Curr Pediatr Res 2012; 16 (1): 69-71

Cat eye syndrome: A mild phenotype with isolated growth hormone deficiency

Sarar Mohamed

Department of Pediatrics, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Department of Pediatrics, Saad Specialist Hospital Al Khobar, Saudi Arabia

Abstract

Cat eye syndrome (OMIM 115470) is a genetic disorder results from abnormality of Chromosome 22. It is characterized by constellation of malformations. Growth is usually normal. We report on a 16 year old Saudi male with Cat eye syndrome (CES) who displayed mild clinical features. The cytogenetic studies confirmed the karyotype as 47XY+del 22q11, which is consistent with the diagnosis of cat eye syndrome. Unlike the majority of reported cases with CES, our patient had severe growth failure. Isolated growth hormone deficiency was confirmed as the patient failed exercise stimulation test in addition to two growth hormone dynamic tests, namely insulin induced hypoglycemia and glucagon tests.

Key words: Cat eye syndrome, short stature, growth hormone

Acepted October 16 2011

Introduction

Cat eye syndrome (CES) is a chromosomal abnormality results from an extra chromosome derived from two identical segments of chromosome 22 [1, 2, 3, 4]. The estimated incidence of CES is I in 50000 to 150000 [5]. CES is characterized by hypertelorism, strabismus, inner epicanthic folds, flat nasal bridge, small mandible and malformed ears [1, 6, 7]. Other anomalies include coloboma of the iris, anal atresia, and variable abnormalities of bladder, rectum, urethra, heart, and kidneys. The diagnosis of CES is confirmed by molecular and cytogenetic studies [7, 8]. We here report on a case of CES presented with mild clinical phenotype and severe growth failure secondary to isolated growth hormone deficiency.

Case report

We report on a 16-year-old Saudi boy who was referred to the endocrine clinic for assessment of short stature. Parents are first degree cousins. Pregnancy and delivery were uneventful. Birth weight was 2.7 kg. He had no history of neonatal jaundice or hypoglycemia. Neonatal examination revealed bilateral multiple ear tags, hypertolerism, bilateral undescended testicles and no evidence of coloboma of the iris. Cardiovascular assessment was normal. At one year of age he presented with chronic constipation. Examination revealed anal fissure, anal stenosis with fibrous ring, and redundant rectum. He was treated with anal dilatation, and anorectoplasty. In view of the anorectal anomalies, cytogenetic and fluorescence in situ hybridization studies confirmed the karyotype as 47XY+del 22q11, which is consistent with the diagnosis of cat eye syndrome. Clinical examination and imaging failed to demonstrate any cardiac or renal malformations. Parents were concerned about growth of their son since early childhood. He continued to be the shortest pupil in his class. Developmental assessment was appropriate for his age with an average school performance..

Assessment of growth at 16 years of age revealed extreme short stature. Height was 129 cm well below the third centile and weight was below the third centile. Midparental height was at 50th centile. Tanner staging showed that our patient was prepubertal with no secondary sex characteristics.

Results

Bone age was significantly delayed and consistent with a 9 year old boy using Greulich-Pyle method. MRI of the brain showed normal pituitary anatomy. Thyroid function test was normal. Celiac screening was negative. Luteinizing hormone releasing hormone (LHRH) test showed that FSH, LH, and testosterone levels were consistent with prepubertal status. Insulin like growth factor 1(IGF1) and IGF binding protein 3 level was within

normal limits. Exercise Stimulation test showed baseline growth hormone of 0.66 mU/l that increased to 1.52 mU/l after 20 minutes of exercise, which is suboptimal response. Table 1 and 2 show the results of Glucagon stimulation test, and insulin induced hypoglycemia test respectively. These pituitary function tests confirmed isolated growth hormone deficiency with intact ACTH-cortisol axis. Growth hormone peaked at 1.1 mU/l (normal >20 Mu/l) with insulin induced hypoglycemia (glucose <1.7 mmol/l). This result indicates severe growth hormone deficiency.

Table 1. *Glucagon stimulation test*

Time	**Growth hormone** (mU/l) N>20	**Cortisol nmol/l** N (160-565)
0	0.58	238
30	1.3	300
60	2.6	300
90	3.16	207
120	2.98	274
150	2.64	481
180	1.13	383

Table 2. *Insulin induced hypoglycemia test*

Time	**Growth hormone** (mU/l) N>20	**Cortisol (nmol/l) N(160-565)**
0	<0.5	733
30	<0.5	658
60	<0.5	512
90	<0.5	467
120	1.0	806
150	0.3	896

Discussion

Cat eye syndrome (CES) is characterized by a typical clinical picture including anal atresia, ocular coloboma, and preauricular tags. Anal atresia and coloboma of the iris, initially considered the hallmarks of the disorder, are present in combination in only a minority of the patients reported [1, 2, 7]. Roias RR et al reported on six patients with CES [6]. The main abnormalities observed were preauricular tags and/or pits and anal atresia (both observed in 83% of cases), coloboma of the iris was observed in only two cases (33%) and congenital heart disease was detected in four patients (67%).

