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CASE REPORT

Nager Syndrome: A Case Report

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Key Words
micrognathia;
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tracheostomy

Nager syndrome (preaxial acrofacial dysostosis) is rare and mostly sporadic. We present a case of Nager syndrome in Taiwan. Craniofacial findings included micrognathia, malar hypoplasia, downslanting palpebral fissures, cleft palate, and ear anomalies. Radial defects consisted of hypoplastic thumb, short forearm, and proximal radioulnar synostosis. Patent ductus arteriosus, atrial septal defect, lower limb deformities, and uncommon flat nasal bridge were noted. Nasal endotube passing through a narrowing oropharynx region or oral airway is life-saving before tracheostomy is performed on patients with Nager syndrome and restricted jaw opening and glossoptosis.

1. Introduction

Nager syndrome was first recognized by Nager and de Reynier in 1948. They used the term acrofacial dysostosis to describe their patient.[1] The syndrome (preaxial acrofacial dysostosis) is due to aberrations in development of the first and second branchial arches and limb buds.[2—4] The main clinical features consist of craniofacial, limb and musculoskeletal anomalies. Less frequently, other malformations have also been reported.[5] Most cases appear to be sporadic, however, autosomal dominant or autosomal recessive inheritance has been mentioned.[4—9] The occurrence of affected siblings with normal parents suggests potential genetic heterogeneity and an additional autosomal recessive form.[5] Thus, the pattern of inheritance remains unclear. Severe airway obstruction is the major cause of morbidity and mortality. Early intervention with tracheostomy has been emphasized.[10] Tracheotomy should be considered to stabilize the respiratory situation promptly. We report here the first case of Nager syndrome diagnosed in Taiwan. A 3-year-old girl presented with severe phenotype and uncommon flat nasal bridge, but did not receive tracheostomy.

2. Case Report

This 3-year-old girl was first transferred to our hospital when she was 3 weeks old. She was born to a healthy

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mother of Gravida 3 Para 3 (G3P3), 40 weeks of gestational age via normal spontaneous delivery; the birth body weight was 2680 g. No specific family history was noted regarding craniofacial disorders. Intubation was attempted soon after birth but failed because of severe micrognathia. Oropharyngeal airway was used first and then shifted to nasopharyngeal airway (3.0 Fr. E-T tube, with room air). On physical examination, the patient presented with severe micrognathia, bilaterally small downslanting palpebral fissures, malar hypoplasia, flat nasal bridge, cleft palate, and low-set, posterior-rotated ears with ear canal atresia (Figure 1). Deformities of both forearms, with radial deviation of the wrists and club feet were found. Cardiac echo showed patent ductus arteriosus of 3.8 mm and atrial septal defect of 3.0 mm, secundum type with left-to-right shunt, which closed spontaneously later. Patent ductus arteriosus was occluded by Amplatzer ductal occluder when the patient was 1 year old. Brain echo and blood karyotyping showed normal results. Imaging study revealed glossoptosis and retrognathia, resulting in oropharyngeal airway narrowing (Figure 2), proximal radioulnar synostosis, and radial hypoplasia (Figure 3). Neither tracheostomy nor gastrostomy was executed by decision of the family.

At 1 year and 6 months old, the patient only needed nasopharyngeal airway when sleeping, but was free during daytime. Rehabilitation proceeded regularly for the limitation of elbow extension and thumb dysplasia (Figure 4). The patient could open her mouth but only to a limited extent, owing to ankylosis of the temporomandibular joint. Hypoplastic, overlapping toes were obvious. At 3 years and 4 months, she still had blurred speech and swallowing incoordination. She could walk and jump. She had normal intelligence. Her body height was 90.8 cm (10—25th percentile); body weight was 11.6 kg (3rd percentile); head circumference was 46.6 cm (10th percentile). She wore a hearing aid due to bilateral conductive hearing loss (50-60 dB), and had received dental management due to abnormal teething and caries.

