STRUCTURAL PITUITARY ABNORMALITY AND DYSFUNCTION ASSOCIATED WITH CHARGE SYNDROME

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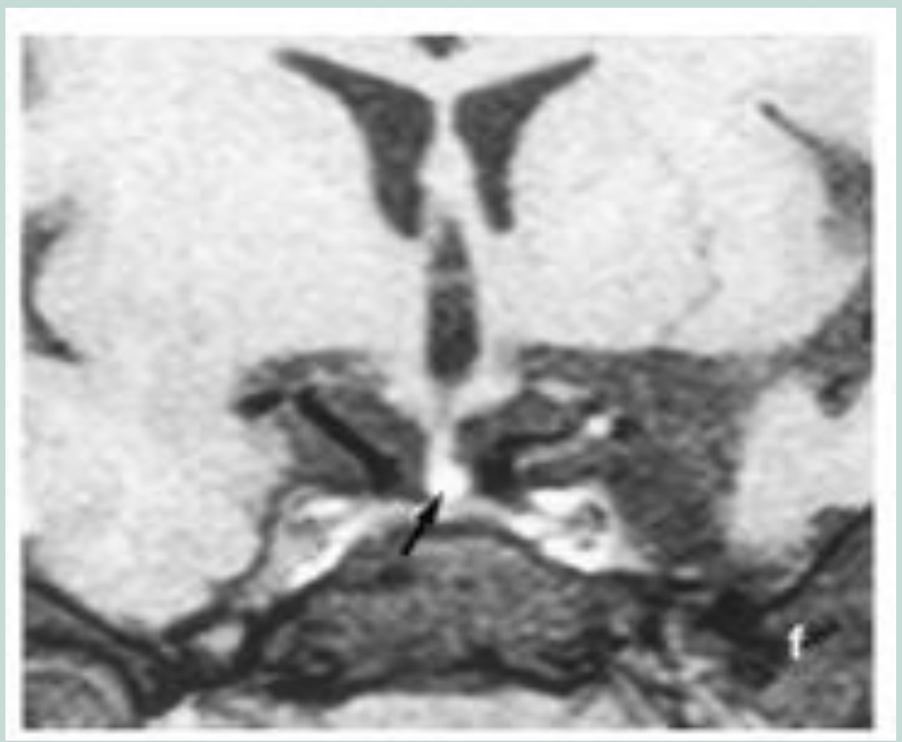
INTRODUCTION

- CHARGE is an autosomal-dominant syndrome which includes a variable combination of coloboma of the eye, heart malformations, atresia of the choanae, retardation of growth and development, and genital and ear abnormalities
- CHARGE syndrome has rarely been associated with anterior pituitary dysfunction and with structural abnormalities of the pituitary gland only twice.
- We report the case of a child with CHARGE association and congenital hypopituitarism due to structural abnormalities of the pituitary gland

CASE PRESENTATION

- The patient was a boy born with IUGR (birth weight 2020gr, 37weeks' gestation)
- Clinical features included
  - retinal coloboma and micropthalmia,
  - choanal atresia, dysplastic auricles with small accessory auricle ,
  - multicystic dysplastic kidney and hypospadias with cryptorchidism.
- Endocrine testing revealed central hypothyroidism and secondary hypoadrenalism. There was inadequate response to low-dose intravenous Synacthen stimulation, with serum cortisol peaking at 10.3μg/dl at 1 hour. He was started on thyroxine and hydrocortisone replacement.
- Because of severe growth impairment by the age of 3.4years (HSDS :-4.71, HVSDS : -3.62), growth hormone secretion was evaluated. A severe GHD was detected (peak GH 1.56ng/ml in both tests) and rhGH therapy was initiated. MRI revealed ectopic posterior pituitary



BLAKE'S CRITERIA

	Major 4C's **	
Ocular coloboma	**C**oloboma -of iris, retina, choroid, disc; microphthalmia	Photophobia; retinal detachment Corneal abrasions
Choanal atresia/stenosis	**C**hoanal atresia (or Cleft palate) – unilateral/bilateral, membranous/bony, stenosis/atresia	Facial growth problems, recurrent closure and resurgeries, unilateral nasal discharge
Cranial nerve anomalies	**C**ranial nerve dysfunction – Olfactory tract anomalies – Facial palsy (unilateral or bilateral), Sensorineural deafness, Velopharyngeal incoordination – swallowing problems	Feeding/swallowing problems; gastroesophageal reflux; hiatus hernia
Characteristic ear anomalies	**C**haracteristic ear abnormalities – External ear (lop or cup shaped),, Middle ear (ossicular malformations, chronic serous otitis), mixed deafness, semicircular canal +/-cochlear defects	Progressive hearing loss; chronic middle ear infections; vestibular problems affecting balance and/or motor skills.
	Minor	
Cardiovascular malformations	Cardiovascular malformations – All types: especially conotruncal defects (e.g. Tetralogy of Fallot), AV canal defects, and aortic arch anomalies	Arrhythmias; angina; further cardiac surgeries
Genital hypoplasia	Genital hypoplasia – Males: micropenis, cryptorchidism; Females: hypoplastic labia, Both: Delayed incomplete pubertal development	Pubertal delay, hormone replacement; fertility (unsure); hypogonadotrophic hypogonadism, osteoporosis
Cleft lip/palate	Orofacial cleft – Cleft lip and/or palate	Cosmetic concerns; self-image
Tracheoesophageal fistula	Tracheoesophageal fistula – Tracheoesophageal defects of all types	Reflux esophagitis; feeding/swallowing problems
Distinctive CHARGE facies	Characteristic face – sloping forehead, flattened tip of nose	Cosmetic concerns; self-image
Growth deficiency	Growth deficiencies – Short stature Borderline growth hormone (GH) stimulation tests	Growth hormone (GH) replacement Obesity
Developmental delay	Developmental delay – Delayed motor milestones, language delay, mental retardation	Educational, behavioural, social adjustment issues; Autistic-like problems; Obsessive compulsive disorders; Attention Deficit Hyperactivity Disorder (ADHD)
	Occasional***	
Renal anomalies	Duplex system, Vesicoureteric reflux	Renal failure
Spinal anomalies	Scoliosis; Osteoporosis	Scoliosis
Hand anomalies	Fifth finger clinodactyly, camptodactyly and cutaneous syndactyly	Fine motor problems; cosmetic concern
Neck/shoulder anomalies	Sloping, Sprengel's deformity, kyphosis	Self-image concern

