



# CHARGE Syndrome: Contribution Of Ear CT Scan And Diagnostic Criteria

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**Abstract:** CHARGE Syndrome is a rare clinical entity of genetic origin associating to varying degrees multiple organ involvement: coloboma, cardiac anomalies, choanal atresia, ear anomalies or deafness, genital anomalies and delayed psychomotor development and growth, necessitating a multidisciplinary approach to its management. We report a case of CHARGE syndrome in a 13-month-old infant.

**Key words:** -CHARGE Syndrome, Choanal atresia, CT Scan, Agenesis of semi-circular canals.

## I. INTRODUCTION

CHARGE Syndrome is a rare clinical entity of genetic origin associating to varying degrees multiple organ involvement: coloboma, cardiac anomalies, choanal atresia, ear anomalies or deafness, genital anomalies and delayed psychomotor development and growth, necessitating a multidisciplinary approach to its management. We report a case of CHARGE syndrome in a 13-month-old infant.

## II. CLINICAL OBSERVATION

A 13-month-old infant with CHARGE syndrome was referred to us for a deafness assessment. She presented to the consultation in the context of a workup for choanal atresia. On physical examination, he showed a staturo-ponderal delay of 3 standard deviations (SD), pre-lingual deafness and delayed psychomotor acquisition with facial dysmorphism. CT scan revealed:

- 1- Bilateral choanal atresia (bony and membranous) "Fig.1"
- 2- Bilateral vestibular hypoplasia with agenesis of the semicircular duct and canals "Fig.2"
- 3- Bilateral hypoplasia of the cochlear nerve"Fig.3"
- 4- Lack of stapes differentiation with densification of the turndable "Fig. 4"

## III. DISCUSION

CHARGE syndrome was first described in 1979 simultaneously by HILL and HUNT, which earned it the name HILL and HUNT syndrome, but in 1981 R. PAGON gave it the name CHARGE syndrome, using the acronym of the initials of the main disorders: Coloboma, Heart defect, Choane atresia, Retarded growth and development, Genital hypoplasia and Ear anomalies or deafness.(1)

The diagnosis could be made if four of the six criteria were met. Due to the lack of specificity of certain criteria, a distinction was made between major criteria (coloboma, choanal atresia, hypoplastic semi-circular canals) and minor ones (the remaining four). (2) Diagnosis is the presence of two major and two minor criteria or one major criterion and three minor ones.

It affects around 1 in 8,500 to 10,000 births, making it one of the 25 most common malformative syndromes, with a pan-ethnic distribution and no gender distinction in frequency. (3) It is most often due to

mutations in the CHD7 gene (chromodomain helicase DNA-binding protein-7 gene). Most cases are sporadic, and rare familial cases with autosomal dominant inheritance have been reported.(4)

## **1- Clinical Features of CHARGE Syndrome:**

### **1-1 Coloboma -C-**

This is a defect in the closure of the colobomic cleft during organogenesis. This is a major criterion of CHARGE syndrome, found in around 85% of patients.

It can affect several structures in the eye. Most frequently, it is purely chorioretinal, but can also involve the optic disc and iris. (5) It is accompanied by microphthalmia in 40% of cases. When isolated, this is considered equivalent to a coloboma. Visual prognosis is essentially determined by the papillary topography of the coloboma, the bilaterality of the lesions and the presence of microphthalmia.(6)

### **1-2 Cardiac malformations -H-**

These are present in 70 to 80% of cases. The most frequent anomaly is tetralogy of Fallot, but other anomalies may also exist, such as persistent ductus arteriosus, isolated septal defects and conotruncal heart disease.(7)

### **1-3 Choanal atresia -A-**

Present in over 40% of cases; it is more frequently bony than membranous and in half of cases bilateral, responsible for respiratory distress in the neonatal period. Its presence indicates a poor prognosis for survival, and requires multiple complex surgical interventions to correct it.(8)

### **1-4 Growth and developmental retardation -R-**

Growth retardation is defined as weight and/or height below  $\sim$ 2 DS (6 standard deviations) or the third percentile. It is found in 75% of patients.

