A PROBABLE CASE OF TRUE HERMAPHRODITE WITH 46,XXq/ XY MOSAICISM

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Abstract

A married women of 35 years age with primary amenorrhoea and poorly developed secondary sex characters but having a frankly feminine external genitalia was found to be a probable case of true hermaphrodite. There was a normal sized testis with epididymis and vasdeferens within the left swollen labia majora. At the position of the overies two greyish white bodies were present, which looked very much like ovaries, but small in size and inter-connected by a band of fibrous tissue. In buccal as well as vaginal smears a very low percentage of cells had a sex-chromation body. The size of the sex chromation was howeevr, much reduced. The G–band analysis of chromosomes, made from leucocyte cultures, revealed a 46, XXq-/46, XY sex chromosome mosaicism with predominance of 46, XY type of cells.

Introduction

Several types of sex-ohromosome constitutions are known amomg hermaphrodites with sex-chromosome mosaicism recorded so far. They are mainly 45, X/46 XY; XX/46, XY and 46, XX/47, XXY types. Individuals with 46, XX/48, XXYY; 45, X/47, XxY; 46, X 'Y'/45,XO; 45 X/47, xYY; 45, X/46, XYqi; 45 X/46, XXY; 46, XX/46, XY/49, XXYYY; 45, X/46, XY/47, XXY; 46, XX/46, XX–q/46, XY dic and 45, X<46 XX<47, XXY-qi have also been reported (Fraccar[1] et al) 1962; Schuster[2] et al., 1962; Boschetti[3] et al., 1968; Miles[4] et al., 1962;, Klevit[5] et al., 1963; Blank[6] et al., 1964; Milcu[7] et al., 1964; Ribas Mundo[8] et al., 1965; Lo[9] et al., 1965; Cox[10] et al., 1967 Ferguson Smith[11] et al.. 1969; Hsu[12] et al., 1970; Polani[13] et al, 1970). A probable case of true hermaphrodite with normal feminine external genitalia bnt possessing 46, XXq46, XY, type of sex-chromosomal mossicism was detected by us which appeared to be a new sex-chromosome constitution in sex.chromosome mosaics so far reported.

Case report

A. D: 35 years old women married for last 15 years was admitted in Gynaecology ward of University Hospital, Banaras Hindu University with a complaint of frequent pain in her left swollen labia majora for one year. According to her the labia majora was swollen from her early childhood but earlier she had experienced no pain. She had primary amenorrhoea but there was no problem in marital relationship. She had married a widower with four children and so psychologically she appeared to be well adjusted women. There was no family history of such illness.

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Examination Findings

She was a thin built tall patient (Fig. 1). Her height was 172 cms. The length of upper and lower arms were 61 and 86 cms., respectively and the distance between umblicus and pubic symphysis was 15 cms. Her breast was poorly developed and the nipples were with less areolar pigmenation and were placed widly apart. There were no axillary hair and pubic hairs were scanty.

Gynaecological examination revealed the external genetalia of feminine type but the left labia majora was swollen and the clitoris was hypertrophied (2, 3 cms.) Fig. 2. In the swollen left labia majora a large (4.6 cms. 3 cms) cystic mass along with a cord-like structure could be felt, urinary opening was normally situated and vagina was only 4 cms. deep ending as a blind pouch. She had male like perineal distance. Uterus was not palpable and cervix was absent.

On laparoscopy almost complete Mullarian agenesis was observed, Except a small ramnant on right side the Mullarian duct had formed no uterus, cervix or even the upper part of vagina. At the normal sites of the ovaries, two small greyish white bodies were present and they were interconnected by a band of fibrous tissue. These bodies looked like ovaries though they were small in size. Biopsy could not be done as patient refused abdominal operation.

Investigations

Urine 17 ketosteriod—was 8.6 gms/24 hrs.

Sex chromation study

Examination of vaginal and buccal muccsal cells strained with Carbol-fuchsin showed presence of small sized sex-chromatin in only about 3% of both types of cells (11 sex-chromation positive cells out of 400 cells counted).

