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Familial True Hermaphroditism*

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True hermaphroditism is a condition in which the patient has either a testis and an ovary or a combined gonad. In ovotestis, testicular and ovarian elements may be intermingled or more or less discrete. A uterus and other Mullerian or Wolffian derivatives in different combinations may be found. The external genitalia are more or less ambiguous. Familial type is very rare, although many sporadic cases have been reported.

Case 1: S. S. (V4 in Figure 1) this 12 year old patient was seen in the Hacettepe Children's Medical Center because of genital ambiguity. She was reared as a female. It was learned that there were two other children showing the same ambiguity in her family (V, 11 and V, 12). These three children were born to a large inbred family. One of them is reported as case 2.

Physical examination showed her height to be 132 cm. and weight to be 27.5 kg. She had masculine type of body muscles. The examination of the external genitalia disclosed no pubic or axillary hair, and a phallic growth of 3 cm. Both gonads were palpated in the inguinal canals. The two labia majora were separate. The urethral opening was in the perineum (Figure 2, 3). There was no breast development.

The X chromatin was negative in the buccal smear. In the peripheral blood lymphocyte and in skin and gonadal fibroblast cultures the chromosome complement was 46, XY. Chromosomal mosaicism was not encountered (Table I).

The bone age was determined as 11 at the age of 14.

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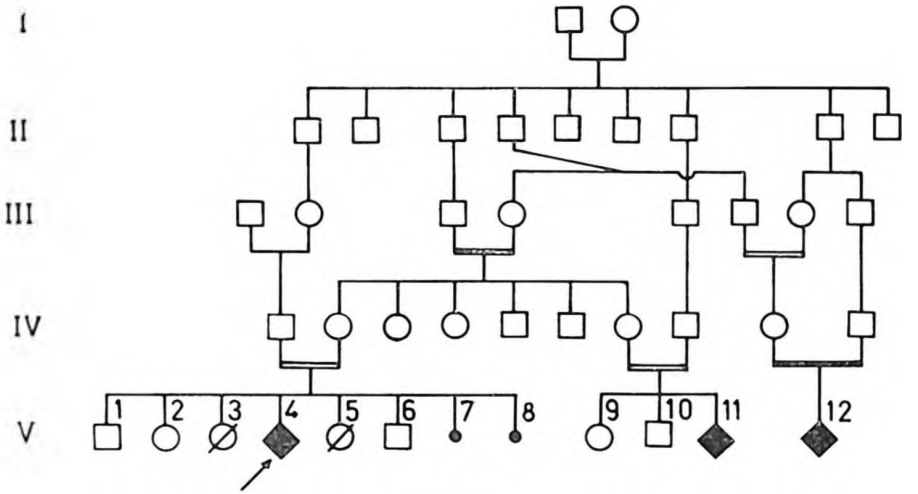

