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RECONSIDERATION OF THE CAT EYE SYNDROME: RECIPROCAL TRANSLOCATION T(11,22) LEADING TO PARTIAL TRISOMY OF 11q AND 22.

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ABSTRACT

We are reporting a case of 47 chromosome complement with an extra rearranged chromosome 22pter → 22q11::11q23 → 11qter in a child with multiple malformations whose mother has a balanced reciprocal translocation t(11,22) with a history of two previous abortions. We emphasize the importance of family study in such cases.

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INTRODUCTION

Cat eye syndrome was the name given to children with multiple congenital anomalies and a small supernumerary chromosome.[6,9] Extensive use of banding techniques has revealed that nearly all cases are in fact a partial trisomy of chromosomes 11 and 22, the result of a 3:1 malsegregation of a balanced parental reciprocal translocation.[1,2,5,8]

CASE REPORT

The patient was born to an unrelated couple, married for 13 years with history of 2 abortions at 1 and 2 months respectively. The two subsequent pregnancies resulted in an apparently healthy boy and the index case. The 4th pregnancy was uneventful and ended in a cesarian section because of placenta praevia at 9 months. Brith weight was 3.0 kg. Exchange transfusion was performed on the 4th day. (serum bilirubin 19.5 mg/100 ml). At examination, the child, a 7 month old female had a head circumference of 39.5 cm (below the 10th percentile) with mild cleft palate, preauricular fistula and peculiar facies (Fig. 1) The child was reported to have ASD, VSD, proximal pulmonary stenosis and right ventricular hypertrophy. The child died of respiratory infection at 23 months of age. Chromosomal study of the child revealed 47, XX + M. chromosome resembling chromosome 22, yet shorter. Chromosomal studies of parents and sib were performed. Karyotype of the father was normal (46, XX), that of mother and brother revealed 46, XX, t(11;22), (11pter → 11q23: : 22q11 → 22qter;22pter →q11: : 11q23 → 11qter), and 46, XX with the same balanced reciprocal 11,22 translocation, respectively. Therefore, it was concluded that the marker chromosome was 22pter → 22q11: : 11q23 → 11qter inherited from the mother (Fig. 2).

DISCUSSION

The cat eye syndrome is the name given to cases reported of patients with some of the following features:[6,9] moderate mental retardation, congenital malformations such as anal atresia, ocular coloboma, palpebral fissures slanting downward and outward, low set ears, mild hypertelorism, epicanthal fold, nystagmus or strabismus, congenital heart defects, microph-

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This case has been presented at the 21st Symposium of the European Society of Human Genetics, May 11-13, 1989, Groningen, the Netherlands.

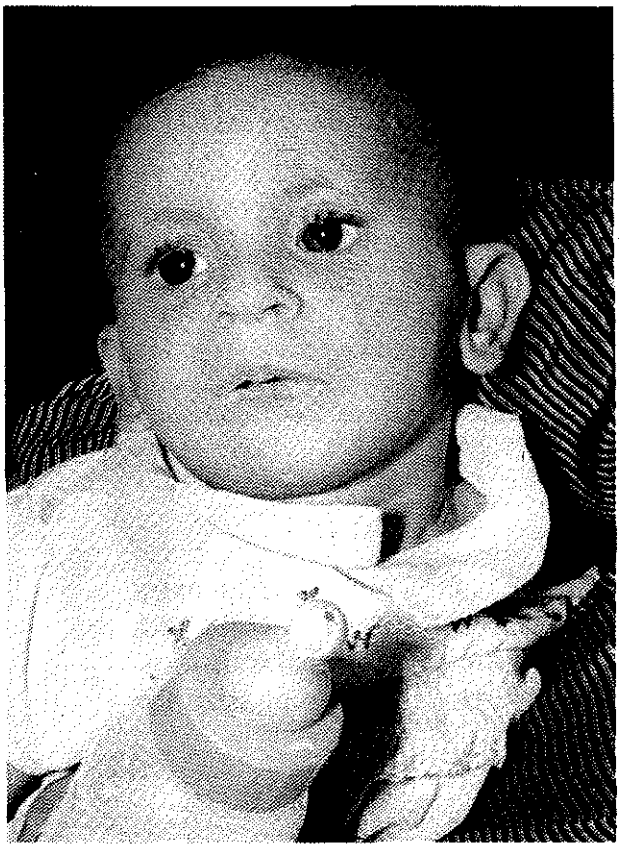


Fig. 1, A. The chubby face and malformed low set ears are evident.