Only a third of cases are revealed antenatally, and most often develop between zero and nine months of age, with catch-up after two years. This does not point to an endocrine pathology, and growth hormone deficiency is exceptional in CHARGE syndrome.(6)

### **1-5 Genitorinary problems -G-**

It is most often micropenis and cryptorchidism in boys (80% of cases), and hypoplasia of the labia minora in girls (16%), delayed development of the external genitalia is easier to recognize in boys than in girls, the main anomalies being microphallus, penile agenesis, cryptorchidism, bifid scrotum, vaginal atresia, hypoplasia of the labia or clitoris.

### **1-6 Ear and hearing problems – E-**

All three parts of the ear can be affected. The outer ear is often small, narrow and poorly implanted (pinna anomalies, ear canal atresia, pre-auricular appendages). The sensory deficit may result in a typical triangular audiogram.

### **1-7 Malformations of the inner ear are common: (9) (10)**

They must be specifically researched for. Hypoplasia or agenesis of the semicircular canals is a sign that has been sign that has remained constant until now, and is specific when associated with other malformations such as ossicular anomalies. It is considered as a major diagnostic sign.

Mondini malformation (cochlea with less than one-and-a-half turns instead of two-and-a-half) is both less frequent and less specific if isolated.

Abnormalities of the ossicles, in particular hypoplasia of the anvil, absence of the stapedial muscle, and anomaly or complete absence of the oval window. Some believe that hypoplasia of the anvil associated with agenesis of the semicircular canals is pathognomonic of CHARGE syndrome. These abnormalities can be investigated by CT scan and MRI.

**Other anomalies:** in addition to these conditions, which give rise to the name CHARGE syndrome, many other congenital anomalies may exist, such as facial paralysis, central nervous system disorders, swallowing anomalies, cleft lip and/or palate, urinary tract malformations or tracheoesophageal fistula.

## 2- Diagnosis: (11)

In view of the multifocal involvement of Charge syndrome, several authors have proposed diagnostic criteria based on a combination of major and minor criteria.

**Major criteria:** coloboma, choanal atresia, ear anomalies and cranial nerve anomalies.

**Minor criteria:** cardiac involvement, genital anomalies, cleft palate, cleft lip, facial dysmorphism, growth retardation and developmental delay. Initially, PAGON et al proposed the presence of 4 criteria for diagnosis, with the mandatory presence of coloboma or choanal atresia.

Finally, given the multiplicity of clinical forms, Verloes proposed the notion of typical, atypical or partial CHARGE syndrome:

- Typical CHARGE syndrome: 3 major criteria or 2 major and 2 minor criteria.
- Partial CHARGE syndrome: 2 major criteria and 1 minor criterion.
- Atypical CHARGE syndrome: 2 major criteria and 0 minor criteria/ 1 major and 3 minor criteria.

Our patient presented typical CHARGE, with 2 major criteria (choanal atresia, ear anomalies) and minor criteria (growth retardation and developmental delay, facial dysmorphism)

