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ORIGINAL ARTICLE

Clinical characteristics of a sample of patients with cat eye syndrome

Clinical Characteristics of Patients with the sample of cat eye syndrome

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ABSTRACT

OBJECTIVE: The cat eye syndrome, a chromosomal disorder is considered rare and phenotypically highly variable. The aim of this study was to describe the clinical characteristics of a sample of patients with the syndrome evaluated at our institution.
METHODS: A retrospective study, six patients diagnosed with cat eye syndrome. All of them showed a karyotype with the presence of an additional marker chromosome, inv dup (22) (pter-> q11.2:: q11.2-> pter). One of them also had mosacismo with a strain with normal chromosome constitution. From the medical records were collected clinical data and outcome. For comparison between the frequencies found in our study and the literature we used the Fisher exact test (P <0.05).
RESULTS: The main abnormalities found were the appendices / pre-auricular pits and imperforate anus (both

observed in 83% of cases). The coloboma of iris, an important finding of the syndrome was observed in two cases (33%). Congenital heart disease, in turn, was observed in four patients (67%), with a primary defect in the atrial septal defect (75%). Unusual findings included microtia associated with hemifacial microsomia, as well as biliary atresia. Terms of clinical development, only one patient died, and this occurred secondary to a framework of chylothorax and sepsis.
CONCLUSION: The phenotype observed in cat eye syndrome is highly variable and may overlap that of the spectrum oculo-auriculo-vertebral. Although people usually make a good prognosis, including the neurological point of view, we believe that every patient with the syndrome should be evaluated early for the presence of cardiac malformations, biliary and anorectal. This would avoid possible complications, including death.

Keywords: Human Chromosome 22 pair. Mosaicism. Goldenhar syndrome. Facial asymmetry.

SUMMARY

OBJECTIVE: The cat eye syndrome is considered a rare chromosomal disease and a condition phenotypically quite variable. The Objective of this study was to describe the Clinical Characteristics of the sample with the syndrome of Patients Evaluated in Our Service.
METHODS: Six Patients with diagnosis of cat eye syndrome Were retrospectively evaluated. All Presented with the karyotype presence of an additional marker chromosome, inv dup (22) (pter-> q11.2:: q11.2-> pter). One of Them Had to still mosaicism with a lineage with a normal chromosomal constitution. Clinical and evolution Were Collected data from Their medical records. Fisher exact test (P <0.05) was used for comparison Between the frequencies found in Our study and literature.
RESULTS: The main abnormalities found Were preauricular skin tags / pits and imperforate anus (both Observed in 83% of cases). Iris coloboma, an important feature of the syndrome was verified in two cases (33%). Congenital heart defect Observed in Patients 4 (67%), atrial septal defect with the (75%) as the most Observed. Uncommon features included hemifacial microsomia Associated to the microtia, biliary atresia Besides. In relation to the evolution, only one of the Patients Died and this occurred secondary to sepsis and quilothorax.
CONCLUSION: The phenotype Observed in the cat eye syndrome is very variable and May Overlap With That of oculo-auriculo-vertebral spectrum. Despite the good prognosis Usually presented by the Individuals, also from the neurological point of view, we believe That All Patients With The Syndrome Should Be Evaluated for Possible early as the presence of heart, biliary and anorectal malformations. This Should Avoid Possible Complications, including death.

Key words: Chromosomes, human, pair 22. Mosaicism. Goldenhar syndrome. Facial asymmetry.

INTRODUCTION

The cat eye syndrome, also known as Schmid-Fraccaro syndrome (*OMIM* 115470), is considered a rare chromosomal disorder with an incidence estimated at 1 in 50,000 to 150,000 live births (Berends et al., 2001). It occurs due to a partial tetrasomy of chromosome 22, resulting in a dicentric supernumerary marker chromosome with satellites at their ends, inv dup (22) (pter-> q11.2:: q11.2-> pter). This, as its description says, involves a duplication of the entire short arm of chromosome 22 (p), and part of its long arm (q) until the band 11. Today we know that this band has several areas of repetitions of low copy number (*low copy repeats - CRLs*) that predisposes to the formation of rearrangements, including chromosome marker observed in cat eye syndrome (Heather et al., 2002). The disease is characterized clinically by the presence of multiple malformations, mainly affecting the eyes, ears, urogenital and anorectal region. However, a highly variable phenotype has been observed, including a description of mildly affected patients (Berends et al. 2001; Rosias et al., 2001).

