Case Report

Trisomy 8p (p11.2-pter) due to maternal translocation t(8;13)(p11;p12) in a child with dysmorphic features

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Here we present a phenotypic description of a male child with trisomy 8p resulting from a maternal balanced reciprocal translocation. The patient presented with dysmorphic face, aplasia of the corpus callosum, and atrophy of cortex, congenital heart defect and marked hypotonia. The father had a normal karyotype. The mother had an apparently balanced translocation involving chromosomes 8 and 13 [46, XX, t(8;13)(p11.2;p12)]. The karyotype of the child was ascertained as 46, XY, der(13)t(8;13)(p11.2;p12).
This is the second reported case of trisomy 8p resulting from a translocation between chromosomes 8 and 13. The chromosomal breakpoints in the two cases differed.

Key words: Cardiac defect; developmental delay; translocation; trisomy 8p.

Trisomy of the short arm of chromosome 8, *de novo* or inherited from a parent carrying a translocation, is associated with craniofacial defects (high forehead, frontal or parietal bossing, carp mouth, full cheeks, and round face), brevicollis with redundant skin folds, mental retardation, absence of the corpus callosum, multiple minor skeletal abnormalities, and other abnormalities.[1] Here we are reporting a new case of trisomy 8p, due to maternal balanced translocation.

Case report

A 3-month-old male child born to non-consanguineous parents referred for cytogenetic analysis because of dysmorphic features. The father was 32 years old and the mother was 24 *at the time of the baby's birth. The mother had two spontaneous miscarriages (at 8 and 12 weeks of gestation). The child was born at term by cesarean. His birth weight was 2800 g and his length was 48 cm. During examination multiple physical deformities were detected. He had large an asymmetric face with full cheeks with partial bossing, temporal retraction, microretrognathia, and chin dimple. The earlobes were slightly simple and large. The eyes were strabismus with very unusual long eyelashes. The nose had everted nostrils with long philtrum. He had a wide mouth with a thin upper lip and an everted lower lips, a highly arched cleft palate, and bifid uvula. X-ray radiography could not detect any abnormal or supernumerary ribs, but the baby had funnel chest.

Proximal thumb placement was seen in both hands. Hypoplastic toenails were noticeable. Skin laxity was obvious. Brain CT scan detected aplasia of the corpus callosum and atrophy of cortex. Echocardiography indicated dilation of the aorta and of the right and left coronary arteries at their origins. Bilateral inguinal hernia was noted. MK had a long and slim trunk* and elongated limbs. The baby was admitted to hospitals several times due to infection and seizure.

At 13 months of age, he is unable to sit without help, cannot talk and has feeding problem. His health conditions have improved with passage of time. He doesn't suffer from infections as much as he used to,

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and after stopped medication for 6 months, no signs of seizure have been seen. [Figure 1] shows the baby at 13 months of age.

Cytogenetic study

The karyotype was done on peripheral white blood cells. The karyotype showed an additional chromosomal fragment on chromosome 13p [Figure 2]. Parental chromosomal analysis was done. The father had a normal karyotype. The mother had an apparently balanced translocation between chromosomes 8 and 13 [Figure 3]. Therefore, the karyotype of the mother was ascertained as 46,XX,rcp t(8;13)(p11.2;p12) and the karyotype of the child identified as

46,XY,der(13), t(8;13)(p11.2;p12).

Discussion

In this report we presented a malformed male newborn with trisomy 8p who unbalanced karyotype was due to a maternal 8p/13p translocation 46,XX,rcp t(8;13)(p11.2;p12). This translocation has been reported once before by Brocker-Vriends et al.[2] but with different breakpoints. Multiple patients with duplication and trisomy of 8p have been reported.[3–7] Many of the previously reported clinical finding were similar. However, the clinical significance of trisomy 8p remains controversial because of the effect of the partial monosomy that may accompany on the partner chromosome. The patients studied by Feldman and his colleagues[3] were all hypotonic at birth, and had feeding difficulties in the neonatal period with significant developmental delay. In some of those patients, prominent forehead, high arched palate, large mouth with a thin upper lip, malformed and/or apparently low-set ears, broad nasal bridge, dental and skeletal abnormalities, and joint laxity were noted. de Die-Smulders et al.[4] reported on five children and two adults with duplication of 8p. They found that minor facial anomalies, hypotonia, and severe developmental delay were noticeable in the children, while in older patients the facial traits were less characteristic. It has to be emphasized that in all patients they examined, the duplication was accompanied by a deletion of the most terminal part of 8p.