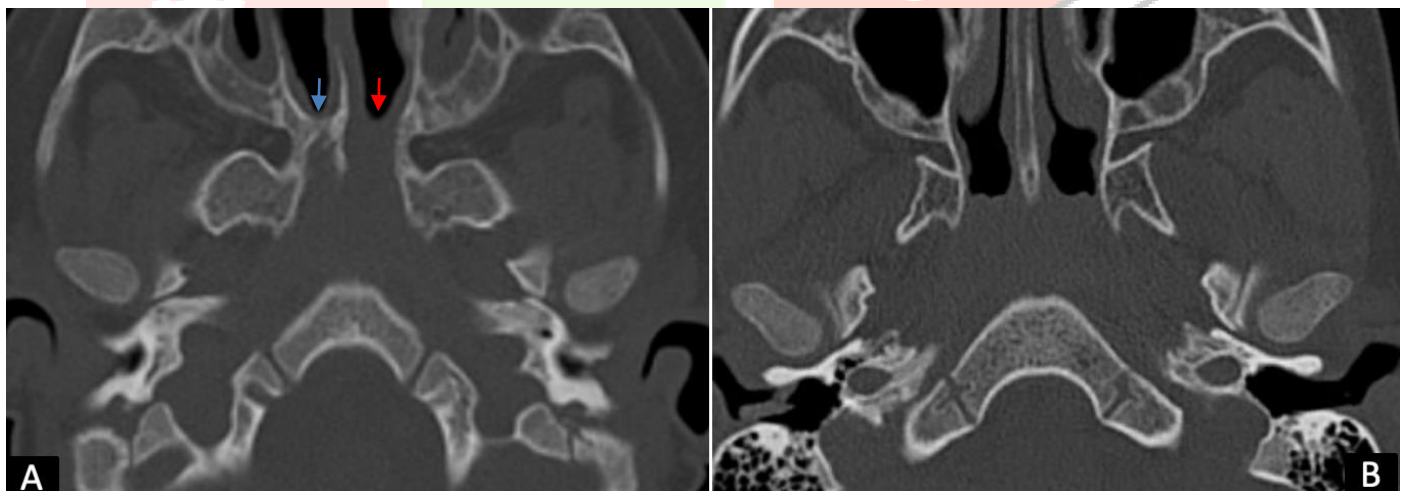
The prognosis of CHARGE syndrome is hampered by the coexistence of heart disease with choanal atresia or trachdo-oesophageal fistula.

## IV. CONCLUSION

All in all, CHARGE syndrome is a frequent polymalformative syndrome, the diagnosis of which is based exclusively on clinical and radiological criteria. Early, multidisciplinary care is vital to limit morbidity in these handicapped children. It is difficult and time-consuming, but essential.

### Figures:

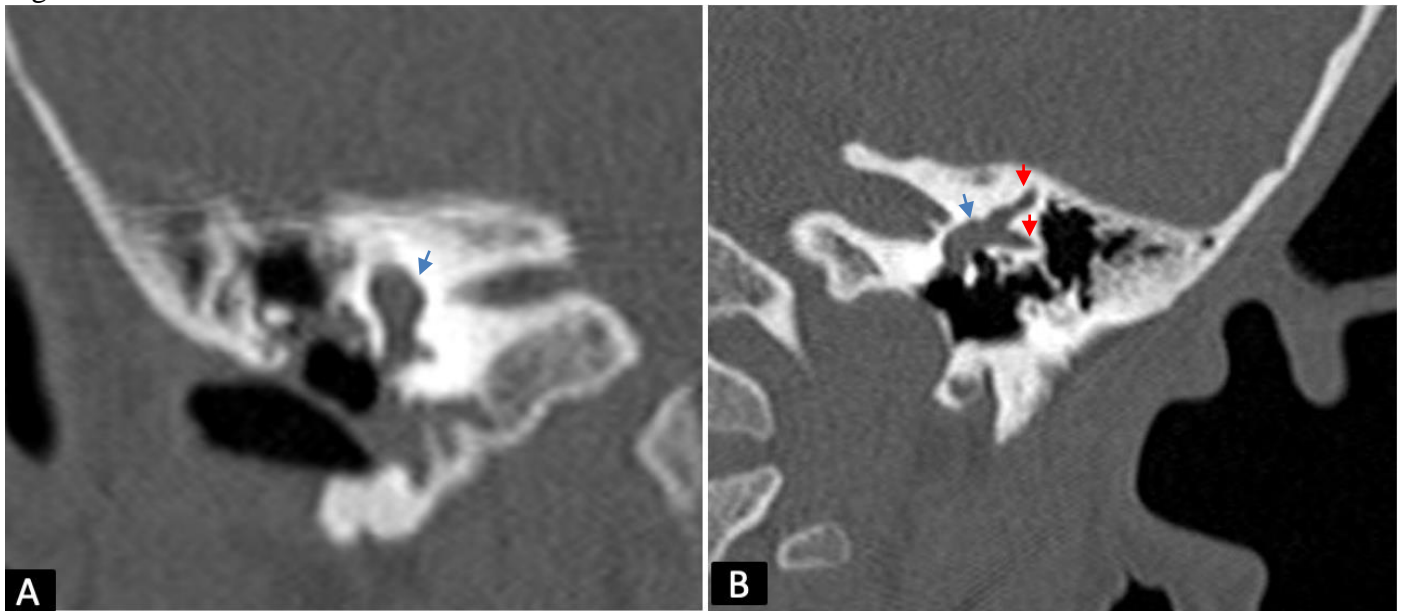
Figure 1



Axial CT section through the choanae:

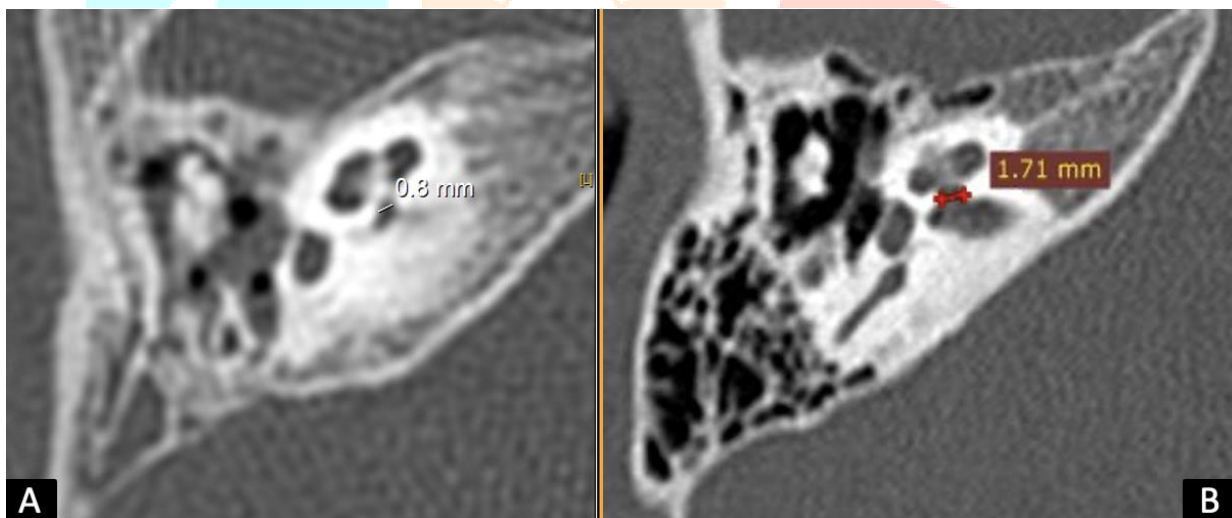
(A) Bilateral choanal atresia (bony on the right (blue arrow) and membranous on the left (red arrow)); (B) Normal appearance

Figure 2



Coronal reconstruction through the vestibular plane:  
(A) vestibular hypoplasia with agenesis of the semicircular canals, (B) Normal appearance  
(blue arrow vestibular, red arrows semicircular canals)

