no response was obtained by an auditory evoked response (ABR) test. Severe hypoplasia of maxillar and man-

Fig. 1. Photograph of the patient with Nager syndrome.

dibular bones was noted from his skull X-ray films, and therefore his upper respiratory tract was narrow. He also had limb anomaly, *i.e.*, short and curved left forearm, a limitation of extension of his left elbow joint, bilateral floating thumbs (left thumb was more severe than right one). His X-ray examination showed an absence of his left radial bone (Fig. 3) and curtailment of his left humoral and ulnar bone. His testis was undescended bilaterally. Brain CT indicated no morphological abnormality. At his birth, mild congenital mitral valve stenosis and insufficiency (MSR), patent ductus arteriosus (PDA), and weakness of the motion of the left ventricular wall were revealed by an echocardiogram. So he was started the treatment with Dopamine for 2 months. As the condition of his heart improved, that is, PDA closed, the ejection fraction of the left ventricle was within normal limits, and mitral valve also showed normal movements, we withdrew the dopamine treatment for him. As he had severe hypoplasia of maxillar and mandibular bones and severe laryngomalasia, he could not keep spontaneous

Fig. 2. 1: Facial aspect of the patient. 2: Clinical aspect of the left hand of the patient.

Fig. 3. Radiographs of the patient's left arm.

respiration. Tracheostomy was performed at the age of 10-month because he could not be released from an intubation.

DISCUSSION

Nager acrofacial dysostosis is a rare syndrome. The severity of this syndrome has wide range from severe type (Stillborn type; Goldstein and Mirkin, 1988) to mild. Our case was severe clinically. The heart is usually normal in Nager syndrome except a few reports (Thompson *et al.*, 1985). Our patient had a heart disease, but the condition of his heart became improved with dopamine treatment for 2 months. It suggested that this heart disease would be transient disturbance of the endocardium caused by hypoxia at his birth. Nager syndrome is resemble to Treacher-Collins syndrome from the aspect of facial manifestations, but facial involvements are also heterogeneous (Palomegue *et al.*, 1990). Our patient has a typical facial feature for Nager syndrome, and complicated with a cleft lip and bifid nasal tip. The sensitive period for the occurrence of a cleft lip and a cleft palate is different (five to six weeks gestation and six to nine weeks, respectively), and a cleft palate is more common than a cleft lip in Nager syndrome (McDonald and Gorski, 1993). This maybe relevant to the fact that the embryologic timing of formation of the organs involved in acrofacial dysostosis is between 32 and 44 days (Goldstein and Mirkin, 1988).

Treacher-Collins syndrome may result from abnormal development of the first and second branchial arch ectodermal placodes (Sulik *et al.*, 1987) or primary interference with neural crest cells (Poswillo, 1975; Willey *et al.*, 1983). Molecular analyses of Treacher-Collins syndrome patients have been developed, and the gene for Treacher-Collins syndrome (TCOF1 gene), located on chromosome 5, was identified (The Treacher-Collins Syndrome Collaborative Group, 1996). TCOF1 encodes the putative nucleolar trafficking protein that is critically required during human craniofacial development (Wise *et al.*, 1997). His chromosome 5 was seemed to be normal so far we examined. It is unknown whether Nager syndrome is the contiguous gene syndrome owing jointly some genes caused of Treacher-Collins syndrome, or not.

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