Prenatal evaluation in a case of familial Y chromosome long arm deletion (Yq-)*

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Summary. A case is reported in which a deleted Y chromosome was found in a fetal karyotype during a prenatal diagnosis performed because of maternal age anxiety. Quinacrine fluorescence studies demonstrated the same deleted Y in the child's father. The possibility of a reciprocal translocation in the father with a genetically unbalanced condition in the fetus was a concern. Careful examination of the father's karyotype and the study of other reported cases involving deleted Y chromosomes led to the conclusion that the fetal karyotype was genetically balanced. The prediction of a normal fetal development was confirmed at the child's birth.

There have been numerous reports of variation in the length of human Y chromosomes, including some cases in which most or all of the fluorescing region appeared to be missing (Bobrow *et al*, 1971; Borgaonkar and Hollander, 1971; Wahlström, 1971; Tishler, Lamborot-Manzur, and Atkins, 1972). Meisner and Inhorn (1972) described a case in which a major deletion of the long arm of a Y chromosome (Yq-) was found to be compatible with normal male phenotypic development and fertility. In the case referred to, ascertainment of the cytogenetic anomaly was made through studies performed on a proband exhibiting mental retardation and several minor physical anomalies. The fact that the phenotypically normal brother of the proband carried the same deleted Y chromosome and has sired four children led Meisner and Inhorn to conclude that a major portion of the Y chromosome long arm is unnecessary for normal male development and fertility.

We report here a case involving a very similar deleted Y chromosome which was ascertained during a prenatal chromosome analysis in a family with no history of developmental anomalies or mental retardation.

Case report

In February 1971, the 40-year-old, pregnant mother of the proband appeared with her husband requesting counselling and management because of the anxiety generated by the knowledge that an 'older mother' runs a higher risk of producing a child with Down's syndrome. It was agreed that a prenatal evaluation of the fetus was appropriate in this case and transabdominal amniocentesis was performed during the 15th week following the onset of the last menstrual period.

Cytogenetic studies

Fetal cell culture was accomplished in the manner standard in our laboratory (Macintyre, Walden, and Hempel, 1971). The cells were fixed in Carnoy's solution and air-dried to obtain metaphase spread preparations.

Partial karyotypes of the fetus (proband) are shown in Fig. 1. The karyotypes included 46 chromosomes, 45 of which appear to be normal and one of which is a minute which was assumed to be a deleted G or Y chromosome (arbitrarily placed in a Y position in Fig. 1).

In an effort to define the origin of the deleted chromosome, fluorescence studies were performed following the protocol of Pearson, Bobrow, and Vosa (1970) utilizing quinacrine dihydrochloride.

Results indicated that the deleted chromosome must be the Y since no small acrocentric chromosome in the spread exhibited the characteristic bright fluorescence of the terminal portion of the Y

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FIG. 1. Partial karyotypes of the G and Y chromosomes from the fetus (proband). Initially, as here, the minute was placed arbitrarily in the Y position.

chromosome long arm. Furthermore, chromosomes 21 and 22 were distinguished by their characteristic fluorescence patterns.

A cytogenetic analysis including fluorescence studies was performed on the proband's father. Quinacrine dihydrochloride was used on some slides and quinacrine mustard (Caspersson, Zech, and Johansson, 1970) on others. His karyotype apparently was identical to that of the fetus. Since no chromosome in the karyotype appeared to have the brightly fluorescing Y chromosome material attached to it (Fig. 2), it was assumed that no translocation existed and that this was a case of a pure deletion of a major portion of the Y chromosome long arm. Because of the phenotypic normalcy of the father, the prediction was made that the fetus would be a normally developed male and the pregnancy was not terminated. Confirmation of the correctness of the prediction was achieved subsequently at the time of birth of the proband, a 3657 g normal male.

Discussion

The finding of a deleted chromosome in the fetus (proband) was unexpected in view of the fact that the prenatal evaluation was being performed solely because of the maternal age factor. Since prenatal analysis was involved, it was important to determine as rapidly as possible which chromosome

was deleted and to arrive at some prediction with respect to the possible effect of the anomaly on fetal development.

When the deleted fetal chromosome was recognized as the Y chromosome because of the missing fluorescing portion, and by positive identification of the G-group chromosome, the following important questions remained to be answered.

1. Is the genetic material in the fluorescing portion of the Y chromosome inactive and unimportant to the normal development of maleness and fertility?
2. If the fluorescing portion is inactive, did the break occur at such a point as to include some active genetic material in the deleted segment?
3. If active genetic material is involved, does a balanced translocation exist in the father rendering him phenotypically normal?
4. If a translocation exists, is the fetus a carrier or genetically unbalanced?
5. Is it possible for the fluorescing portion of the Y chromosome to be translocated to another chromosome and in the process somehow lose its fluorescing qualities?

There had been several cases reported in which the fluorescing portion of the Y chromosome was small or absent with no apparent effect upon the phenotype of the individual (Bobrow *et al*, 1971; Borgeonkar and Hollander, 1971; Wahlström, 1971).

Based on the above findings we were prepared to assume that the fluorescing portion of the Y chromosome is of no consequence to the normal development of the individual; however, the size of the deletion in our case was rather great and we had no proof that active genetic material was not included in the deleted segment.

The only way to exclude the possibility of active genetic material having been lost to the fetal karyotype was to determine that the phenotypically normal father was not a carrier of a balanced translocation involving the deleted Y segment. A careful examination of all other chromosomes in the father's karyotype (Fig. 2) failed to demonstrate the presence of the highly fluorescing segment of the Y chromosome. We were prepared to accept the situation in the father's karyotype as being a pure deletion, providing the distal long arm of the Y maintains its fluorescing qualities after translocation. The case of Noel *et al* (1971), in which a Y long arm was translocated to a D chromosome and continued to demonstrate fluorescence, gave us some assurance that no translocation existed in the father in our case.

Based on the above data it was assumed that the fetal karyotype was essentially the same as that of the

FIG. 2. Fluorescent metaphase cell from the proband's father. Note the absence of brightly fluorescing Y chromosome material.

phenotypically normal father, and the prediction was made that the child would be developmentally normal. As mentioned above, the prediction was proven correct at the child's birth. Subsequent studies have continued to support the assumptions on which we acted in this case (Bühler, Müller, and Stalder, 1971; Friedrich and Nielsen, 1972; Fründ *et al.*, 1971; Krmpotic *et al.*, 1972; Meisner and Inhorn, 1972; Tishler *et al.*, 1972; Lundsteen and Philip, 1973; Siebers *et al.*, 1973).

The importance of the use of fluorescence tech-

nique in this case cannot be too greatly stressed. The size of the deleted chromosomal segment relative to the size of large chromosomes to which it might have been translocated, precluded a definitive evaluation based on the older standard techniques of staining and karyotype analysis. The fluorescence of the terminal portion of the Y chromosome long arm is so distinct that fluorescence methods may prove to be superior to Giemsa-banding techniques in cases involving possible Y chromosome deletions or translocation.

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