Chromosomal studies

Peripheral whole blood counts were used for chromosomal preparation. The slides were made by ignition method. The chromosomes were stained for G-band by Seabright's[14] (1971) trypsin method with slight modifications.

The chromosomes counted in a total of 30 well spread metaphases under oil immersion lens consistently showed 46 chromosomes per plate. However, in 22 (70. 3%) plates there were 5 G-group small acrocentric elements whereas in the remaining 8 (29. 6%) plates there were 4 G-group small acrocentric elements. On karyotyping 3 plates with 5 G-group chromosomes, it appeared that there was a Y chromosome besides the 4 smallest acrocentric autosome (Fig. 5) and on karyotyping 3 plates with 4 G-group chromosomes a small sub-metacentric element was unpairable in all the three plates with any other chromosomes of the complement (Fig. 6). In G band analysis the presence of Y in the cells with 5G-group chromosomes was confirmed (Fig. 7) and the small sub-metacentric element of the cells containing 4 G-group acrocentric was identified as long-arm deleted X-chromosome (Fig. 8).

Management

A longitudinal incision was given on left labia majora and normal sized testis with epididymis and vas deferenace (Fig. 3) leading into the inguinal canal was found. The testis was removed and labia was reconstructed. The removed testis on histology revealed under developed degenerated and

hyalinized seminiforms tubules. Some identifiable cells of sortoli were present but no spermatozoa could be seen. On the other hand, leyding cells were present in abundance (Fig. 4).

Discussion

The condition of external and internal genitalia are known to vary considerably in human with different sex–chromosomal mosaicism. In general, the condition of gonads and accessory sexual charecters of such individuals depend upon the proportion and distribution of cells with different sex–chromosome constitution during development (See Polani, 1970). In the present case chromosomes of only one tissue (blood) were studied but the existance of two cell lines, one XY and another with XY–q, in the individual was established. The presence of a cell line with one normal X and the other cell line with 46, XY in human mosaic seems to be not reported earlier. The small size of the sex chromatin body observed in the buccal and voginal smears of this individual could be due to the long arm delitition of one the X's, since it is known in human that the structurally abnormal X in invariably form the Barr body (See Hamerton,[15] 1969). The extremely low frequency of sex-chromation positive cells in buccal and vaginal smears observed could be due to very low propertion of 46, XXq, cells in those tissues as encountered in the leucocytes culture of the individual. Also, because of reduction in the size of the sex.chromatin, its detection might have often been obscured.

The exact nature of the gonads located at the normal position of ovaries is unfortuately not known. On laporoscopy the two grayish-white bodies had looked more like ovaries. According to polani (10C. cit.) sometimes the two elements of ovotestis may be so discrete that the two constitute separate but adjoining gonads on the same side.

It could be possible that on the left side of the present individual extreme segragation of testicular and ovarian tissues-might have taken place. This seems to be therefore a case of true hermaphroditism rather than testicular feminization or so called mixed gonadal dysgenesis.

Acknowledgement

We are thankful to the Medical Superintendent, S.S. Hospital, Banaras Hindu University for allowing us to publish this case.

Fig. 1 Showing photograph of the patient.

Fig. 2 Showing hypertrophide clitoris and opening of the blind vagina.

Fig. 3 Showing external genetilia and just vivisected testis with epidedymis and vas difference from left labia majora.

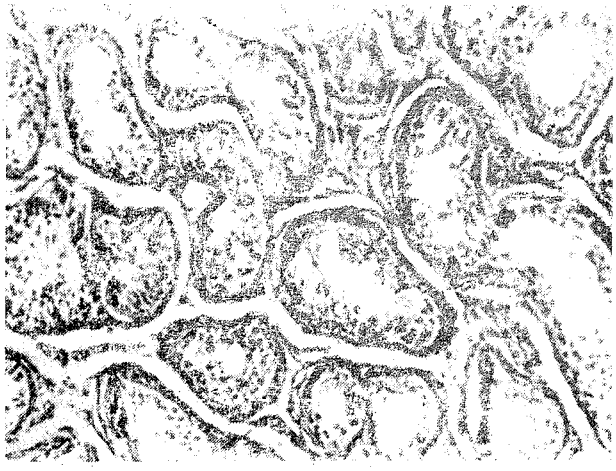


Fig. 4 Showing section of testicular tissue showing under-developed (U.D.) hyalanized (H) and degenerated (D) seminiferous tubules with sertoli (Ser) and Leydig (L) cells but no spermatozoa X 160.

