CASE REPORT

Cat eye syndrome

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Accepted 16 April 2014

SUMMARY

A full-term female baby, a product of non-consanguineous marriage, was born at 37 weeks of gestation with a birth weight of 2.08 kg. Antenatal scan at 31 weeks revealed complex congenital heart disease with a hypoplastic right ventricle, pulmonary atresia and an intact septum. Immediately after birth, the infant was shifted to the nursery and was started on intravenous fluids and infusion prostaglandin E1 (Alprostadil). On examination, she had microcephaly, periorbital puffiness, a long philtrum, a broad nasal bridge and retrognathia, up slanting palpebral fissures, widely spaced nipples, a sacral dimple and right upper limb postaxial polydactyly. Postnatal echocardiography confirmed a large ostium secundum atrial septal defect with left to right shunt, right ventricle hypoplasia, pulmonary atresia with an intact septum and a large vertical patent ductus arteriosus. Ophthalmological examination showed a bilateral chorioretinal coloboma sparing disc and fovea. Karyotyping showed an extra small marker chromosome suggestive of the Cat eye syndrome.

BACKGROUND

The Cat eye syndrome (CES) associated with a partial tetrasomy of chromosome 22 is a rare genetic syndrome with a known incidence of 1 in 150 000 live births. This syndrome is known by other names which include chromosome 22 partial tetrasomy (22pter-22q11) or chromosome 22 Inv dup (22pter-22q11) or Schmid-Fraccaro syndrome (OMIM 115470) or chromosome 22 partial trisomy (22pter-22q11).¹ The syndrome was named 'Cat Eye' due to the typical ophthalmological finding of vertical colobomas in few patients. There are about 100 patients reported till now with CES in the literature. It is usually caused by a partial tetrasomy of chromosome 22 which is the result of a supernumerary dicentric marker chromosome with satellites at the ends, and inverse duplication of chromosome 22.² The classical triad consists of iris colobomas, anal malformations and ear anomalies.

CASE PRESENTATION

A full-term female baby at 37 weeks of gestation was born to a non-consanguineous couple (G3P2L2 mother) with a birth weight of 2.08 kg (<10 centile) through an elective Caesarean section. The baby cried immediately at birth and had an Appearance, Pulse, Grimace, Activity, Respiration (APGAR) score of 7/8/8 at 1, 5 and 10 min respectively. At birth, the infant's head circumference was 31 cm (<10 centile), the length was 39 cm (<10 centile) and had features of symmetrical intrauterine growth restriction. Antenatal

scan at 31 weeks revealed a complex congenital heart disease with a hypoplastic right ventricle, pulmonary atresia and an intact septum. There was no history of any teratogenic drug intake or medical disorders in the mother. The rest of the antenatal course was uneventful. Parents and elder siblings of the baby were normal with no malformations or congenital heart defects. The baby was shifted to the nursery and was started on intravenous fluids and infusion prostaglandin E1 (Alprostadil). The infant's oxygen saturation (SaO₂) of 87% in room air was maintained. The blood pressure at the time of admission was 54/25(34) mm Hg in the right upper limb with a heart rate of 120 bpm. On examination, the infant had microcephaly, periorbital puffiness, a long philtrum, a broad nasal bridge, retrognathia, upslanting palpebral fissures, widely spaced nipples, a sacral dimple and right upper limb postaxial polydactyly. On cardiac evaluation, she had a murmur which was continuous and more prominent at the base of the heart. Investigations performed on the infant showed a packed cell volume of 52.2%, a total leukocyte count (TLC) of 12 800/mm³ and platelets of 3.22 lakhs/mm³, serum sodium 141 meq/L, potassium 4.9 meq/L and calcium 8.7 mg/dL. Postnatal echocardiography confirmed a large ostium secundum atrial septal defect (ASD) with left to right shunt, right ventricle hypoplasia, pulmonary atresia with an intact septum and a large vertical patent ductus arteriosus (PDA). The baby was started on feeds at 22 h and fluids were stopped. Ophthalmological examination showed a bilateral chorioretinal coloboma sparing disc and fovea. She was continued on alprostadil infusion. The abdomen ultrasound, neurosonogram and infantogram were normal. The karyotype showed an extra small marker chromosome, suggestive of the diagnosis of CES (figure 1). Parents were explained about the need for further evaluation of the baby's genetic composition with fluorescence in situ hybridisation (FISH) or microarray techniques but they refused in view of financial constraints. The baby was shifted to the cardiac centre for management from where she was discharged and was kept in follow-up. The baby expired at home.

