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THE CHARGE ASSOCIATION IN A NEWBORN INFANT*

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SUMMARY: Akısü M, Özkınay F, Özyürek R, Küçüktaş A, Kültürsay N. (Department of Pediatrics, Ege University Faculty of Medicine, Bornova-İzmir, Turkey). The CHARGE association in a newborn infant. Turk J Pediatr 1998; 40: 283-287.

CHARGE association is the nonrandom association of congenital anomalies, including choanal atresia, coloboma, heart defects, retardation of growth and development, genital hypoplasia and ear abnormalities. We report a male newborn infant with CHARGE association. Other congenital abnormalities include micrognathia, high-arched palate, facial asymmetry, broad nasal bridge, hypertelorism, asymmetric eye size, and left microphthalmia. On radiologic examination, hemivertebrae were detected on the thoracal vertebrae. Although both autosomal and recessive transmission have been reported, most cases of CHARGE association have been sporadic (karyotype analysis is generally reported to be normal as in our patient). Transmission and recurrence risk of this association are not known. The presence of choanal atresia and/or coloboma must alert the clinician to search for other abnormalities for diagnosis of CHARGE association. *Key words: CHARGE association, choanal atresia, hemivertebra, microphthalmia, newborn, patent ductus arteriosus, vertebral anomaly.*

Hall[1] first reported a nonrandom association of congenital malformations occurring with choanal atresia, but CHARGE association (coloboma, heart defect, choanal atresia, growth and/or developmental retardation, genital hypoplasia, ear abnormalities) was described by Pagon et al.[2] in 1981. Additional features may include asymmetric face, micrognathia, cleft palate, facial weakness, difficulty in swallowing, hydronephrosis, and tracheoesophageal fistula[1,2]. These nonrandom anomalies were named as an "association" rather than as a "syndrome"[2].

Although autosomal dominant and recessive inheritances are also suggested by occurrence in some families, this association is mostly reported in sporadic cases[1-4]. CHARGE association may be a good example of genetic heterogeneity. A newborn with CHARGE association is reported here.

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Case Report

A male infant was born to a 28-year-old mother after 37 weeks of gestation at Ege University Medical School Hospital. No maternal drug exposure, infectious disease, alcohol or parental consanguinity was reported (Fig. 1). The mother had a phenotypically normal stillborn of 30 weeks' gestation one year previously. That pregnancy was complicated by oligohydramnios. One-minute and five-minute Apgar scores were 5 and 7, respectively.

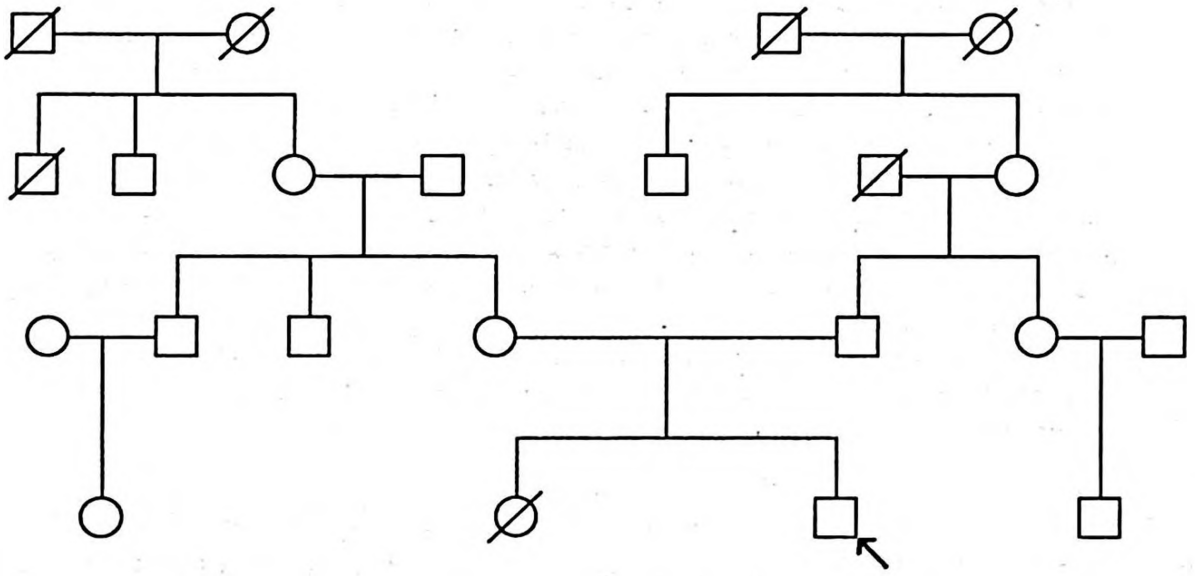

Fig. 1: The pedigree of the patient.