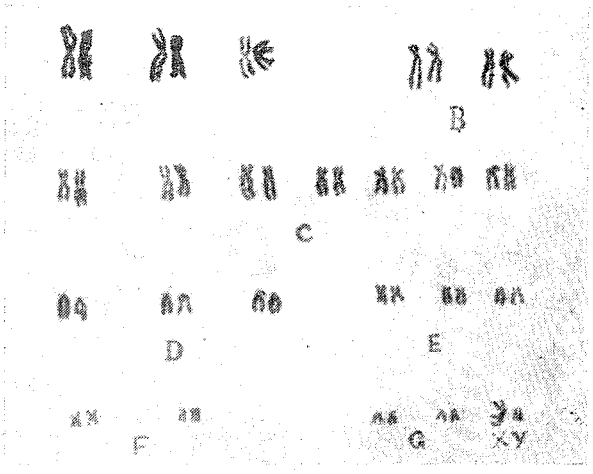
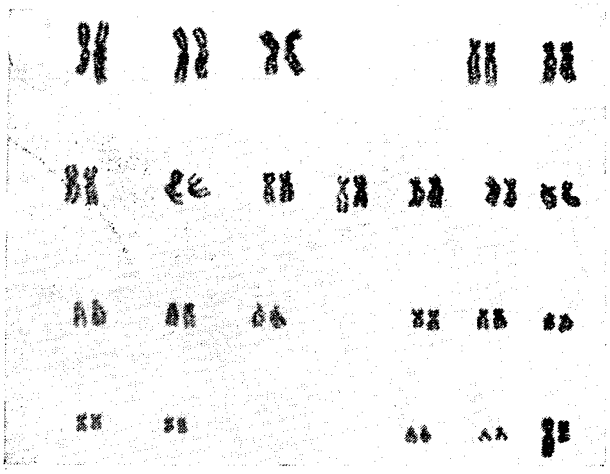


Fig. 5 Karyotype showing XY Chromosomes X1600.



Fig, 6 Karyotype showing XX-q Chromosomes X 1600.

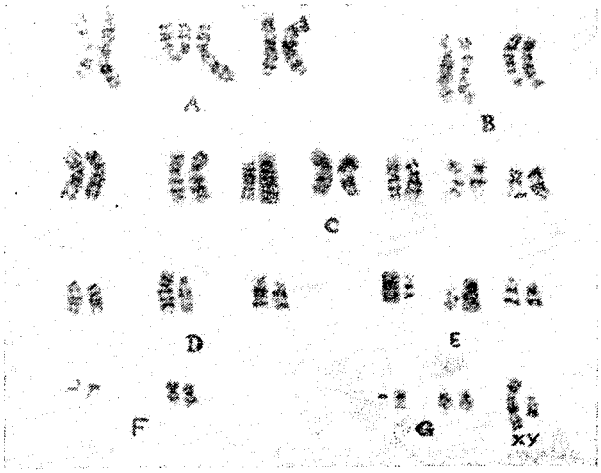


Fig. 7 G–Band Karyotype showing XY Chromosomes X 1600.