It seems that a severe abnormal phenotypes appeares when the duplication involves a longer, more proximal segment. For example Guo et al.[5] reported on the clinical and cytogenetic findings of cases carrying an inverted duplication of region 8p11.2p23. Ther phenotypes included severe mental retardation (in 100% of cases), minor facial alterations (in 97% of cases),

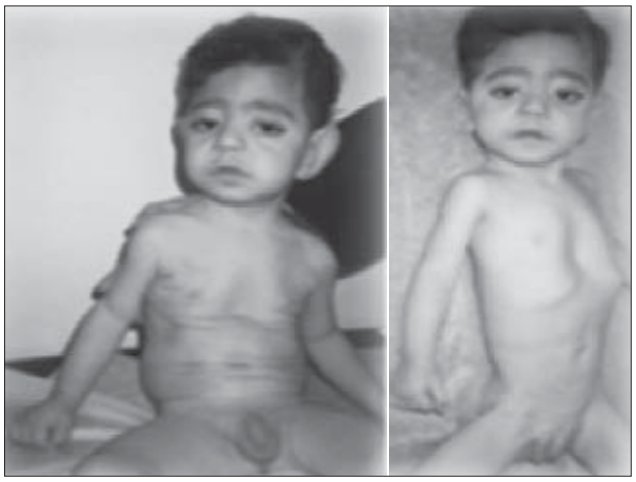

Figure 1: Photographs showing the proband at 13 months of age

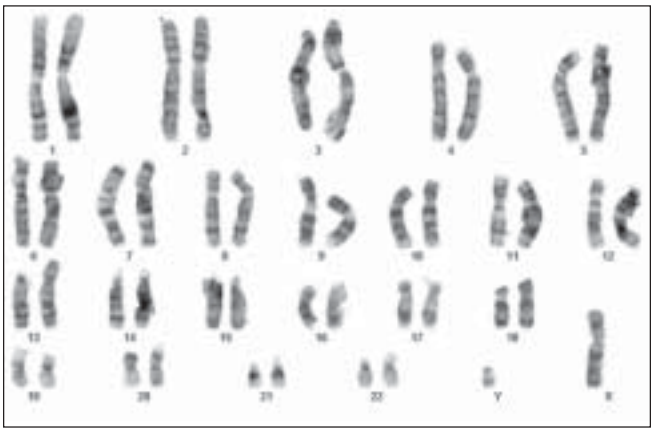

Figure 2: The karyotype of the patient

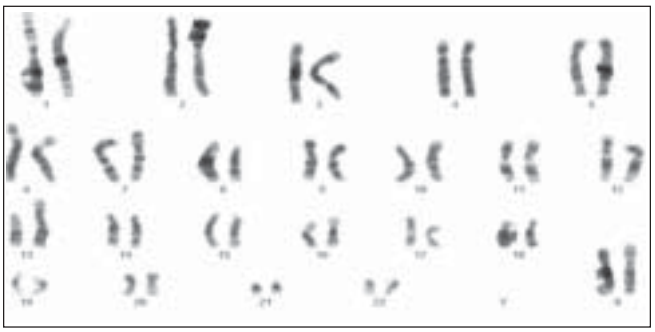

Figure 3: The karyotype of the mother

agenesis of the corpus callosum (in 80% of cases), hypotonia (in 66% of cases), orthopedic abnormalities (in 58% of cases), scoliosis/kyphosis (in 40% of cases) and congenital heart defect (in 26% of cases). But patients with trisomy 8p22pter had only a mild clinical presentation, consisting mainly of learning disability.[6]

Of course, it needs to be noted that in some cases, a single phenotype results in different phenotypes, as reported by Plomp et al.[7] There are several reported cases of trismy 8p findings during prenatal diagnosis. For example Chiyo et al.[8] reported on a prenatal investigation on a fetus who was the brother of a 2-year-old boy trisomic for 8p. The 2-year old boy was severely mentally retarded and had multiple minor anomalies. The prenatal study on the fetus was showed him to carry the same 8p trisomy as his brother. The pregnancy was terminated in the 22nd eek; however, the autopsy revealed no major anomalies. On the other hand, Pezzolo et al.[9] described a female fetus in which prenatal diagnosis of 8p trisomy was established after amniocentesis at 16 weeks of gestation. Several malformations including an anomalous lobature of the right lung, a little and high atrio-ventricular communication, and an anomaly in the number and shape of the aortic semilunar valves were found in the fetus. Several studies have shown that the 8p23 band contains a gene or genes critical for normal cardiac development and function.[8] Features of the patient presented here are consistent with results of studies, which indicate the presence of genes for normal cardiac development on 8p. Agenesis of the corpus, a previously reported feature of trisomy 8 syndrome, was also found in our patient. A review of published reports indicates that this defect might be the result of duplication of a gene located within 8p21-pter.[1]

In summary, in this patient with a trisomy of 8p, clinical findings characteristic of a duplication of 8p were present, including facial features and development delay. The manifestations in this patient were very severe with major internal organ malformations (such as congenital heart defects). These findings, together with previously reported cases carrying trisomy/duplication of 8p define a syndrome that suggests the existence of genes on the 8p region specially important for the development of brain and heart. Inv dup(8p) causes a distinct phenotype, whereas the phenotype of trisomy 8p due to translocation is much more variable, probably because of the accompanying monosomies. By studying additional individuals with this condition, trisomy 8p may emerge as a more recognizable clinical phenotype.

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