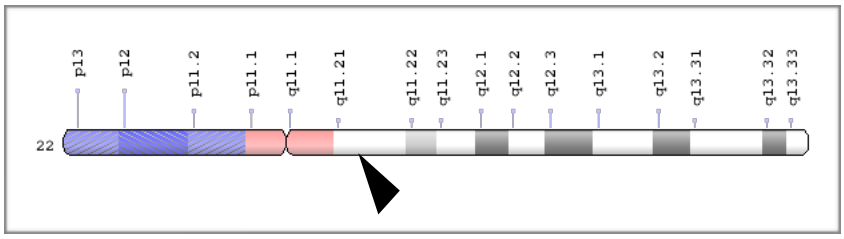
CAT EYE SYNDROME INFORMATION

Cat Eye Syndrome

In 1965 Schachenmann et al.[1] reported a small additional chromosome in several patients with combination of coloboma iris and anal atresia. Coloboma is a defect of the iris when the patient has a slit-like hole usually in its lower segment. Such defect may be similar to the appearance of a cat's eye. Several months before this publication Lejeune et al. published the article about another chromosomal disease, which they called "cat cry syndrome". Schmid and Fraccaro (co-authors in the original Schachemann's publication) coined the term "cat eye" syndrome for the disorder they described. Later it became clear that coloboma is neither obligatory nor the most frequent manifestation of the syndrome. However, the term "cat eye syndrome" still used for designation of this condition. Sometimes "Schmid-Fraccaro syndrome" may be used as a synonym.



Of course, in 1960s-1970s the nature of the additional chromosome could not be precisely identified, and several patients reported in this period may actually had other forms of chromosomal pathology. More sophisticated methods of cytogenetic examination which appeared in 1980s allowed to recognize that the additional chromosome in patients with this syndrome is an isochromosome of the proximal (near-centromeric) area of chromosome 22q [2]. [Isochromosome is a structure where the chromosome consists of two identical segments on both sides of the centromere]. As a result the patient has four copies of this segment (two from his/her normal chromosomes 22 and two from an additional isochromosome). The newest investigations showed that tetrasomy for the relatively small ~2 Mb segment of 22q11.21 is sufficient to produce the full clinical picture. The occurrence of an additional isochromosome 22q11.21 is an obligate condition for the diagnosis of the syndrome. If the person has this additional chromosome he/she should be qualified

as “cat eye syndrome” patient independently of the presence or absence of main clinical manifestations.

Cat eye syndrome is a relatively rare condition, it occur less than 1:50,000 births. For 40 years after first publications where nature of the additional chromosome was precisely determined there are 115 observations available for the detailed clinical analysis.

Coloboma is frequent but not constant manifestation of the syndrome. It was found in 43 out of 115 patients (~37%). Coloboma iris is the most common. Sometimes the patients have also colobomas of the choroid, retina or optic nerve. Of course ophthalmological examination is necessary to recognize these forms of colobomas. There are 5 reports of microphthalmia (small size of the eyeball). At least 4 patients had Duane retraction syndrome (form of strabismus caused by abnormal development of the n. abducens (VI cranial nerve)). Other eye defects are not characteristic.

Second cornerstone manifestation is anal atresia. It was found in ~60% of reported patients (66/115). This abnormality has to be treated by surgery. Other defects of gastro-intestinal system are relatively uncommon, although biliary atresia and Hirschsprung’s diseased were diagnosed 5 times, each.

Defects of the external ear are the third group of main manifestations. Usually the patients have preauricular tags or preauricular pits. It is the most frequent abnormality found in 86/115 (~ 75%) of patients. More serious defects – atresia of the external auditory canal or even aplasia of the ear were reported in several cases. Hearing impairment is common for the persons with atresia of auditory canals but not typical in most other patients.

Heart defects were not considered as main manifestation of the syndrome. However more than half patients (60/115) has different forms of heart defects. Surprisingly one relatively rare form of heart defect – total anomalous pulmonary veins return (TAPVR) – is very common for cat eye syndrome patients. In normal conditions four pulmonary veins (two from each lung) take blood from lungs to the heart. These veins bring oxygenated blood to the left atrium. In persons with TAPVR these veins bring blood to other parts of the heart. As a result the organs may receive insufficient amount of oxygenated blood. TAPVR was found in 22 patients with cat eye syndrome. Almost 40% of patients with heart defects have TAPVR. Some scientists[3] consider this defect as the hallmark of this syndrome. Surgical correction of this defect may be necessary. At least 6 patients with cat eye syndrome had interrupted aortic arch – very rare form of heart defect causing serious hemodynamic problems[4].

Many patients with cat eye syndrome have abnormalities of the kidneys (30/115). Sometimes it is very serious defect, including absence of one kidney or cystic dysplasia leading to kidney failure. Vaginal atresia and aplasia of uterus were diagnosed in four female patients with this syndrome. Actually this defect may be

more common because clinical manifestations of these abnormalities occur only at puberty, and prepubertal girls usually are not examined regarding these organs. Developmental defects of the kidneys and agenesis of Müllerian structures (uterus and vagina) are closely related, and this association is frequent in Mayer-Rokitansky-Küster-Hauser syndrome.

There are 6 reports of cleft palate. At least 3 patients had polydactyly. There are numerous sporadic reports of other defects – cerebellar hypoplasia, absent thymus, diaphragmatic hernia, branchial cyst, a- or polysplenia, etc. It is unclear however whether these defects are rare components of the syndrome or just random associations. And of course patients with unusual manifestations may be preferentially reported.

Typically patients with cat eye syndrome reveal mild intellectual disability, although some patients may be intellectually normal whereas other may be significantly impaired. Defects of the brain are not characteristic. Several patients with this syndrome had seizures, which may be drug resistant.

Except rare severe heart defects and dysplastic kidneys most abnormalities in persons with cat eye syndrome are not life-threatening. Therefore vital prognosis is relatively good. There are many reports of adults with this condition.

Adults with cat eye syndrome are fertile and they may have their own children. There are several familial cases of the syndrome with direct intergenerational transmission of the marker chromosome. Of course, most patients having their own children are only mildly affected, although their children may have full picture of the syndrome.

In most cases marker chromosomes are sporadic events. For such families risk of recurrent birth of the affected child is close to zero. However parental examination should be recommended because occasionally manifestations of the syndrome are very mild. Adult with an additional isochromosome 22q11.21 has a 50% risk of transmission of the abnormal chromosome to the next generation.

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