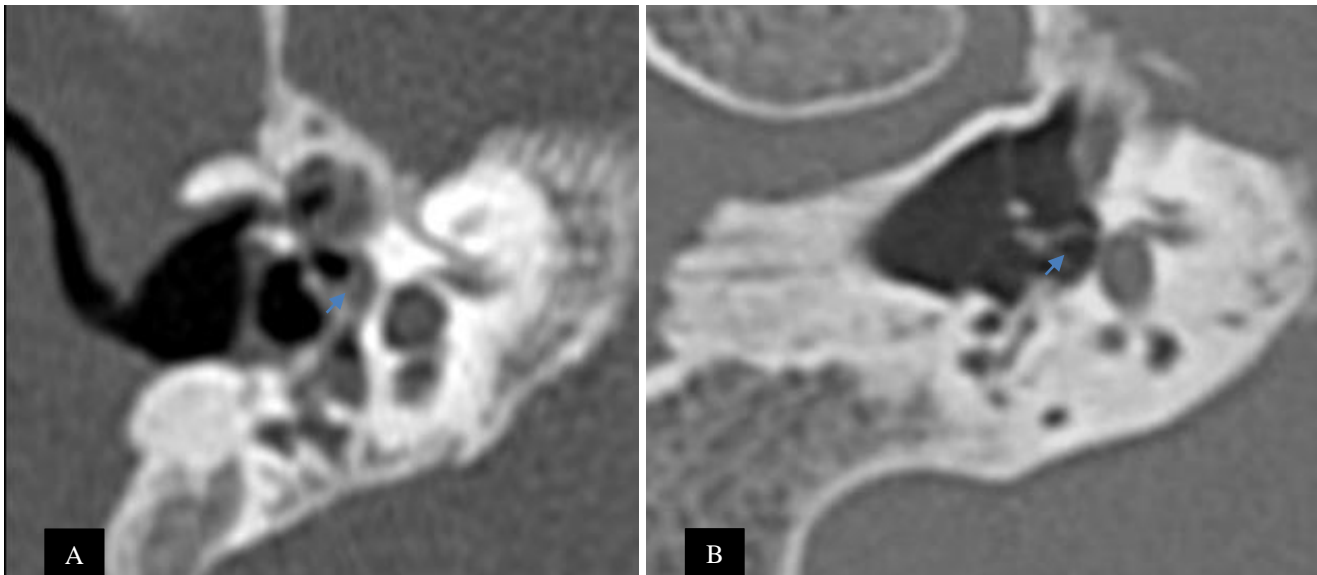
Figure 3



Axial section through the hypoplastic cochlear nerve canal measured at 0.8 mm (B) Normal measurement (1.5 - 2 mm).



Figure 4



Reconstruction through the plane of the stapes (blue arrow):

(A) Densification of the platinum + Lack of differentiation of the stapes (B) Normal appearance

## REFERENCES

- [1] Pagon RA, Graham JM, Jr, Zonana J, Yong SL. Coloboma, congenital heart disease, and choanal atresia with multiple anomalies: CHARGE association. *J Pediatr*. 1981 Aug;99(2):223–7.
- [2] Mitchell JA, Davenport SL, Hefner MA, Shei MM. Use of an expert model to test diagnostic criteria in CHARGE syndrome. *J Med Syst* 1985 ; 5-6 : 425-36.
- [3] Karina A Issekutz, John M Graham, Jr, Chitra Prasad, Isabel M Smith, Kim D Blake. To enhance easy recognition of the syndrome by all clinicians An Epidemiological Analysis of CHARGE Syndrome: Preliminary Results From a Canadian Study. *American Journal of Medical Genetics*. 2005 Mar;133A(3):309–317.
- [4] Vissers LE, van Ravenswaaij CM, Admiraal R, Hurst JA, de Vries BB, Janssen IM, van der Vliet WA, Huys EH, de Jong PJ, Hamel BC, Schoenmakers EF, Brunner HG, Veltman JA, van Kessel AG. Mutations in a new member of the chromodomain gene family cause CHARGE syndrome. *Nat Genet*. 2004 Sep;36(9):955–7.
- [5] McMains K, Blake K, Smith I et al. Ocular features of CHARGE syndrome. [Erratum appears in *J AAPOS*. 2008 Dec;12(6):630]. *J. AAPOS* 2008; 12: 460–5.
- [6] Finel E, Parent P, Giroux JD, de Parscau L. The CHARGE association. *Arch Pediatr*. 1996 Oct;3(10):1020–5.
- [7] Blake KD, Prasad C. CHARGE syndrome. *Orphanet J. Rare Dis*. 2006; 1: 34.
- [8] Leclerc JE, Fearon B. Choanal atresia and associated anomalies. *Int. J. Pediatr. Otorhinolaryngol*. 1987; 13: 265–72.
- [9] Amiel J, Attiee-Bitach T, Marianowski R, CormierDaire V, Abadie V, Bonnet D, et al. Temporal bone anomaly proposed as a major criteria for diagnosis of CHARGE syndrome. *Am J Med Genet* 2001 ; 9: 124-7.
- [10] Admiraal RJ, Huygen PL. Vestibular areflexia as a cause of delayed motor skill development in children with the CHARGE association. *Int. J. Pediatr. Otorhinolaryngol*. 1997; 39: 205–22.
- [11] Verloes A. Updated diagnostic criteria for CHARGE syndrome: a proposal. *Am J Med Genet A*. 2005 Mar 15;133A(3):306–8.