

## CHARGE Association

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### ABSTRACT

We present here a case of 17-year-old boy from Kolkata presenting with obesity, bilateral gynecomastia, mental retardation, and hypogonadotropic hypogonadism. The patient weighed 70 kg and was of 153 cm height. Facial asymmetry (unilateral facial palsy), gynecomastia, decreased pubic and axillary hair, small penis, decreased right testicular volume, non-palpable left testis, and right-sided congenital inguinal hernia was present. The patient also had disc coloboma, convergent squint, microcornea, microphthalmia, pseudohypertelorism, low set ears, short neck, and choanalatresia. He had h/o VSD repaired with patch. Laboratory examination revealed haemoglobin 9.9 mg/dl, urea 24 mg/dl, creatinine 0.68 mg/dl. IGF1 77.80 ng/ml (decreased for age), GH <0.05 ng/ml, testosterone 0.25 ng/ml, FSH-0.95  $\mu$ U/ml, LH 0.60  $\mu$ U/ml. ACTH, 8:00 A.M cortisol, FT3, FT4, TSH, estradiol, DHEA-S, lipid profile, and LFT was within normal limits. Prolactin was elevated at 38.50 ng/ml. The patient's karyotype was 46XY. Echocardiography revealed ventricularseptal defect closed with patch, grade 1 aortic regurgitation, and ejection fraction 67%. Ultrasound testis showed small right testis within scrotal sac and undescended left testis within left inguinal canal. CT scan paranasal sinuses revealed choanalatresia and deviation of nasal septum to the right. Sonomammography revealed bilateral proliferation of fibroglandular elements predominantly in subareolar region of breasts. MRI of brain and pituitary region revealed markedly atrophic pituitary gland parenchyma with preserved infundibulum and hypothalamus and widened suprasellar cistern. The CHARGE association is an increasingly recognized non-random pattern of congenital anomalies comprising of coloboma, heart defect, choanal atresia, retarded growth and development, genital hypoplasia, ear abnormalities, and/or deafness.<sup>[1]</sup> These anomalies have a higher probability of occurring together. In this report, we have described a boy with CHARGE association.

**Key words:** CHARGE, congenital malformations, Hypogonadotropic hypogonadism

### CASE REPORT

A 17-year-old boy presented with complaints of obesity, bilateral gynecomastia, hypogonadism, and mental retardation. During examination, the patient had facial asymmetry due to unilateral facial palsy that inspired us for a detailed history and examination.

The patient was the first child of his parents and he was born after 10 years of infertility. He was born at term through LUCS with uneventful antenatal history. There

was no history of drug intake or radiation exposure in the antenatal period. Family history was not significant. The mother gave history of delayed attainment of milestones.

He was admitted in hospital 2 months after birth with feeding difficulty and inadequate weight gain. He was diagnosed with heart failure and treated with digoxin, captopril, and frusemide. Echocardiography at that time revealed a large perimembranous ventricular septal defect (VSD) with large L→R shunt and severe pulmonary arterial hypertension and normal cardiac valves. Closure of VSD was performed with Dacron patch. He also had right-sided congenital inguinal hernia that was operated when he was 3 years old. The patient weighed 70 kg (>97<sup>th</sup> percentile) and had a height of 153 cm and BMI of 29.90. He had bilateral gynecomastia, sparse facial and axillary hair, pubic hair was at Tanner stage 3. The patient had decreased right testicular volume (4 ml) and absent left testis. Scrotal rugosity, thinning, and hyperpigmentation were present.

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The patient had mental retardation and attention deficit hyperactivity disorder. Binetkammat test showed a prorated IQ of 61, indicating mild mental retardation. On the Vineland Social Maturity Scale, he obtained a social age of 5 years and 9.6 months.

The patient also had disc coloboma, convergent squint, microcornea, microphthalmia, pseudo hypertelorism, low set ears, short neck, and bilateral choanal atresia.

