LETTER TO THE EDITOR

CONGENITAL TRACHEAL STENOSIS IN A BOY WITH THE 22q13.3 DELETION SYNDROME

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The propositus was the second child of a healthy unrelated Taiwanese couple. The father was 35 years and mother 26 years at his birth. There was no family history of congenital malformations. He was born uneventfully at 41 weeks of gestation with a birth weight of 3,200 g. Hypotonia, poor neck control, suprasternal retraction, noisy breathing and recurrent bronchiolitis were noted postnatally. Chest X-ray showed evidence of tracheal stenosis, and computed tomography scan of the trachea with three-dimensional reconstruction showed a focal narrowing of trachea at the level of the vocal cord. A ventilation bronchoscopic examination at age 6 months revealed a stenotic ring at the cricoid level. Intelligence testing at 3 years and 5 months of age revealed severe mental retardation and marked speech and language delay. Brain and heart ultrasound examinations were normal. On examination at 7 years of age, his body weight was 15 kg (25th centile), and head circumference was 49.8 cm (50th centile). He manifested absent speech, mental retardation, unstable gait, long eyelashes, prominent dysplastic ears, dolichocephaly, a flat midface, a bulbous nose, a pointed chin, full cheeks, a wide nasal bridge, relative long hands, clinodactyly of fingers and hypoplastic toenails (Fig. 1). However, there was neither autistic behaviour nor epilepsy. Cytogenetic investigation on metaphase cells from peripheral blood lymphocytes of the proband and his parents revealed a karyotype of 46,XY,del(22)(q13.2) in the proband (Fig. 2) and normal karyotypes in the parents. Fluorescence *in situ* hybridization (FISH) experiments were performed using bacterial artificial chromosome (BAC) clones on metaphase cells. The deletion was confirmed by using probes RP11-91O6 (22q11.21) and RP11-232E17 (22q13.33) (Fig. 3). Polymorphic DNA marker analysis revealed that the deletion was paternal in origin (Table I).

We have described a patient with congenital tracheal stenosis, tracheal hypoplasia, marked speech and language delay, severe mental retar-

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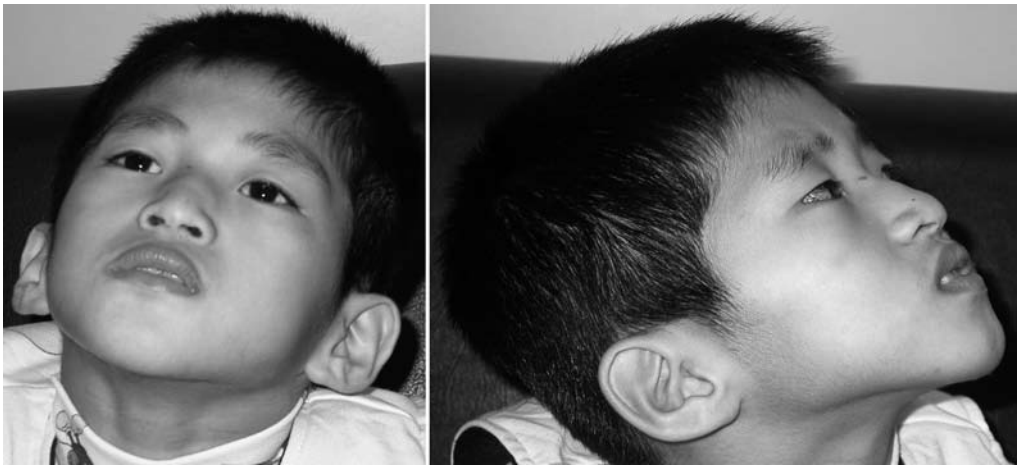

Figure 1: Characteristic facial dysmorphism of prominent dysmorphic ears, dolichocephaly, a flat midface, a bulbous nose, a pointed chin, full cheeks and a wide nasal bridge.

