Introduction

CHARGE Syndrome (CS) is a complex syndrome, an autosomal dominant condition, with variable expressivity and no family history with a prevalence ranging from 1/8,500 to 1/17,000 live births and depends on professional recognition. In approximately 90% of cases, it is caused by mutations in the CHD7 gene on chromosome 8q12.1 or can be isolated in less cases. Management involves early medical, surgical, and multidisciplinary (occupational, speech, and physical therapy) interventions.

We report an eleven months female infant presented to our emergency department with history of cough, otitis media with effusion, unilateral nasal discharge associated with congenital heart disease, right side choanal atresia, other abnormalities detected right eye coloboma with growth retardation and development delay. In our case the pronounced clinical finding was majority matched to those reported criteria.

Keywords: CHARGE Syndrome; Growth Retardation; Coloboma

Abbreviations

CS: CHARGE Syndrome; CA: Choanal Atresia; CN: Cranial Nerve

Case Report

Fatima is an eleven months old female infant presented to our ED, due to history of cough, runny nose associated with ear discharge, one day before presentation. She was diagnosed as CA at age of (5 months), associated with CHD (mild pulmonary stenosis), She is the third baby in the family and is the product of young positive consanguinity, NSVD, birth weight is 2400 gm, on breast milk till (6 months), then mixture feed, the actual body weight is (6 kg, below the third percentile), height (64 cm, below the third percentile). No history of similar cases in the family. Prenatal and natal history was normal, and some developmental millstone delay.

Physical examination of chest, abdomen, head were normal. Heart: systolic murmur on the left parasternal, at the third intercostal space, echocardiography reveals (pulmonary valve stenosis, aortic coarctation and patent foramen ovale). Ears show low set without pinna deformity. Investigation: CBC, S/E, Ca, Phosphorus, KFT, LFT, serum glucose, serum GH, T4 and TSH were within normal average according to the age and sex. Abdominal U/S and chest x-ray were normal findings, temporal bone CT show CA and mild stenosis of right ear canal, echocardiography reveal PFO, mild pulmonary valve stenosis and aortic coarctation.

Discussion

We report a female infant with CHARGE syndrome through physical examination, and other diagnostic procedures include radio imaging, echocardiography and through diagnostic criteria were found in our case: unilateral iris coloboma, CA composed of both bone and membranes defect, mild right ear canal stenosis with otitis media with effusion and low seat ears, Congenital heart disease (pulmonary stenosis, aortic coarctation, and patent foramen ovale), growth retardation.

CS is a recognizable genetic disease, caused by dominant loss-of-function mutations of the CHD7 gene with most cases being de novo [11]. The prevalence of this syndrome varies between 1/8,500 to 1/12,000 live births [1]. The true incidence of CS reported internationally may therefore be underestimated [12,13]. This syndrome remains a clinical diagnosis causing a variety of clinical expression with a based on major and minor criteria as outlined by Blake, et al. [14] modified by Verloes [15] and summarized in table 1. Fatima clinical findings was majority matched to those reported criteria, three major and three minor criteria.

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<td>Definite (4 major or 3 major and 3 minor)</td>
<td>Typical: 3 major or 2 major and 2 minor</td>
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<td>Probable/possible CHARGE (1 or 2 major and several minor features)</td>
<td>Partial: 2 major and 1 minor</td>
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<td>Atypical: 2 major but no minor, or 1 major and 2 minor</td>
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<td><strong>Major criteria</strong></td>
<td><strong>Major</strong></td>
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<td>Coloboma</td>
<td>Coloboma (ocular)</td>
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<td>Choanal atresia/stenosis</td>
<td>Choanal atresia/stenosis</td>
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<td>Characteristic ear anomalies</td>
<td>Hypoplasia/aplasia of semicircular canals</td>
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<td>Cranial nerve dysfunction (especially CN VII and VIII)</td>
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<td><strong>Minor criteria</strong></td>
<td><strong>Minor criteria</strong></td>
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<td>Genital hypoplasia</td>
<td>Rhombencephalic dysfunction (brainstem and cranial nerve anomalies).</td>
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<td>Developmental delay</td>
<td>Hypothalamo-hypophyseal dysfunction</td>
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<td>Cardiovascular malformation</td>
<td>Malformation of the internal/external ear</td>
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<td>Growth deficiency</td>
<td>Malformation of mediastinal organs (heart, oesophagus)</td>
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<td>Orofacial cleft</td>
<td>Intellectual disability</td>
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<td>Tracheoesophageal fistula</td>
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<td>Distinctive facial features</td>
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*Table 1: CHARGE syndrome diagnostic criteria.*