Laboratory examination revealed haemoglobin 9.9 mg/dl, urea 24 mg/dl, creatinine 0.68 mg/dl, fasting venous plasma glucose 58 mg/dl, total bilirubin 0.6 mg/dl, conjugated bilirubin 0.2 mg/dl, unconjugated bilirubin 0.4 mg/dl, SGPT 32 IU/L, SGOT 46 IU/L, ALP 262 IU/L, total protein 8 gm/dl, albumin 4g/dl, globulin 4g/dl, P Time 13.6 seconds (control 11.8 seconds), INR 1.15, totalcholesterol 167 mg/dl, HDL 53 mg/dl, LDL 97 mg/dl, VLDL 17 mg/dl, triglyceride 142 mg/dl.

IGF1 77.80 ng/ml (decreased for age) (N range for 17 years: 193–731 ng/ml). GH <0.05 ng/ml (normal males, upto 3 ng/ml), testosterone 0.25 ng/ml (males, 1.75–7.81 ng/ml), FSH 0.95  $\mu$ IU/ml (1–14  $\mu$ IU/ml), LH 0.60  $\mu$ IU/ml (0.7–7.4  $\mu$ IU/ml). Therefore, the patient had growth hormone deficiency and hypogonadotropic hypogonadism.

Other hormone assays showed ACTH 39.70 pg/ml (0–46 pg/ml), FT3 6.42 pmol/l (3.10–6.80 pmol/l), FT4 1.36 ng/dl (0.93–1.7 ng/dl), TSH 2.79  $\mu$ IU/ml (0.27–4.2  $\mu$ IU/ml), 8:00 A.M. cortisol 8.71 mcg/dl (6.2–19.4 mcg/dl), DHEA-S 96.2 mcg/dl (males, 80–560 mcg/dl), estradiol 23.1 pg/ml (males, 20–75 pg/ml). Prolactin was elevated at 38.50 ng/ml (2.1–17.7 ng/ml). The patient karyotype was 46XY.

Imaging echocardiography revealed ventricularseptal defect

closed with patch, grade 1 aortic regurgitation and ejection fraction of 67%.

USG of both testes revealed small right testis within the scrotal sac (size 16  $\times$  12  $\times$  8 mm approximately) with preserved shape. Undescended ill developed small left testis present within left inguinal canal with thin and narrow spermatic cord attached to it. Sonomammography revealed bilateral proliferation of fibroglandular elements predominantly in subareolar region of breasts. No focal space occupying lesion was noticed.

Computed tomography scan paranasal sinuses revealed choanalatresia [Figure 3] and deviation of anterior cartilaginous nasal septum.

MRI of the brain showed markedly atrophic pituitary gland parenchyma with preserved infundibulum and hypothalamus. Suprasellar cistern was widened.

Thus, the patient had a combination of abnormal facies, discoloboma, retardation of growth and development, genital hypoplasia, ventricular septal defect, and ear anomalies, which is consistent with diagnosis of CHARGE association.

## DISCUSSION

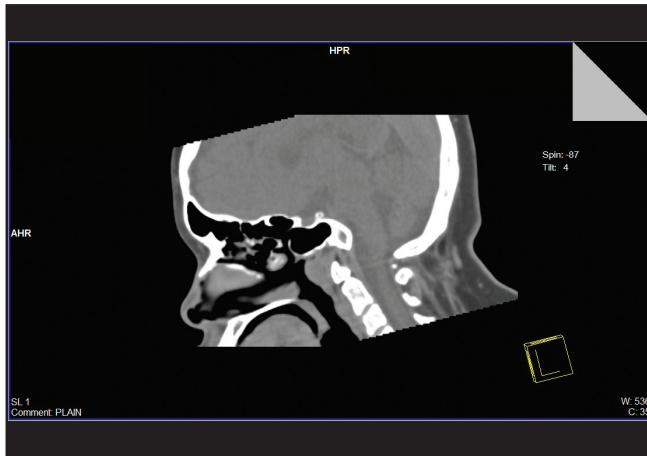
CHARGE association was first described by Hall in 1979 in children with multiple congenital anomalies along with choanalatresia.<sup>[2]</sup> But it was Pagon *et al.* in 1981 who first coined the acronym CHARGE association<sup>[1]</sup>. This multiple congenital anomaly condition has an estimated prevalence of 1:10000. Various diagnostic criteria have been proposed for CHARGE association. Pagon *et al.* proposed that to make a confident diagnosis of the CHARGE association,