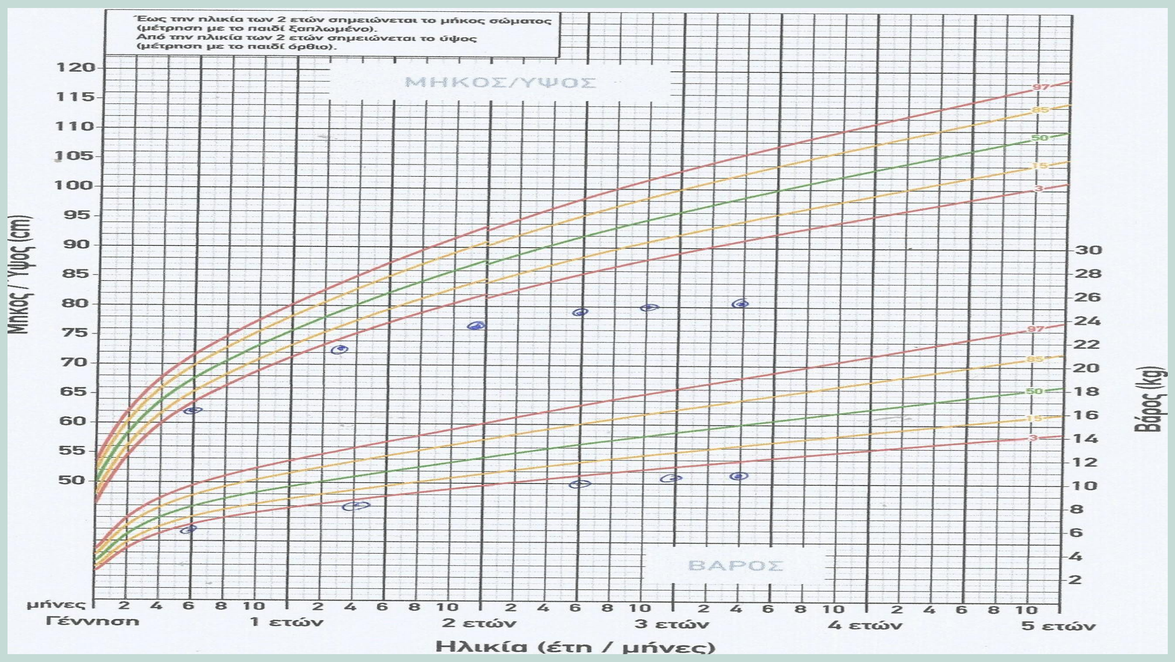
TABLE I. Major and Minor Signs of CHARGE Syndrome

Major signs ("the 3 C")
Coloboma (iris or choroid, with or without microphthalmia)
Atresia of Choanae
Hypoplastic semi-circular Canals
Minor signs
Rhombencephalic dysfunction (brainstem dysfunctions, cranial nerve VII to XII palsies and neurosensory deafness)
Hypothalamo-hypophyseal dysfunction (including GH and gonadotrophin deficiencies)
Abnormal middle or external ear
Malformation of mediastinal organs (heart, esophagus)
Mental retardation

VERLOE'S UPDATED CRITERIA, 2005

TABLE II. Definition of Typical, Atypical, and Partial CHARGE Syndrome

Typical CHARGE
3 majors signs
2/3 major signs + 2/5 minor signs
Partial/incomplete CHARGE
2/3 major + 1/5 minor
Atypical CHARGE
2/3 major + 0/5 minor
1/3 major + 3/5 minors



CONCLUSION

- We describe the case of a boy fulfilling citeria of CHARGE association (Blakes 1998, Verloes 2005) presenting with multiple anterior pituitary hormone deficiencies and structural pituitary abnormality.
- To our knowledge this is the 3rd case in the literature where congenital hypopituitarim in CHARGE syndrome is associated with pituitary structural abnormalities and especially ectopic posterior pituitary