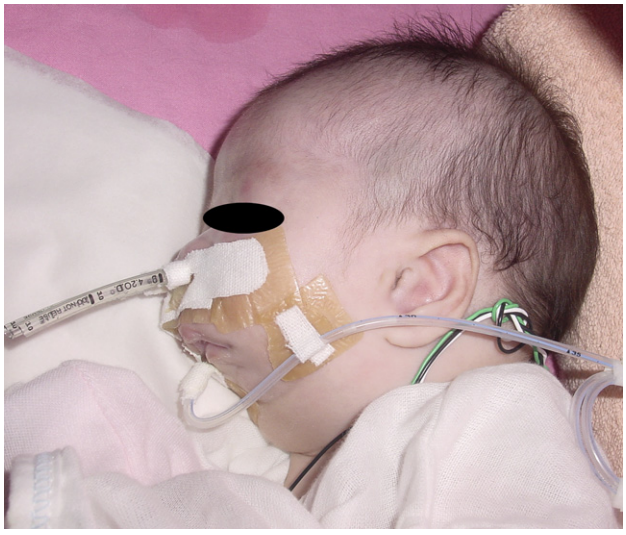

Figure 1 Severe micrognathia and low-set ear.

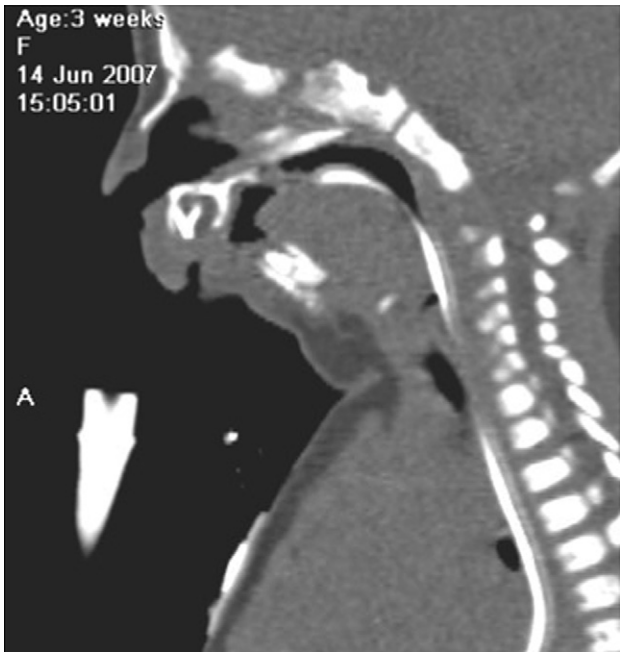

Figure 2 Glossoptosis and retrognathia, resulting in oropharyngeal airway narrowing.

3. Discussion

Nager syndrome shares similar craniofacial features with Treacher Collins syndrome, including micrognathia, malar hypoplasia, downslanting palpebral fissures, and ear anomalies, but mandibular hypoplasia tends to be more severe.[4] It can be distinguished from Treacher Collins syndrome by preaxial upper-limb deformities, such as thumb anomaly, radial defect and radioulnar synostosis. Limb anomalies are a cardinal sign of Nager syndrome and, in combination with the characteristic facial features, are diagnostic.[5] In Finland, the incidence of Nager syndrome has been estimated as 3:1,000,000.[11] No more than 80 cases have been reported to date.[4,5,12] Nager syndrome is so rare that this is the first reported case in Taiwan.

A distinct acrofacial dysostosis case, which might be a new form of the disease, has been proposed by Zhang et al.[13] To investigate the etiology of the phenotype, whole-genome, high-resolution array comparative genomic hybridization analysis was carried out, revealing two cryptic duplications, 1p36.33 and 1q21.3-q22. They also suggested that two genes, *VWA1* and *PYGO2*, might be the candidate genes for the abnormal phenotype of this case.[13] However, the etiology of Nager syndrome is still unclear, without any gene having been identified to date.

In the case presented here, craniofacial findings included micrognathia, malar hypoplasia, downslanting palpebral fissures, cleft palate, and ear anomalies, as well as radial defects consisting of hypoplastic thumb, short forearm, and proximal radioulnar synostosis, fulfilling the diagnostic criteria for Nager syndrome. The patient had a severe typical phenotype with uncommon flat nasal bridge, which was different from other reported cases.[5] For psychological and physiological issues, she might need surgical correction of micrognathia eventually. However,