Figure 1: Showing bilateral gynecomastia



Figure 2: Showing absent left testes



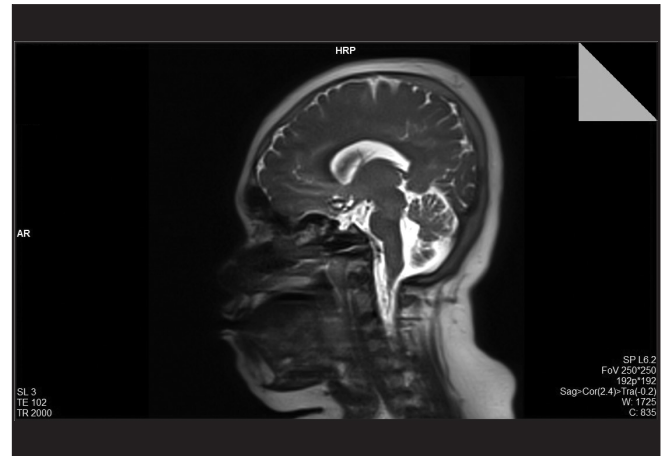
**Figure 3:** CT scan of paranasal sinus showing choanal atresia

at least four of the seven major features included in the mnemonic have to be present and these should include either coloboma or choanal atresia or both.<sup>[1]</sup> An expert group of geneticists and developmental pediatricians defined the major and minor criteria of CHARGE syndrome in 1998.<sup>[3]</sup> Patients with four major characteristics or three major and three minor characteristics are likely to have CHARGE syndrome.

CHARGE is a mnemonic for coloboma, heart defects, choanal atresia, retarded growth and development, genital abnormalities, and ear anomalies. CHARGE syndrome is characterized by the following:

1. Unilateral or bilateral coloboma of the iris, retina-choroid, and/or disc with or without microphthalmos (80–90%)
2. Unilateral or bilateral choanal atresia or stenosis (50–60%)
3. Cranial nerve dysfunction resulting in hyposmia or anosmia, unilateral or bilateral facial palsy (40%), impaired hearing, and/or swallowing problems (70–90%)
4. Abnormal outer ears, ossicular malformations, absent semicircular canals
5. Cryptorchidism in males and hypogonadotropic hypogonadism in both males and females
6. Cardiovascular malformations (75–85%)
7. Growth deficiency and developmental delay (70–80%)

The diagnosis of CHARGE syndrome is based on clinical findings. CHD7, encoding the chromodomain



**Figure 4:** MRI brain showing atrophy of pituitary glands with preserved infundibulum and hypothalamus

helicase DNA binding protein, is the only gene currently known to be associated with CHARGE syndrome.<sup>[4]</sup> Overall, CHD7 analysis in individuals with either typical CHARGE syndrome or a milder phenotype (i.e., fewer major characteristics) detects mutations in about 65–70% of all cases.

Our patient had three major (coloboma, choanal atresia, and cranial nerve dysfunction) and three minor criteria (cardiovascular malformation, genital hypoplasia, and distinctive facies with sloping forehead and flattened tip of nose). Genetic study could not be conducted. Therefore, our patient probably had CHARGE syndrome.

## REFERENCES

1. Pagon RA, Graham JM, Zoana J, Yong SL. Coloboma, Congenital heart disease and choanal atresia with multiple abnormalities—CHARGE association. *J Pediatr* 1981;99:223-27.
2. Hall BD. Choanal atresia and associated multiple anomalies. *J Pediatr* 1979;95:395-98.
3. Blake KDI, Davenport SL, Hall BD, Hefner MA, Pagon RA, Williams MS, *et al.* CHARGE association: An update and review for the primary pediatrician. *Clin Pediatr* 1998;37:159-71.
4. Johnson DS, Morrison N, Grant L, Turner T, Fantes J, Connor JM, *et al.* Confirmation of CHD7 as a cause of CHARGE association identified by mapping a balanced chromosome translocation in affected monozygotic twins. *J Med Genet* 2006;43:280-4.

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