The infant had intrauterine growth retardation with a birth weight of 1530 g (below 10%) and height of 43 cm (below 10%). Micrognathia, high-arched palate, facial asymmetry, broad nasal bridge and hypertelorism were observed on physical examination. Asymmetric eye size and left microphthalmia, but no other ocular abnormality such as coloboma of iris and retina, were detected. The ears were small, cup-shaped and low-set but the external auditory canal was normal on otoscopy (Figs. 2 and 3). The infant showed respiratory distress and cyanosis. Bilateral choanal atresia was considered since a nasogastric feeding tube failed to be advanced through both nares. On cardiac auscultation a systolic murmur was heard. The infant was hypotonic and had weak and poorly organized neonatal reflexes. External genitalia were normal.

Complete blood count and other biochemical laboratory studies were normal. Blood gas analysis showed mild hypoxemia. Cytogenetic study showed normal male karyotype (46, XY).

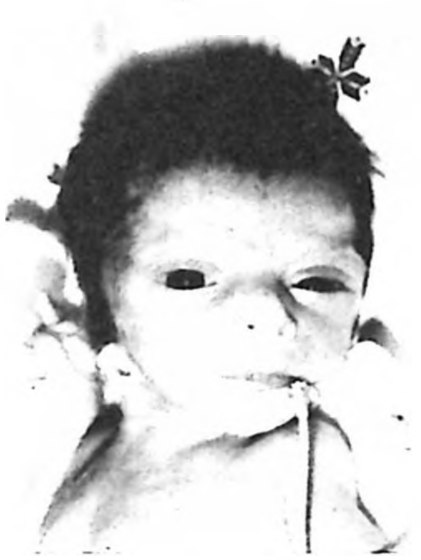

Fig. 2: Photograph of the case showing facial asymmetry, facial weakness, broad nasal bridge, hypertelorism, asymmetric eye size, left microphthalmia, and small, cup-shaped and low-set ears.

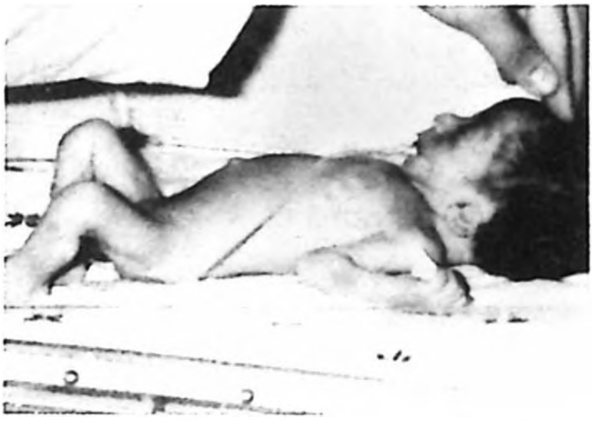

Fig. 3: Photograph of the case showing micrognathia, depressed nasal bridge, and small, cup-shaped and low-set ears.

Bilateral choanal atresia was visible on lateral skull x-ray with opaque medium given through nares and was also confirmed by fiberoptic rhinoscope (Fig. 4). Chest radiogram showed cardiomegaly and increased pulmonary circulation, in addition to hemivertebral appearance of 5^{th}, 7^{th}, and 9^{th} thoracal vertebrae (Fig. 5). Abdominal ultrasonography showed normal urogenital structure. Patent

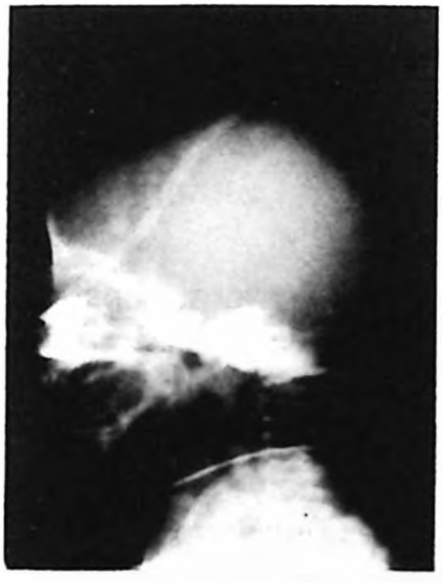

Fig. 4: Lateral skull x-ray with radioopaque material demonstrates choanal atresia.