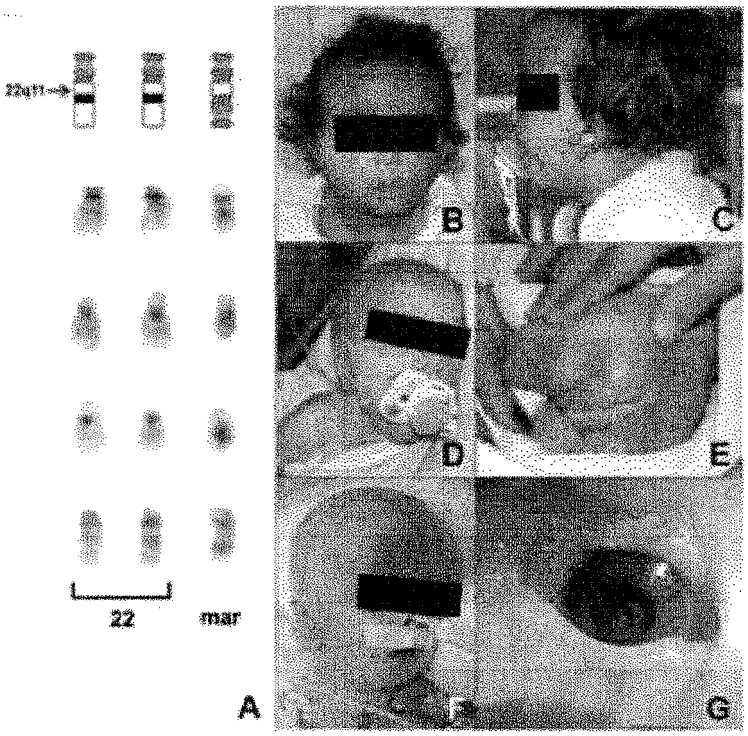
Thus, due to lack of related studies in our environment (Belangero et al., 2009), the objective was to describe the clinical characteristics of a sample of patients with cat eye syndrome evaluated at our institution.

METHODS

Retrospectively reviewed six patients diagnosed with cat eye syndrome, referred to the Department of Clinical Genetics for imperforate anus, pits and / or preauricular tags associated with other malformations. All patients had a karyotype with the presence of an additional marker chromosome, similar to dicentric chromosomes found in the partial tetrasomy 22: inv dup (22) (pter-> q11.2:: q11.2-> pter) (see Figure 1). One of them also had mosacismo with a strain with normal chromosome constitution: 47, XX, inv dup (22) (pter-> q11.2:: q11.2-> pter) [30] / 46, XX [14] . In three cases it was able to conduct the evaluation of the karyotype in a mother and

a father, and all of them the result was normal.

Figura 1 - Ideograma e cariótipo parcial por bandas GTG mostrando exemplos de cromossomos 22 citogeneticamente normais e de marcadores apresentados pelos pacientes. Notar que o ponto de quebra para a formação do cromossomo marcador ocorre na região 11 do braço longo (q) do cromossomo 22, levando a uma inversão duplicação do segmento pter->q11 (A). Características clínicas de alguns pacientes da amostra. Notar principalmente na microssomia hemifacial (B), apêndices e fossetas pré-auriculares (C, D e F), imperfuração anal (E), micrognatia (F) e coloboma de íris com epicanto (G) (B e C: paciente 2; D e E: paciente 3; F e G: paciente 5)



From the medical records data were collected regarding gender and age, that the service sent to Genetics, anthropometric measures and parental age at birth, clinical features observed on physical examination, results of exams, and deaths.

For comparison between the frequencies found in our study and the literature we used the Fisher exact test, from the PEPI program. Only P values <0.05 were considered statistically significant.

This study was approved by the Ethics Committee of the Institution.

RESULTS

Of the six patients who comprised the sample, four were female and two male. Their ages at the time of initial evaluation ranged from five days to two years and six months (mean 234 days), four of whom had been sent by the Pediatric Surgery, Pediatrics and one by one by the Pediatric Cardiology. The paternal age ranged from 36 to 50 years (mean 41.2 years), maternal and 31 to 39 years (mean 36 years). Birth weight ranged from 2178 to 3640 g (mean 2896 g), length 44 to 51.5 cm (mean 47.9 cm) and head circumference 32-36 cm (average 33.9 cm) .

The clinical features presented by patients are shown in Table 1 and Figure 1. The main abnormalities found were

the appendices / pre-auricular pits and imperforate anus (both observed in 83% of cases). The coloboma of iris, an important finding of the syndrome was observed in two cases (33%). Congenital heart disease, in turn, was observed in four patients (67%), and that the main defect was observed in atrial septal defect (75%). Terms of clinical development, only one patient died (patient 5). This was due to complications during the postoperative congenital heart disease with chylothorax and sepsis.

