A CASE OF 18q-DELETION WITH BALANCED TRANSLOCATION
\textit{t(15;18)(p13;q21.3)} IN THE MOTHER

CHANDEL, D.

Division of Human Genetics, Department of Zoology, Gujarat University, Ahmedabad - 380 009, India.
E mail: divya_chandel@yahoo.com

Received: June 27, 2007; Accepted: September 5, 2007

Abstract: The 18q deletion syndrome can be caused by several terminal and interstitial deletions of which terminal deletions of the distal part of 18q are known as the De Grouchy syndrome. A female infant with distal 18q deletion confirmed by G-banding is reported, who was referred for delayed development. Subsequent karyotyping in parents revealed that the deletion was inherited from the mother who carried a balanced reciprocal translocation between chromosome 15 and 18 - 46,XX,t(15;18)(p13;q21.3).

Key words: 18q deletion, Reciprocal translocation, \textit{t(15;18)}.

INTRODUCTION

Change in genetic dosage of one or more genes is one of the most common causes of mental retardation. Examples of known important loci include the subtelomeric regions and the areas involved in microdeletion syndromes. The cause for mental retardation is established only in approximately 50\% of cases, limiting the efficiency of genetic counseling, detection of carriers, and prenatal diagnosis in these families.

18q- syndrome is a partial aneuploidy syndrome caused by the deletion of part of the long arm of chromosome 18 with an estimated prevalence of about 1 in 40,000 live births [1]. Typically patients with this syndrome exhibit decreased growth, characteristic facial dysmorphologies, extremity abnormalities, hearing loss, developmental delay and mental retardation. However, the clinical presentation of this syndrome is extremely variable and many of the patients exhibit only a small number of the features associated with the syndrome.

MATERIALS AND METHODS

The child was referred at 10 months for chromosome analysis as a case of delayed development. The proband was born full term by breech delivery to non consanguineous parents aged 35 years and 30 years. The proband was given oxygen after birth. There was no family history of spontaneous abortions, mental retardation or any other congenital anomaly.

The milestones of the proband were delayed with head holding at 5 months and no turning over or sitting at 10 months. She had low birth weight (2.0kg) and reportedly poor weight gain. Physical examination revealed height as 64 cms, weight as 4.5 kg and head circumference as 38 cms. The child had microcephaly, hypotonia, lowset ears, high arched palate and umbilical hernia. Since birth the child had a history of recurrent infections, with frequent cold, cough, constant temperature and frequent vomiting.

The proband was examined by a consultant physician. Clinical features and detailed family history was recorded in a proforma. 2-3 ml of intravenous blood was collected in heparinized syringes from the proband and her parents for karyotyping. Peripheral Blood Lymphocyte Cultures were set up in duplicate in RPMI 1640 medium (Hi-media, India) and harvested at 72 h, after which the slides were
Fig. 1: Metaphase preparations from Peripheral Blood Lymphocyte Cultures of the proband and mother showing:

a. G-banded partial karyotype of proband with two normal chromosomes 15 and normal and deleted (right) chromosomes 18.
b. Maternal chromosomes – normal 15 and t(15;18)(p13;q21.3) and normal and deleted 18.
c. Silver nitrate stained preparations showing NOR activity in the deleted chromosome 18 and its involvement in acrocentric chromosome associations.

Fig. 2: Partial ideogram showing breakpoints on chromosome 15(p13) and chromosome 18(q21.3). The bands distal to these points are exchanged in the reciprocal translocation.
prepared as per the routine protocol [2]. Routine GTG banding was performed on the slides for chromosome analysis [3].

Silver nitrate staining [4] was performed in the mother and the proband to ascertain the breakpoint in 15p. Metaphases were studied under oil immersion lens (100X) of Nikon microscope. For each sample 100 metaphases were scored according to ISCN guidelines [5].

**RESULTS**

Chromosome analysis of the proband revealed partial deletion of 18q and was interpreted as 46,XX,del(18)(q21.3). Subsequent chromosome analysis carried out in the parents showed that the abnormal chromosome was maternal in origin. The mother carried a balanced reciprocal translocation 46,XX,t(15;18)(p13;q21.3) interpreted as:

\[46,XX,t(15;18)(18qter \rightarrow 18q21.3::15p13 \rightarrow 15qter;18pter \rightarrow 18q21.3::15p13 \rightarrow 5pter)\]

Silver nitrate staining in the cultures of mother showed NOR activity in both the chromosomes involved in translocation, although greater activity was observed on the 18q arm than on the 15p, indicating that a large part of NOR was translocated to the chromosome 18. The chromosome constitution of father was normal (46,XY), while the chromosome analysis in the phenotypically normal sister of proband could not be carried out.

Subsequently, silver nitrate staining revealed that the derived 18q- chromosome in the proband also had NOR activity. Thus, the chromosome constitution of the proband was interpreted as:

\[46,XX,der(18pter \rightarrow 18q21.3::15p13 \rightarrow 15pter).\]

Figure 1a and b show partial karyotypes representing chromosome 15 and 18 in the proband and mother respectively. The silver nitrate preparations showing NOR activity and satellite associations in the terminal region of 18q is given in figure 1c.

**DISCUSSION**

Reciprocal translocation is one of the most common chromosome abnormality, being found in one in 500 people [6]. Such translocations have no phenotypic effect in most carriers, but have an increased risk of an unbalanced progeny due to imbalances and delays in meiosis [7]. Typically the imbalance in progeny is due to partial trisomy and partial monosomy in regions that are involved in reciprocal translocation. This is also observed for the present case, where the child has a deletion 18 because of balanced reciprocal translocation (15;18)(p13;q21.3) in the mother.

Partial deletion of the long arm of chromosome 18 was first described by de Grouchy et al. in 1964 [8]. More than 80 cases are on record [9]. It is responsible for a distinctive syndrome of facial dysmorphism and mental retardation. Some of the other common features are hypotonia, ‘carp shaped’ mouth and some ocular anomalies. Majority of the patients have IQ between 30 and 50. Reproduction in these patients is possible and Subrt and Pokorny [10] have reported a female patient with six pregnancies.

In the present case as the family history was otherwise negative for spontaneous abortions, mental retardation or congenital anomalies, the balanced translocation is thought to have occurred de novo in the mother. Her parents and sibs were not available for confirmation. Though cytogentic analysis could not be carried out in the proband’s sister, her normal intelligence and phenotype suggests that either she has a normal chromosome complement or she has inherited the balanced rearrangement of her mother.

To our knowledge, no translocation with such breakpoints [(15;18)(p13;q21.3)] has been described previously. The abnormal karyotype of the proband 46,XX,der(18pter \rightarrow 18q21.3::15p13 \rightarrow 15pter) is due to the balanced rearrangement in the mother. The risk of further such aneusomic births and miscarriages is high due to large segments of duplication/deletion caused by unequal segregation. It can be concluded that the couple has an increased risk of progeny with an unbalanced karyotype, as both partial trisomies and monosomies of 18q are probable. The proband showed severe abnormalities. Hence, prenatal diagnosis should be performed and genetic counseling offered in case of a future pregnancy.

**ACKNOWLEDGEMENTS**

This paper is dedicated to late Prof. N.J. Chinoy. Author is also grateful to the Council for Scientific and Industrial Research, New Delhi for financial grant.
REFERENCES