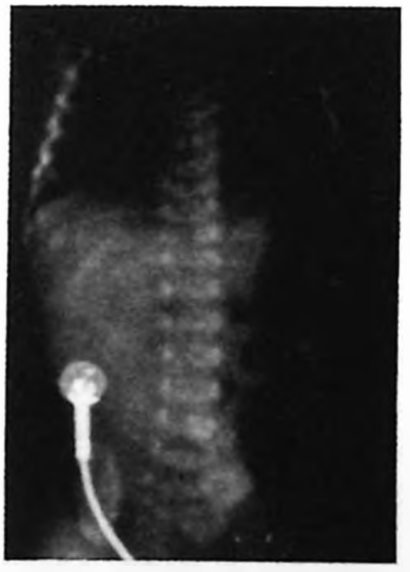

Fig. 5. Chest x-ray of the case showing cardiomegaly, increased pulmonary circulation and thoracal hemivertebrae.

ductus arteriosus (PDA) of 3 mm, patent foramen ovale of 3 mm and pulmonary hypertension were diagnosed on echocardiography.

The patient was diagnosed with CHARGE association. Any further intervention and investigation was refused by family because of the high expectancy of mental retardation in patients with CHARGE association.

Discussion

Major abnormalities in CHARGE association may be outlined as follows:

Ear Abnormalities: lop-or cup-shaped pinnae, low-set ears, small ears, deafness, and external ear abnormalities.

Choanal Atresia: bilateral or unilateral, membranous or bony obstruction.

Ocular Manifestation: coloboma of iris, coloboma of retina/choroid, asymmetric eye size, microphthalmia, nystagmus, strabismus, and refractive errors.

Genital Abnormalities: micropenis, undescended testes, and hypogonadism.

Heart Defects: PDA (very common, either alone or associated with more severe lesions), tetralogy of Fallot (very common), ventricular septal defect, atrioventricular canal, double-outlet right ventricle, and aortic arc anomalies.

Growth: (commonly due to the problems of feeding and swallowing) and developmental retardation (mental retardation is independent from the presence of microcephaly, and IQ scores range from 30 to 80)[1-7]: Blake et al.[3] reported that one-third of neonates with CHARGE association had intrauterine growth retardation and all subsequently continued to be growth retarded. The diagnosis of CHARGE association requires at least four of the six major diagnostic criteria (choanal atresia, heart defect, coloboma, growth and/or developmental retardation, genital hypoplasia and ear abnormalities)[3, 5, 8]. In addition to these major abnormalities, a number of anomalies were also described in this association, such as: micrognathia, facial weakness, asymmetric face, cleft palate, short neck, microcephaly, small mouth, difficulty in swallowing, hydronephrosis, tracheoesophageal fistula and skeletal abnormalities (hemivertebrae, scoliosis, syndactyly, clinodactyly)[1-3, 7].

Because our patient had choanal atresia, heart defects, ear abnormalities and intrauterine growth retardation, the diagnosis of CHARGE association was established. Microphthalmia and asymmetric eye size were detected as eye abnormalities. PDA, the most common cardiac anomaly in this association, was established, in addition to patent foramen ovale and pulmonary hypertension, external auditory canal was normal on otoscopy in spite of abnormal pinnae. Other minor abnormalities of the patient were micrognathia, high-arched palate, facial asymmetry, broad nasal bridge, and hypertelorism. X-ray study of thorax showed hemivertebrae, an uncommon abnormality in CHARGE association.

Although both autosomal and recessive transmission have been reported, most of the cases with CHARGE association have been sporadic. Transmission and recurrence risk of this association are not known. Karyotype analysis is generally reported as normal as in our patient[9]. The presence of choanal atresia must alert the clinician to search for other abnormalities for diagnosis of CHARGE association.

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