DISCUSSION

Despite the supernumerary marker chromosome derived from the 22 molecular size could vary according to the *CRLs* of the q11 region where the rearrangement occurred (more proximal or distal), there is, so far, a direct correlation between the phenotype displayed by patients with cat eye syndrome and the size of the region is in excess (Mears et al. 1994; Berends et al., 2001).

The phenotypes observed in our patients, despite the small size of our series were not different from those described previously in the literature. Although the syndrome is called the cat eye syndrome, due to the appearance of the iris coloboma iridocoroidal secondary to vertical (which resembles the iris of a cat), malformations that are associated with the disease most often are the appendices and / or pre pits earphones and anorectal malformations (Rosias et al., 2001). These were the main findings of our patients, both observed in 83% of cases. On the other hand, some of malformations have been rarely reported in the syndrome, such as biliary atresia. In the series of Rosias et al. (2001) was reported in four out of 48 evaluated cases (8%) with this abnormality.

We could not find descriptions in literature of another patient with the cat eye syndrome and hemifacial microsomia associated with unilateral microtia (patient 2). The sum of your findings, together with appendices / pre-auricular pits, strongly suggested the clinical spectrum of oculo-auriculo-vertebral (OAVS) or Goldenhar syndrome (*OMIM* 164210) (Strömland et al. 2007; Engyz et al., 2007). To our knowledge, this is the first reported case of a patient with cat eye syndrome and this phenotype. However, interestingly, we found the report in the literature of other patients with the phenotype of OAVS and chromosomal abnormalities with the addition of parts or the whole chromosome 22. These included trisomy 22 mosaicism (Pridjian et al., 1995), the supernumerary chromosome der (22) t (11; 22) (Engiz et al., 2007) and the duplication of the long arm of chromosome 22 (Hathout et al., 1998). Moreover, in some cases described by Berends et al. (2001) found the report of facial asymmetry / a hemifacial hypoplasia. However, we can not exclude the possibility that this finding may have an association with chromosome mosaicism presented by the patient, where areas of hyperplasia and hypoplasia may be present (Woods et al., 1994).

The frequency of cardiac defects observed in our sample (67%) when compared to other series described in the literature, was statistically similar to them, ranging from 50% to 63% (Berends et al. 2001; Rosias et al. 2001). However, as pointed out by well Rosias et al. (2001) and Berends et al. (2001), these frequencies are possibly subject to bias, since patients mildly affected may escape detection. The main cardiac defect described among individuals with cat eye syndrome is the total anomalous pulmonary venous drainage (29% to 43%), which was observed in only one patient in our sample (25% of cases with congenital heart disease). The most common malformation in our series, atrial septal defect (75%) has been described in approximately 30%, and patent ductus arteriosus in 14% of patients with the syndrome (Berends et al. 2001; Rosias et al. 2001). The persistent left superior vena cava, observed in one patient in our sample, is an uncommon finding (Berends et al., 2001). On the other hand, another common defect, but absent in our series, is the tetralogy of Fallot, which has been described in about 8% to 14% of cases (Berends et al. 2001; Rosias et al., 2001). Less common defects include aortic abnormalities (such as interrupted aortic arch), pulmonary stenosis, tricuspid atresia, a hypoplastic left heart syndrome, hypoplasia of the mitral valve, atrium or ventricle, and single ventricle (Berends et al. 2001; Rosias et al. 2001; Belangero et al., 2009).

Regarding neurological findings, structural changes in the central nervous system are infrequently found among individuals with cat eye syndrome. Examples include cerebral hypoplasia (as seen in patients 2 and 6) and cerebellar atrophy and micropoligiria (Berends et al. 2001; Rosias et al., 2001). Developmental delay has been described in about 50% of patients (Berends et al., 2001), and this was observed in three patients in our sample (60%). Mental development, in turn, varies from normal to severely affected (Berends et al. 2001; Rosias et al., 2001). In our sample, this aspect can not be adequately evaluated because all patients were still at a very early age.

Usually, individuals with cat eye syndrome have a good prognosis. Nevertheless, the main complications that may lead to death include the presence of heart failure, liver / biliary atresia, pneumonia and sepsis (Rosias et al., 2001), as observed in the only case in our sample.

CONCLUSION

The phenotype observed in cat eye syndrome is highly variable and may overlap with that of OAVS. Although people usually make a good prognosis, including the neurological point of view (mental deficit, when present, is usually mild to intermediate) (Berends et al., 2001), we believe that every patient with the syndrome should be evaluated for early presence of cardiac malformations, biliary and anorectal. Some may require intervention and treatment. This could prevent possible future complications, including death of patients.

Conflict of interest: no

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