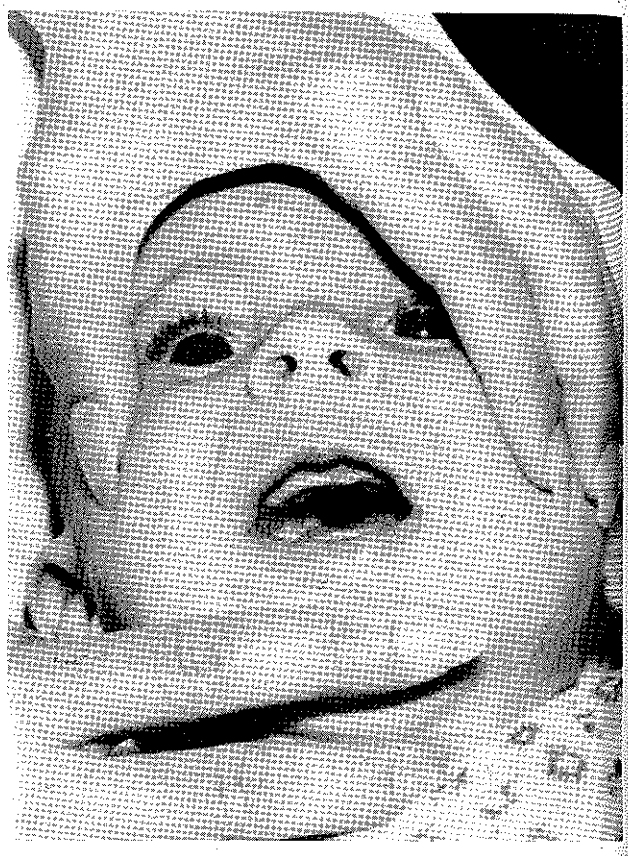


Fig. 1, B. Cleft palate is noticeable.

thalmia, pretragian tags and/or pits, anomalies of the urinary tract, and of the skeleton.

Few of the sixty reported cases of cat eye syndrome have the complete syndrome.[6,7,9] Their karyotypes reveal a supernumerary chromosome that varies in size from a small metacentric chromosome to a G-like chromosome thought to be a chromosome 22, In 5/6 of the reports the supernumerary chromosome is smaller than chromosome 22 and is designated as a non-21 G-chromosome.[7]

In 1972, Buhler, et. al.[4] reported the first observation of a familial translocation between chromosomes11 and chromosome 22,leading to a shorter chromosome 22, and suggested that the supernumerary chromosome in the cat eye syndrome was a 22 q-. Aurias in 1975 reported the first reciprocal parental t(11;22) leading to an offspring bearing a karyotype with the extra small acrocentric chromosome.[1] Since then, approximately 51 more cases of such parental t(11;22) have been reported.[2,5] In the parent, the chromosome is the product of a reciprocal translocation between chromosomes 11 and 22 wherein the terminal segment of the long arm of chromosome 22 is exchanged for a slightly shorter terminal segment from chromosome 11, resulting in a slightly shorter chromosome 22 and a longer chromosome 11 (Fig. 3). Therefore, the parent is a carrier of a balanced reciprocal translocation.[8,11] Because of the rearrangements within these chromosomes, a 3:1 malsegregation may occur at nuclear division resulting in an abnormal gamete with the extra rearranged chromosome.[10]

From 51 reported cases, three have inherited from the father and the remainder from mother with no incidence of nonfamilial or *de novo* translocation.[2,5] According to the literature, the low incidence of father-to-offspring inheritance is due to a decrease in fertility in the male. However, the frequency of abortion is high regardless of the sex of the carrier (35.5% ± 5.0).[2,5,6] The frequency of recurrence is estimated between 2%-6% and 2%-4% for female and male translocation carriers respectively,[5] although data for males are inconclusive due to the few number of cases reported. The features noted in children with the rearranged chromosome (22pter → 2211::11q23 → 11qter) in an unbalanced karyotype are as follows: microcephaly, wide face with chubby cheeks, short, broad, flat nose, a long prominent philtrum, retraction of the lower lip, microretrognathia, high arched palate or cleft palate, glossoptosia, low set deformed ears with blind pits, preauricular tag, hypoplastic genitalia in the male and or cryptorchidism.

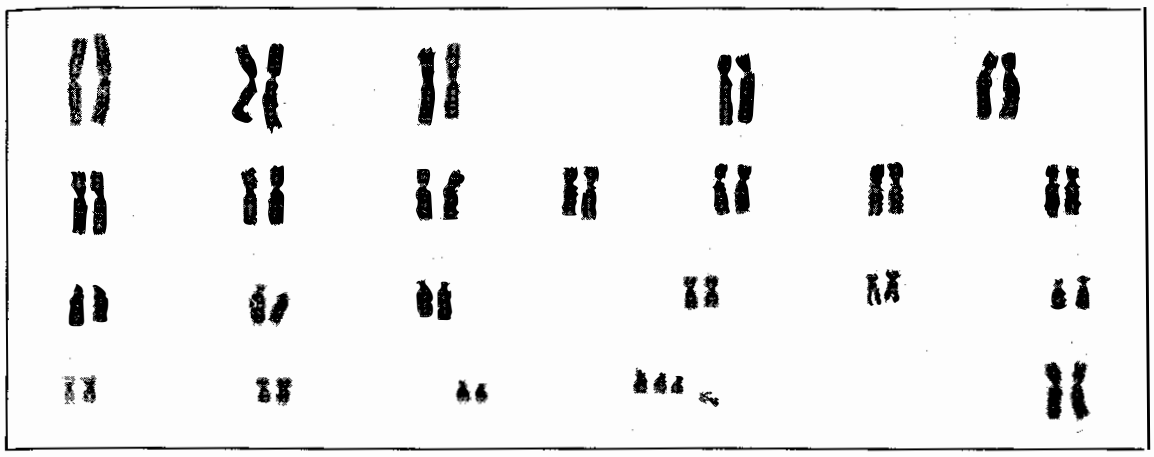


Fig. 2, A. Karyotype of child showing the supernumerary chromosome in the 22 group (arrow).