Choanal atresia is a blockage of the passages between the nasal cavity and the naso-pharynx, may be membranous or bony; bilateral or unilateral, and the obstruction may be partial/unilateral or complete [1,2]. Majority of cases are unilateral or bilateral bony or membranous septum in approximately 10% [5]. If CA is unilateral may go undiagnosed until the child presents with persistent unilateral rhinorrhea, but bilateral CA causes respiratory distress and may requiring resuscitation at birth [6]. In our case the CA was suspected at age of five months when the family noticed persistent unilateral rhinorrhea, high resolution temporal bone CT, showed mixed membranous and bone CA and mild right ear canal stenosis, seen in figure 2. Chronic otitis media and deafness can be seen as a complications of CA [8].

Coloboma is a missing pieces of eye tissue structures that may be small size, unilateral or bilateral and may affect either iris, retina, or both. Eye malformations are reported in up to 80% of patients with CS [9]. Other anomalies include hypoplasia of optic nerve, anophthalmia, nystagmus, squint and refractive errors [16]. Vision may be normal or impaired but mostly patients have preserved vision [11]. The incidence of retinal coloboma is more common than iris coloboma [6].

Ear abnormalities one of the major criteria and is common finding in the CS, may involve the all the three segments of the ear can be affected, with external ear dysmorphology being a classical finding in CS [17]. Distinctive malformations mostly include abnormal shape and position of the pinnae, specifically, reduced vertical height of the pinna and a cup-shaped, hypoplastic incus, decreased numbers of cochlear turns, and absent semicircular canals [9,18,19]. The early diagnosis of hearing impairment is crucial in patients diagnosed with CS, so early use of appropriate auditory aids, allowing for optimal language and communication development [20].

Growth restriction affects 60 - 80% of children with CS, is thought to be multifactorial and usually normal at birth but later on show growth retardation owing to repeated infections, feeding problems and frequent surgeries [14,15], growth hormone deficiency [6,3,21], therefor may have adverse outcome on growth and bone mineralization, therefor needs early intervention for feeding difficulties [12]. In our patient the growth and thyroid hormones were within normal range.

Cardiac malformations occur in the majority (50 - 85%) of patients, defects include tetralogy of Fallot, aortic arch abnormalities, patent ductus arteriosus, double outlet right ventricle with atroventricular canal, aberrant subclavian artery, ventricular septal defect and atrial septal defect. Severe heart defects are a major cause of death in children with CS [6,22]. Echocardiography reveals mild pulmonary valve stenosis and it’s not mentioned before in medical literature, in association with aortic coarctation, and patent foramen oval.

Genito-urinary anomalies: 50 - 70% of cases have genital anomalies [11] and anomalies of the urinary tract may be present in 10 - 40% [18]. Hypoplastic external genitalia is the most common anomaly, micropenis and/or cryptorchidism, secondary to hypogonadotropic hypogonadism [23].

CNS abnormalities: Nearly 55 - 85% of patients have definite CNS anomalies. CNS abnormalities in CS are highly variable and typically result from a dysfunction of one or more cranial nerves (CN). Dysfunction of CN I, VII, IX, X, and XI, VIII are reported commonly in patients diagnosed with CS [24,25].

Occasional findings: Polyhydramnios esophageal atresia and tracheoesophageal fistulas, cleft lip and/or palate, abnormalities of skeletal muscle, limb anomalies, spine malformation, vertebral anomalies, abnormal cervico-cranial junction, abnormal number of ribs and scoliosis [14,26,27].

The life expectancy of patients with CS varies widely, with individuals living anywhere from five days [2], to at least 46 years [21], with the highest rate of mortality in the first year of life [28]. The rate of mortality is highest with a combination of bilateral CA, complex heart defects or tracheoesophageal fistula, severe T-cell deficiency, and brain anomalies.

Conclusion

We report an eleven months Palestinian female patient presenting with classic features of CS. Based on clinical diagnostic criteria this case is fulfilling with definite CS. The presence of coloboma, CA, ear abnormalities, congenital heart disease, developmental delay and growth retardation should alert the clinician to the possibility of CHARGE syndrome. In this case we report pulmonary valve stenosis, that is not mentioned before in the medical literature as part of CHARGE syndrome.

Bibliography

CHARGE Syndrome in Palestinian Infant: A Case Report


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