CHARGE Syndrome

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Introduction

CHARGE syndrome is a rare, recently well recognized entity with non-random pattern of congenital anomalies. The syndrome associations consist of C-coloboma of the eyes, H-heart disease, A-atresia of the choanae, R-retarded growth and development, G-genital hypoplasia/genitourinary anomalies and E-ear anomalies and/or hearing loss. All anomalies are not seen in every case and a varied spectrum of associations is seen in most of the cases. The exact incidence is not known. However, the reported prevalence is approximately 1:10,000 births [1]. We report one such case.

Case Report

A male child aged 6 years was brought to the OPD by the parents with complaints that the size of left eye was unusually small compared to the right eye and the growth of the child was not commensurate with his peers. Otherwise, the perinatal history and developmental history was normal.

On examination, the height and weight of the child was less than 5th percentile and was stunted. Child had microphthalmia left and bilateral inferior nasal coloboma of the irises (Fig 1). Examination of the eye including fundoscopy, was normal. Examination of the ear, nose and throat was essentially normal. Radial pulse was normal but the right femoral artery was weakly palpable and there was radio-femoral delay. Blood pressure in right upper limb was 150/98 mm Hg and in the right lower limb 100/50 mm Hg, suggesting presence of Coarctation of the Aorta. General examination, including genitalia, was within normal limits. Systemic examination revealed, cardiac apex shifted to the left 6th intercostal space, a grade IV/VI long systolic murmur in the left lower sternal edge. Abdominal, respiratory and central nervous system examination were within normal limits.

Child was investigated and radiography of the chest revealed cardiomegaly (Fig 2). Echocardiography revealed significant co-actation of the aortic arch and a small non restrictive ventricular septal defect (VSD). Due to the possibility of CHARGE association, ultrasonography (USG) of the abdomen was carried out, which showed absent right kidney and a hydronephrotic left kidney. Further investigations were conducted in the form of intravenous urography (IVU) (Fig 3) and dimercaptosuccinic acid

(DMSA) scan which confirmed the USG findings and also showed a dilated pelvicalyceal system on the left side with vesico-ureteral reflux (VUR) (Fig 4). Other investigations included hematological and renal parameters, which were essentially normal. An ENT and ophthalmologic consultation did not reveal any added abnormalities. Karyotyping was normal. The child had coloboma of the irises, heart defect, growth retardation and urinary anomalies, thus satisfying the criteria for CHARGE syndrome.

Child was managed with anti-hypertensives and antibiotics (for VUR). Subsequently, he was taken up for left ureteric re-implantation and surgical correction of VUR. Cardiac surgery is being planned to deal with the coarctation of aorta and VSD.

Discussion

Pagan et al first coined the term CHARGE syndrome in 1981. This syndrome/association was named for its seven major clinical features. They are : coloboma of the eye, heart defects, atresia of the choanae, retarded

Fig. 1 : Facial photograph of the patient showing microphthalmia left eye associated with coloboma of iris

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Fig. 2 : Radiograph PA view of the chest showing cardiomegaly

Fig. 3 : Intravenous urography showing absent left kidney with dilated pelvicalyceal system and tortuous ureter of right kidney

growth and development including central nervous system anomalies, genital hypoplasia and / or urinary tract anomalies and ear anomalies and / or hearing loss. At least 4 of the 7 major criteria should be present to diagnose CHARGE syndrome [2]. Since then, various literature has been published describing the various associated anomalies, prevalence and possible etiology. Tellier et al reviewed 47 cases of CHARGE syndrome and the prevalence of various associations described by them are, coloboma 79%, heart malformation 85%, choanal atresia 57%, growth and / or mental retardation 100%, genital 34%, ear anomalies and or deafness 60%-

Fig. 4 : DMSA scan showing absent left kidney with right sided hydronephrosis

90%. In addition, facial palsy, micrognathia, cleft palate, swallowing difficulties and tracheoesophageal fistula were also reported. This non-random pattern of congenital anomalies occurs together more frequently than expected by chance. The combination of malformations in CHARGE syndrome strongly supports the view that this multiple congenital anomalies/mental retardation syndrome is a polytopic developmental field defect involving the neural tube and the neural crests cells [3].

Consensus diagnostic criteria have been proposed which incorporate both major and minor features of CHARGE association. Though, the various components in CHARGE syndrome occur as constellation, to be meaningful, it has been suggested that the terminology should be restricted to infants with coloboma and/or choanal atresia and three other malformations, such as heart, ear, genitourinary and retardation of growth [1].

Our case had bilateral coloboma of the irises, heart defect (coarctation of the aorta), growth retardation and urinary anomalies (4 major anomalies), thus satisfying the criteria of CHARGE syndrome.

The major eye changes described in this syndrome are - coloboma of the iris, retinal dysplasia, ectopic / glial tissue in sclera, microphthalmia and hypoplasia of the head of the Optic nerve [4]. Wyse et al in their study of spectrum of congenital heart disease, found Fallot's tetralogy and atrioventricular septal defects as more common compared to other cardiac lesions [5]. Other anomalies seen were, patent ductus arteriosus, double outlet right ventricle etc.

Ragan et al have described various genitourinary abnormalities, which can be seen in CHARGE association [6]. In the study of 32 cases, 69% had

genitourinary abnormalities. It included, genital anomalies such as micropenis, penile agenesis, chordee, cryptorchidism, bifid scrotum, atresia of cervix / vagina, labia majora and clitoris. The renal anomalies included solitary kidney, hydronephrosis, renal hypoplasia, vesico-ureteral reflux, neurogenic bladder and duplex kidney.

Most common ear abnormality is small, square, triangular and apparently low set ears, small helices and small or absent lobes. Other ear anomalies include bilateral vestibular defects, internal ear abnormalities such as semicircular canal defects, malformed pinnae, hypoplastic uncus, conductive hearing loss [7].

Management of such cases involves multidisciplinary approach. Presence of congenital heart disease, bilateral posterior choanal atresia or tracheoesophageal fistula and male sex have been associated with poor prognosis [5]. Choanal atresia requires emergency procedure such as tracheostomy and subsequently definitive repair as soon as possible [7].

Risk of recurrence of similarly affected child of normal parents is fairly low. But all known entities including chromosomal anomalies should be excluded and proper genetic counselling offered to parents [1,8].

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From a Sunday Newspaper :-

'The surgeon said he'd removed my momentum - the funny apron of fat that covers the intestines'.

The Workshop Bugle recently carried a news report about a chap who'd happily

'recovered from a tuna of the kidney'.

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