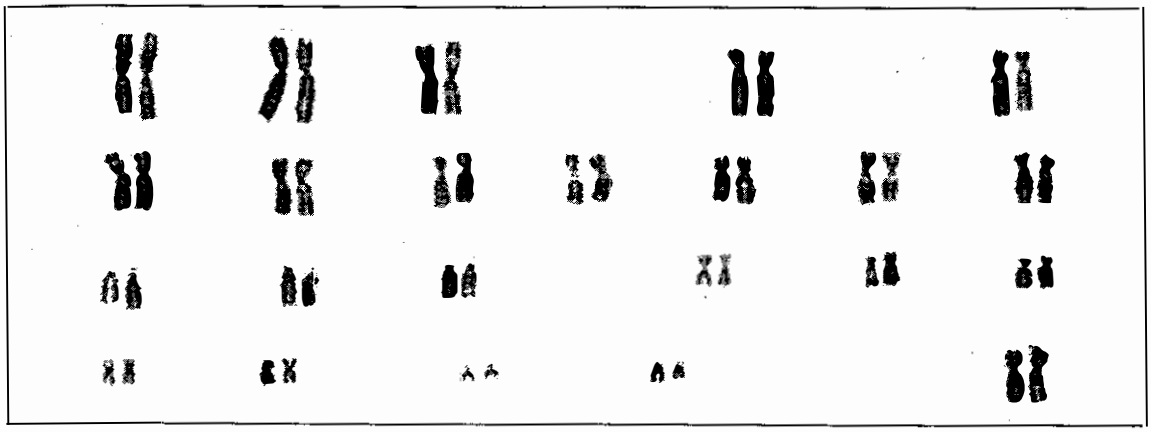
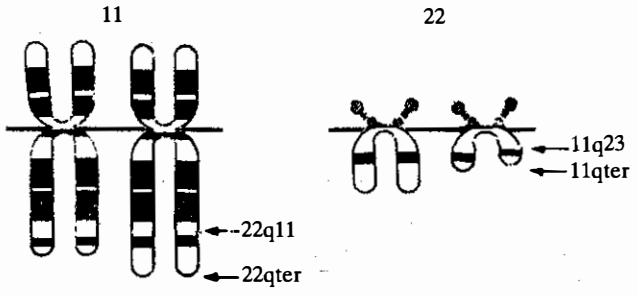


Fig. 2, B. Karyotype of the mother with balanced translocation (11;22). Arrows indicate chromosomes 11 and 22, one which is slightly longer and the latter which is slightly shorter than its homologue.

The most common malformations are complex heart defects, renal anomalies, and hip dislocation, and less frequently, malrotation of the intestine, uterine anomalies, diaphragm hypoplasia, and atresia of the collar bone. These children are usually hypotonic and have severe psychomotor and growth retardation.[1,2,5-10] These features are similar to the findings in children with trisomy 11q2. Presumably associated with the small segment that is chromosome 22, are the following features: anal anomalies, auricular maldevelopment, and palpebral fissures slanted downward and outward.[2] Whether complete trisomy 22 as such exists is at present debatable. There has not been a trisomic 22 child born to parent who is carrier of a balanced Robertsonian translocation involving chromosomes 22. All offsprings from the carrier of a balanced translocation t(22,22) are aborted in very early stages of gestation. According to Boue, et. al. trisomy 22 is frequent in spontaneous abortion.[3] Since using modern banding techniques, no further reports of trisomy 22 have been made and all cases considered to have the cat eye syndrome are ascertained to be trisomic for 11q.

The case we report is typical of the process of understanding the etiology of these cases. When first



Reciprocal Translocation
Between Chromosomes 11 and 22

Fig. 3. Schematic representation of the exchange between chromosomes 11 and 22 and the resultant chromosomes with the balanced translocation.

presented with the child and upon examination, we considered the cat eye syndrome as a likely diagnosis and cytogenetic findings seemed to confirm this, although the smaller size of the chromosome we assumed to be chromosome 22, led us to study the karyotypes of the entire family. As we were able to detect the translocation in the mother, we could identify more accurately the supernumerary chromosome of the child and recognize the child's symptoms as those of partial trisomy 11q and 22q.

As this translocation is the most common reciprocal translocation in human beings leading to live abnormal offspring, we would like to emphasize the importance of familial study in its detection.

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Addendum

While the article was under print, 2 recent reports of complete trisomy 22 in liveborn infants who died perinatally was published.

These are the only two reports of trisomy 22 employing high-resolution banding and therefore certain as to the trisomy. This indicates the presence of trisomy 22 in live births but once again emphasizes the importance of chromosomal study in distinguishing between trisomy 22 and the partial trisomy 11;22.

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