AN UNUSUAL CASE OF GONADAL DYSGENESIS WITH A DELETED LONG ARM CHROMOSOME

by

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Kallio (1973) and Sarto (1974) in an extensive study of women with primary ovarian failure, have demonstrated that the majority of patients have 46 XX karyotypes and a minority of these cases reveal a spectrum of sex chromosome karyotypes ranging from 45 X to 45 X/46 XX; translocations involving the 'X' chromosome and autosome. Partial deletion of either of the arms of the X chromosome are however rare and still rare are the cases showing complete absence of short or long arms. In this present paper attempts have been made to determine (1) "The genes responsible for stature and ovarian function on the X chromosome" and (2) "Barr body (X chromatin) condensation center" by analysing the clinical and cytological data of a patient having total deletion of the long arm of the X chromosome.

CASE REPORT

The patient (R.A.) aged 15 years was referred to the Endocrine Clinic at the Tata Memorial Hospital for delayed puberty and complete absence of secondary sex characteristics. Mother was 21 and father was 28 years at the time of her birth. She has 1 sister (10 yrs) and 2 brothers (21 and 8 yrs), all apparently normal looking. The phenotypically female patient was 53.6" tall, weighed 88 lbs and did not reveal any stigmata of Turner's syndrome. Skull X-ray revealed normal sella turcica. Urinary gonadotrophins were repeatedly elevated and ranged in the menopausal levels.

X chromatin was 8% and 16% in the buccal and vaginal smears respectively and in both these instances, this mass was significantly small as compared to that seen in normal females. No Y-chromatin was found. The analysis of 52 metaphase plates revealed 46 (XXq-) Fig. 1.

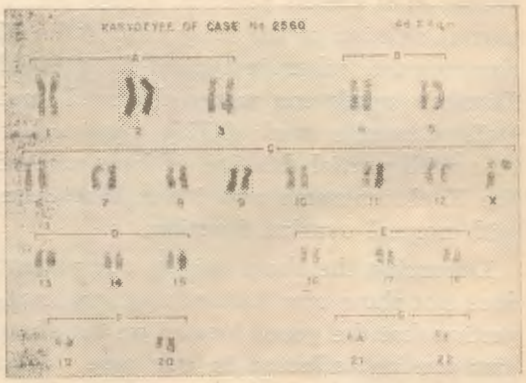

Fig. 1. Metaphase plate showing XXq- in a patient with gonadal dysgenesis.

and 45 X in 19 and 33 plates respectively. The deleted Xq- was confirmed by G-banding (Sun et al, 1974) autoradiography and BrDU banding technique (Pearson and Van Egmond-Cowan 1976).

Discussion

Specific deletions involving the 'X' chromosome in cases of gonadal dys-

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Accepted for publication on 17-7-80.

genesis aid in determining their relationship to phenotypic features and/or subsequent regions contributing the formation of the X chromatin.

Jacobs (1960) reported a case with primary amenorrhoea, sexual infantilism with 'streak' gonads but absence of features typical of Turner's syndrome; cytogenetic studies showed a small X chromatin mass with partial deletion of long arm of one of the X chromosome. Ferguson-Smith (1965) in his extensive review on gonadal dysgenesis has postulated that while genes in the short arm are responsible for stature, genes in the long and short arm of the 'X' chromosome are involved in ovarian differentiation. However, more recent work using banding techniques have revealed some inconsistencies which naturally doubt the postulations of Ferguson Smith. For example, Weber *et al* (1970) reported a case with a partial deletion of the long arm of the X chromosome wherein typical features of Turner's syndrome were observed and DeLa Chapelle *et al* (1975) reported a case with partial deletion of long arm of the X chromosome and intact short arm with normal ovarian function.

Debarring the short height, our patient does not show any Turner stigmata, suggesting that the genes located on the short arm are not affected in our case. It is quite probable that short height in our case may be due to complete loss of one of the 'X' chromosomes in 72% metaphase plates.

Based from the data on partial and complete deletion of the short arm, partial deletion of the long arm, isochromosome of the long arm and ring chromosomes, Therman *et al* (1974) postulated that the inactivation centre responsible for X-chromatin is located on the long arm of X chromosome at a region close to the centromere. According to their hypothesis 'X' chromatin will not be formed if this region is completely deleted. This hypothesis has not been tested since cases showing total deletion of the arm have been very rare. Further, DeLa Chapelle *et al* (1972) reported 2 cases (46 XX pi and 46 XXp$^-$) in which X chromatin mass was smaller than normal. Presence of small X chromatin in the absence of long arm of the X-chromosome in the present case as well as two cases reported by DeLa Chapelle (1972) indicate that even short arm contributes to the formation of the Barr body or the X chromatin mass. From this observation it appears that Therman's hypothesis is not fool proof. It is quite probable that two loci, one at the proximal end of the short arm or the entire region between the two loci around the centromere is responsible for inactivation and formation of X-chromatin mass.

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