INVESTIGATIONS

Echocardiography showed a large ostium secundum ASD with left to right shunt, right ventricle hypoplasia, pulmonary atresia with an intact septum and a large vertical PDA.

The karyotype revealed 47,XX,+idic(22)(q11.2) or 47,XX,+idic(22)(pter->q11.2::q11.2->pter) suggestive of CES.

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To cite: Sharma D, Murki S, Pratap T, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-203923

Figure 1 Showing karyotype of baby which is 47,XX,+idic(22)(q11.2) or 47,XX,+idic(22)(pter→q11.2::q11.2→pter) suggestive of cat eye syndrome.

TREATMENT

Supportive care and correction of cardiac anomaly.

OUTCOME AND FOLLOW-UP

The baby was discharged from the hospital but the baby succumbed to death at home.

DISCUSSION

CES which is a partial tetrasomy of chromosome 22 is a rare genetic syndrome with a known incidence of around 1 in 150 000 live births. It is caused by a partial tetrasomy of chromosome 22 which is the result of a supernumerary dicentric marker chromosome with satellites at the ends, and inverse duplication of chromosome 22. The formation of the small extra Inv dup 22 chromosome is thought to be mediated by recombination between low copy repeats in meiosis.² The classical triad consists of iris colobomas, anal malformations and ear anomalies. This is found in around 41% of the affected neonates. The disease manifests with multiple malformations, primarily involving the eyes, ears, cardiac, anorectal and urogenital systems.³ In CES patients, the short arm (p) and a small portion of the long arm (q) of chromosome 22 (the critical region being 22pter-22q11.2) are present three (trisomy) or four (tetrasomy) times rather than twice in all cells of the body.^{3, 4} The proximal part of the long arm of chromosome 22 (22q11.2) is the critical area for chromosomal rearrangements and contains genes which are responsible for the cat eye and the Di-George syndrome.^{5, 6} The additional chromosome 22 usually arises spontaneously and in such cases karyotypic analysis of the parents is normal. Few cases can occur due to a balanced translocation in either of the parents and in such cases the recurrence rate is high. The malformations and abnormalities common to CES were first catalogued in 1898.⁷ The malformations involve all systems and predominantly include cardiovascular system (anomalous pulmonary venous return, the tetralogy of Fallot, the ventricular septal defect, the persistence of the left superior vena cava, the absence of the inferior vena cava, tricuspid atresia); eye anomalies (coloboma, hypertelorism, down slanting palpebral fissures); ear anomalies (preauricular skin tags or fistulae, prominent antihelices, hypoplastic ear lobes and atresia of auditory canals); nasal malformations (broad and depressed nasal bridge, minimal

epicanthal folds); gastrointestinal malformations (anorectal malformations) and urogenital malformations (kidney hypoplasia or aplasia, bladder fistula and hydronephrosis). The affected infants have mild-to-moderate mental retardation, abnormal neurodevelopmental outcomes with growth retardation. Schachenmann *et al*⁸ described this syndrome in association with a small marker chromosome in 1965. Mc Taggart *et al* have classified CES chromosomes on the basis of the location of the two breakpoints which are required to generate them:

1. *Smaller type 1*: chromosomes are symmetrical, with both breakpoints located within the proximal interval.
2. *Larger type 2*: they are of two subtypes
 - A. asymmetrical, with one breakpoint located in each of the two intervals;
 - B. symmetrical, with both breakpoints located in the distal interval.⁹

Confirmatory diagnosis is multimodal including chromosomal analysis, FISH testing, whole chromosome paint, array genomic hybridisation or the Multiplex Ligation-dependent Probe Amplification assay.¹⁰⁻¹² The index patient had many major features suggestive of CES. These patients usually have good prognosis, including good neurological outcomes (when mental deficiencies are present they are usually mild to moderate), but all patients with the syndrome should be assessed for the presence of cardiac, biliary and anorectal malformations.³

Learning points

- Cat eye syndrome (CES) is a rare syndrome in which newborns have varied presentation.
- Karyotyping is the gold standard for diagnosing these syndromes.
- Prognosis of these babies depends mainly on the associated malformations such as cardiac anomalies.
- Genetic counselling is essential in such families. Some cases of CES are not secondary to an idic (22) but rather to a familial translocation involving chromosome 22, in which case the recurrence rates may be higher. In such cases, the parental karyotyping should be performed.

Contributors DS wrote the primary manuscript. TP and MV analysed the manuscript and carried out the corrections. SM analysed the manuscript and carried out final corrections.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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