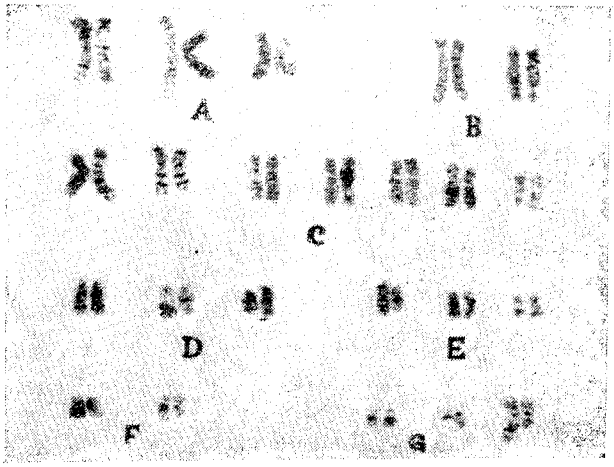


Fig. 8 G–Band Karyotype showing XX–q Chromosomes X 1600.

REFERENCES

1. Fraccaro, M., Taylor, A.I. Bodian, M and Newns, G.M. A Human Intersex ('true hermaphrodite") with XXYYY sex–chromosomes. *Cytogenatics* (Basel) 1 : 104–112. 1962.
2. Schuster, J., and Motulsky, A.G., 1962. A New Karyotype (XX/XY/XO Mosaic) in True Hermaphrodite. Clin. Res., 101–110; 1962.
3. Miles, C.P., Luzzatti, L., Storey, S.D. and Pet-erson, C.D., *Lancet,* 2:455; 1962.
4. Boschetti, R., Gilbertas, A., Nool, B., and Quack, B., Pseudohermaphroditisme Masculin et Mosaic 45, X/46, XY dic/46, XX. *Ann. Genet Semaine Hop.*, 2:62–65, 1968.

5. Klevit, H.D., Mallman, W.J. and Eberlein, W.R., Triple Mosaicism with an Isochromosome Derived From Partially Deleted Y in a Male Pseudohermaphrodite. *Pcdiatrics*, 32:56–62; 1963.

6. Blank, C.E., Zachary, R.B., Bishop, A.M., Emery, J.L., Dewhurst, C.J., and Bond, H.H. Chromosome Mosaicism. In A Hermaphrodite. Brit. Med. J. 2:90–93; 1964.

7. Milcu, St. M., Stoenescu, D., Maximilian, C., Demian, A., Danila–Muster, A., Iliescu, I., and Ghiur, M. Pseudohermafroditism Masculen Cu·mosaic Cromozomial XO/XY/XXY, *Fiziol. Patol.* (Bucharest), 10:145–151, 1964.

8. Ribas–Mundo, M. and Prats, J., Hermaphrodite with Mosaic XX/XY/XXY. *Lancet*, 2:294., 1965.

9. Lo, M.T., and Kobernick, S.D., (X' Y'/X) Mosaicism in Phenotypic Intersex. Report of a Case. *Am. J. Clin. Pathol.*, 43:251–255; 1965.

10. Cox. D., and Berry C.L., A Patient with 55, XO/XYY Mosaicism. *J. Med. Genet.*, 4:132–133; 1967.

11. Ferguson–Smith, M. A., Boyd, E., Ferguson–Smith, M.E., Pritchard, J.G., Yasuf, A.F.M., and Gray B. Isochromosome for Long Arm of Y Chromosome in Patient with Turner's Syndrome and Sex-chromosome Mosaicism (45,X/XYqi). *J. Med, Genet.* 6:422–425; 1969.

12. Hsu, L.Y.F., Hirschhorn, K., Golstein, A. and Barcinski, M.A., Familial Chromosomal Mosicism, Genetic Aspects. *Ann. Hum. Genet.*, 33:343; 1970.

13. Polani, P.E., Hormonal and Clinical Aspect of Hermaphreditism and the Testicular Feminizing Syndrome in Man. *Phil. Trans. Roy. Soc. Lond.*, B 259: 187–204, 1970.

14. Seabright—Rapid Banding Technique for Human Chromosome, Lancet. 2:971–972.

15. Hamerton, J.L., Hand Book of Melecular Cytology. Ed. Lima–de–Faria. North Holland Publishing Co., Frontiers of Biolegy Vol. 15, PP–751–803.