A FAMILIAL TRANSMISSION OF HETEROZYGOUS NO. 17 CHROMOSOMES IN RELATION TO SPONTANEOUS ABORTION 1)

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Received July 29, 1968

Recent human cytogenetics have indicated that certain chromosome abnormalities are important factors as a cause of spontaneous abortions, because of high incidence of chromosomal abnormalities occurring in spontaneously aborted conceptuses (Geneva conference 1966, Carr 1967). Further, evidence has been provided that some parental chromosome abnormalities may play a significant role in etiology of recurrent abortions (refer to Makino et al. 1965, Ikeuchi 1966, Inhorn 1966).

In the course of a chromosomal survey having been made on spontaneous abortions in the Makino Laboratory, a chromosome abnormality showing a heterozygous pair of no. 17 chromosomes was detected in an abortus and its mother. We undertook a familial survey of this chromosome abnormality with particular concern to the transmission pattern of the abnormal chromosome, its possible origin, and genetic significance.

CASE REPORTS

The pedigree of the family involving the carriers of the abnormal chromosome is presented in Figure 1. The members of the family were all mentally and physically normal in clinical examination. Five members of them and an abortus from the propositus were studied chromosomally. The propositus is a healthy woman aged 28 years. Her first pregnancy was terminated by spontaneous abortion 11 weeks after the last menstrual period. The aborted specimen consisted of small pieces of the chorionic membrane involving normal villi without any fragments of fetal tissues. The specimen was scanned for chromosome abnormality. Afterwards, she had again a spontaneous abortion, but no chromosomal study was made on the conceptuses. Except one each record of spontaneous abortion in two aunts, there was in this family no member who cast a spontaneous abortion.

Dermatoglyphic studies in the propositus’ mother, brother and sister revealed in them no significant departure from normal.

CYTOLOGICAL FINDINGS

The chromosomes of an aborted specimen from the propositus was studied with

1) Contribution No. 819 from the Zoological Institute, Faculty of Science, Hokkaido University, Sapporo, Japan.
cultured cells of the chorion without decidual cells (Makino et al. 1967). Chromosomes of five members of the family were studied exclusively on the leucocyte cultures in combination with the air-drying method.

The results of chromosomal observations in 7 members of the family including an abortus are given in Table 1. All the cases studied showed a normal diploid number of 46. Karyotype analyses revealed the occurrence of an extra small metacentrics in group 19-20 with the absence of an element in group 17-18 in the propositus, her abortus and mother. The remaining chromosomes showed no morphological abnormality within the scope of this study. The karyotype of the propositus is shown in Figure 2 as example. Further, some excellent metaphases showed that one of 5 small metacentrics had a centromere located less medially than the remaining elements, and that its short arm was similar in size to that of no. 17 chromosomes rather than that of no. 18 chromosomes (Figs. 3-8). Evidently one of the no. 17 chromosomes is thus affected.

Table 1. Results of chromosome studies in 6 members, including an abortus, of the family under study

<table>
<thead>
<tr>
<th>Case (age)</th>
<th>Chromosome counts</th>
<th>No. of cells obs.</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propositus (28 yrs.)</td>
<td>1 4* 44 —</td>
<td>49</td>
<td>46, XX; heterozygosity of no. 17</td>
</tr>
<tr>
<td>Husband (27 yrs.)</td>
<td>— — 15 —</td>
<td>15</td>
<td>46, XY</td>
</tr>
<tr>
<td>Abortus (11 wks.*)</td>
<td>3* 1 18 1</td>
<td>23</td>
<td>46, XX; heterozygosity of no. 17</td>
</tr>
<tr>
<td>Mother (51 yrs.)</td>
<td>— — 20 —</td>
<td>20</td>
<td>46, XX; heterozygosity of no. 17</td>
</tr>
<tr>
<td>Brother (23 yrs.)</td>
<td>— — 20 —</td>
<td>20</td>
<td>46, XY (long Y = nos. 13-15)</td>
</tr>
<tr>
<td>Sister (13 yrs.)</td>
<td>— 1 21 —</td>
<td>22</td>
<td>46, XX</td>
</tr>
</tbody>
</table>

*: missing elements were those from random groups. **: gestational age.
An autoradiographic study was undertaken for supplement of the above findings in the propositus and her mother. Tritiated thymidine was added to the leucocyte cultures 7 hours before preparation, giving a final concentration of 1 µc per milliliter medium. The slides coated with Sakura NR-M1 emulsion were exposed for 7-10 days at 4°C. Most metaphases labelled with triated thymidine indicated that one chromosome and the aberrant one out of 4 chromosomes in group 17-18 showed minimal labelling, in striking contrast to the remaining 2 elements which showed a definitely heavier labelling pattern. Based on the above finding, the said aberrant chromosome was identified with considerable certainty as a member of the no. 17th pair.

The three members here studied, namely the propositus’ husband, brother and sister, were found to possess a normal karyotype. Exceptional was the brother who had a very long Y chromosome apparently similar in size to 13-15 chromosomes.

REMARKS

The present study revealed that no. 17 chromosomes formed a heterozygous pair. The heterozygous manifestation of no. 17 seems to be the first record in both prenatal and postnatal populations.

To date, a variety of partial deletion has been recorded in autosomes; for example, a short arm deletion of a B chromosome, a long arm deletion of D or G chromosomes, long and short arm deletion of a no. 18 chromosome, and so on. It is a rather general feature that those chromosome anomalies are associated with severe congenital malformations. The propositus and her mother concerned here showed a heterozygosity of
no. 17 chromosomes, but they were clinically and mentally normal within our examinations. At the present status of knowledge, a speculative interpretation for the said abnormality, though not very appropriate, is that the heterozygosity occurring in the propositus and her mother may be recognized as partial monosomy for the long arm of a no. 17 chromosome. However, it is problem that the partial long arm deletion of a no. 17 chromosome is essentially associated with a particular disease, since reported cases with a short arm deletion of a G chromosome were associated with different diseases (Shaw 1962, Neu et al. 1966, Ito and Makino 1966).

Referring to related data, a probable interpretation for the origin of the aberrant autosome is as follows: the propositus and her mother might be carriers of the reciprocal translocation between one of no. 17 chromosomes and a certain other element though not morphologically detectable, and a partial monosomy for the long arm of a no. 17 chromosome may lead to spontaneous abortion. There is, however, no chromosomal proof for the above interpretation in the material so far studied.

Figs. 3-8.
SUMMARY

A clinically and mentally normal woman and her aborted specimen had the 17th chromosome pair showing a heterozygous condition. A familial survey related to the woman revealed that her mother of normal phenotype was also a carrier of the same aberrant chromosome. A possible origin of the abnormal chromosome and its some genetical significance were discussed.

ACKNOWLEDGEMENT

We are very grateful to Professor Sajiro Makino for his direction and going through of the manuscript, and to Dr. Motomichi Sasaki for his invaluable advice and suggestion. Thanks are also due to Dr. T. Kajii for analysing the dermatoglyphic feature.

LITERATURE CITED