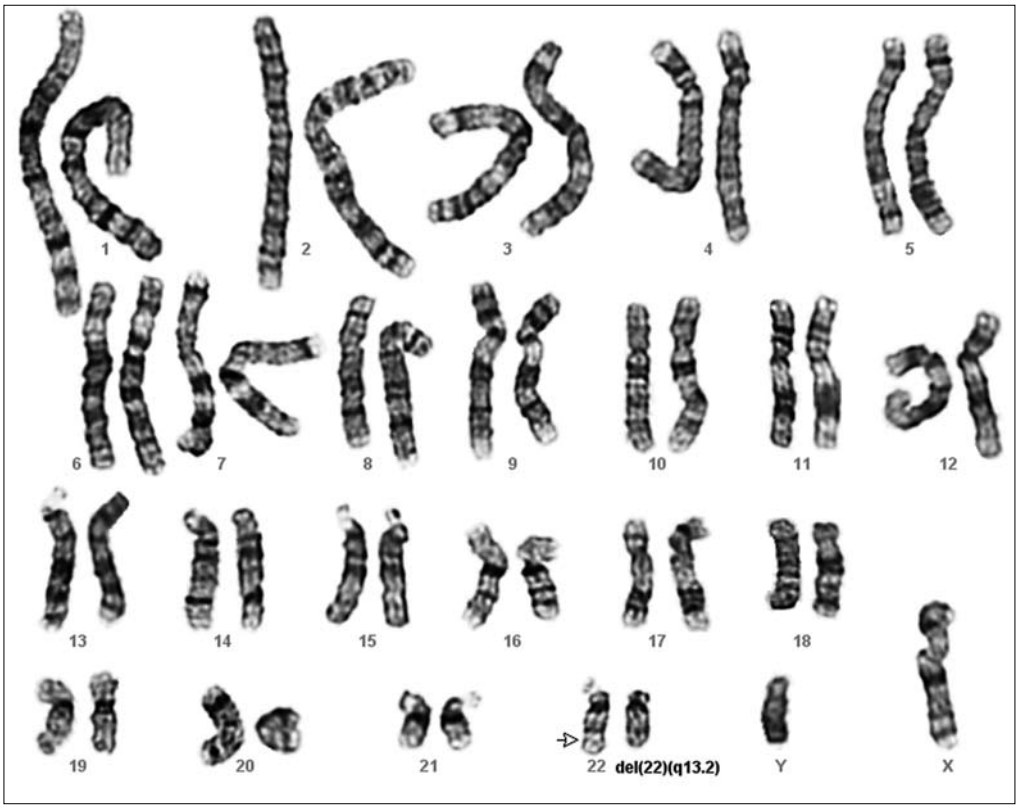

Figure 2: The karyotype of the proband.

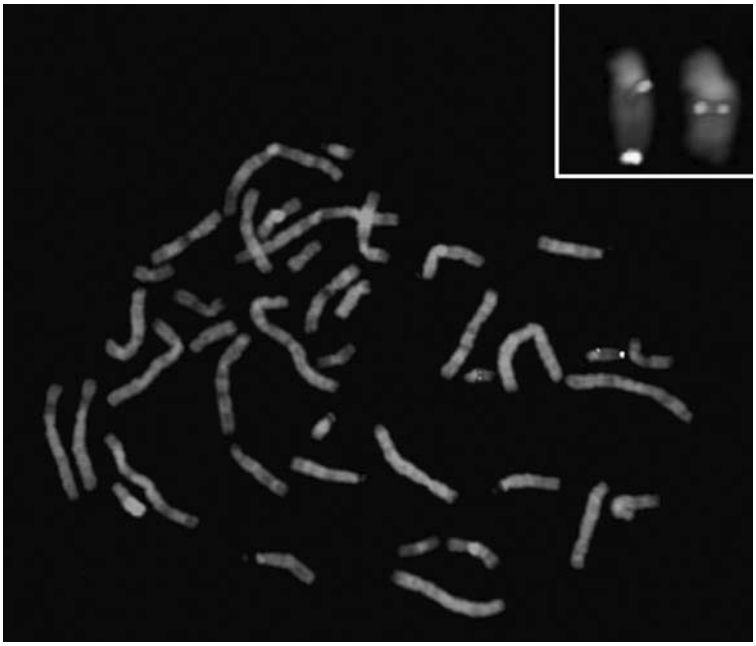

Figure 3: Fluorescence *in situ* hybridization (FISH) using bacterial artificial chromosome (BAC) clones RP11-91O6 (22q11.21) (red signal) and RP11-232E17 (22q13.33) (green signal) shows absence of the green signal of the RP11-232E17 probe on the aberrant chromosome 22.

Table I: Genotypic information of the family members at short tandem repeat (STR) markers specific for chromosome 22q by quantitative fluorescent polymerase chain reaction (QF-PCR)

STRs	Position*	Locus	Father	Mother	Proband
D22S417	41,434,402 - 41,434,575	22q13	182,210	182,194	194
D22S274	43,647,816 - 43,648,021	22q13	204,212	222	222
D22S532	44,501,825 - 44,501,995	22q13.31	188	180,188	180

* Human Build 36.3

dation and a deletion of chromosome 22q13.2→qter. The patient manifested characteristic features of the 22q13.3 deletion syndrome or Phelan-McDermid syndrome (OMIM 606232) which has clinical characteristics including long eyelashes, large or unusual ears, relatively large hands, dysplastic toenails, full brow, dolichocephaly, ptosis, full cheeks, a bulbous nose, a pointed chin, autistic behaviour, neonatal hypotonia, global developmental delay, normal or accelerated growth and absent to severely delayed speech (5). Marked speech and language impairments are the most reproducible features of the 22q13.3 deletion syndrome (5). In a meta-analysis of 64 cases with the terminal 22q deletion syndrome, Manning *et al.* (4) found that 60 cases (94%) were associated with delayed/absent speech. In a meta-analysis of 107 cases with the terminal 22q deletion syndrome, Cusmano-Ozog *et al.*

(1) found that 103 cases (96%) were associated with delayed/absent speech. Haploinsufficiency of the *SHANK3* gene has been shown to be a major causative factor in the neurological symptoms of the 22q13 deletion syndrome (6). Durand *et al.* (2) reported evidence showing the abnormal gene dosage of *SHANK3* is associated with autism spectrum disorders and language and speech disorders. An increased incidence of respiratory infections has also been observed in patients with the 22q13 deletion syndrome (3). Wilson *et al.* (7) suggested the general non-specificity of the 22q13 deletion syndrome by the findings that haploinsufficiency for the 22q13 genes other than the *SHANK3* gene can have major effects on cognitive and language development. Although the finding of congenital tracheal stenosis and tracheal hypoplasia in our patient may be coincidental, the real prevalence of tracheal abnormalities in patients with the 22q13.3 deletion syndrome and the role of the genes at 22q13.3 in the normal development of trachea are still required to be evaluated in further studies.

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