Our patient as many of CES cases reported recently did not show ocular coloboma which was thought to be essential for the diagnosis in the early reports. Clinical presentation of our patient is keeping with the recent reports showing wide phenotypic variations associated with Cat eye syndrome [1, 2, 3]..

The majority of reported CES cases showed normal growth [1]. Mild prenatal growth retardation may occur, however postnatal growth is usually normal. Our case showed significant short stature. The cause of short stature was isolated growth hormone deficiency documented by pituitary function tests. Growth failure was reported in few cases with cat eye syndrome. Pierson M et al reported a case of Cat eye syndrome with pituitary dwarfism and normal mental development [7]. Masukawa H reported on a 17-year-old male with Cat Eye Syndrome (CES) and hypogonadotropic hypogonadism who showed short stature and absence of secondary sex characteristics and responded to growth hormone combined with human chorionic gonadotrophin replacement therapy [8]. Matsumoto R reported on a 34 year old man with CES who presented with idiopathic hypogonadotropic hypogonadism and normal stature [9]. We opted to start our patient on growth hormone therapy aiming to gain more height before inducing puberty by using gonadotropin or androgen. Combining growth hormone with androgen may lead to early closure of epiphyses resulting in short final height.

In conclusion, we report on an unusual case of cat eye syndrome presented with few dysmorphic features, anorectal anomalies, normal developmental milestones and severe growth failure caused by isolated growth hormone deficiency. This case alerts physicians to consider the possibility of CES in patients with anrectal malformations despite absence of other typical features of this syndrome. It also highlights the importance of early assessment of growth including growth hormone testing for patients with CES who deviate from normal growth pattern.

References

1. Online Mendelian Inheritance in Man, OMIM (TM). [cited 2011 Aug 12]. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine. Available from: http://www.ncbi.nlm.nih.gov/omim/Cat eye syndrome.
2. Lindsay EA, Shaffer LG, Carrozzo R, Greenberg F, Baldini A. De novo tandem duplication of chromosome segment 22q11-q12: clinical, cytogenetic, and molecular characterization. Am J Med Genet 1995; 56: 296-299.
3. Rosias PR, Sijstermans JM, Theunissen PM, Pulles-Heintzberger CF, De Die-Smulders CE, Engelen JJ, Van Der Meer SB. Phenotypic variability of the cat eye syndrome. Case report and review of the literature. Genet Couns 2001; 12: 273-282.

4. Jung MKin, Kim JB, Pai KS, Yun JN, Park SJ. Partial tetrasomy of chromosome 22q11.1 resulting from a supernumerary isodicentric marker chromosome in a boy with Cat-eye syndrome. J Korean Med Sci 2010; 25: 1798-1801.
5. Berends MJ, Tan-Sindhunata G, Leegte B, Van Essen AJ. Phenotypic variability of cat-eye syndrome. Genet Couns. 2001; 12: 23-34.
6. Rosa RF, Mombach R, Gazzola Zen PR, Graziadio C, Paskulin GA. clinical characteristics of a sample of patients with cat eye syndrome. Rev Assoc Med Bras 2010; 56 (4): 462-466.
7. Pierson M, Gilgenkrantz S, Saborio M. Cat eye syndrome with pituitary dwarfism and normal mental development. Arch Fr Pediatr. 1975 Nov; 32(9):835-48.
8. 8.Masukawa H, Ozaki T, Nogimori T. Cat eye syndrome with hypogonadotropic hypogonadism. Intern Med 1998; 37 (10): 853-856.
9. 9..Matsumoto R, Shimizu C, Nagai S, Taniguchi S, Umetsu M, Kimura Y, Atsumi T, Yoshioka N, Kubo M, Koike T. Cat-eye syndrome with isolated idiopathic hypogonadotropic hypogonadism. Intern Med. 2005; 44(10):1069-1073.

Correspondence:

Sarar Mohamed
Department of Pediatrics (39)
College of Medicine
King Saud University
P.O. Box 2925, Riyadh11461
Saudi Arabia