Figure 1
The pedigree of the family

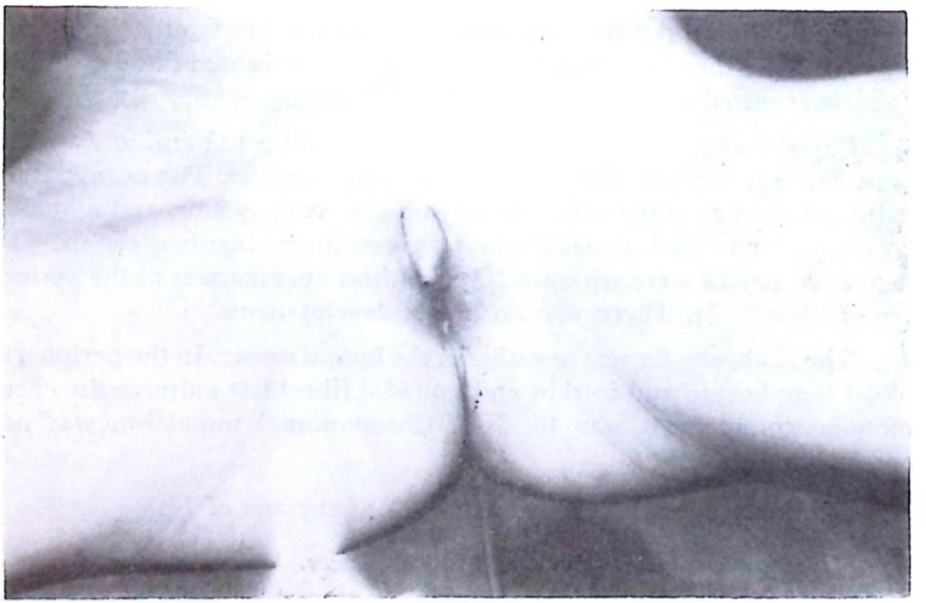

Figure 2
External genitalia of Case 1

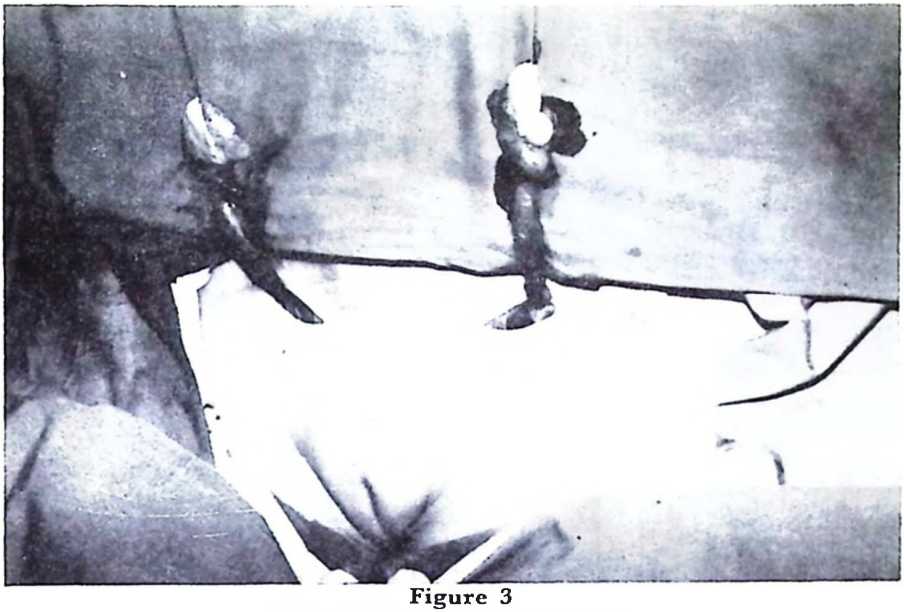

Figure 3
The gonads during the operation

TABLE I

THE CHROMOSOME COMPLEMENT OF THE PATIENT

	No of metaphases with 46, XY chromosome
Peripheral blood	72
Skin	50
Gonad	30

FSH and LH levels were 20 U/l and 17 U/l respectively. 17 KS was 3.10 mg/l and 17 OH 2.94 mg./l.

The patient underwent surgery, both gonads found in the inguinal canal were removed.

Histologically, the biopsy of the right gonad showed well-formed, immature testicular tubules with some inactive spermatogonia in the basement membrane. The interstitium was loose and fairly vascular with small epithelioid cells. A nodule of ectopic adrenal cortical tissue was found adjacent to the testis.

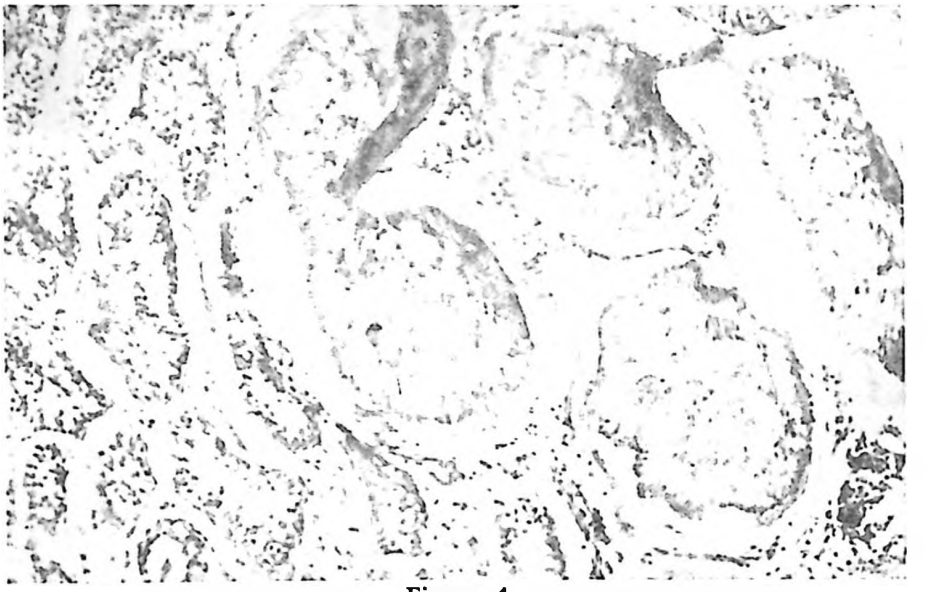

Figure 4
Well formed immature testicular tubules (left) with small island of ovary (right)

The left gonad showed well-formed immature testicular tubules with small island of ovary. The follicles were all anovular and atretic with cystic distension and were reduced in number. Primordial follicles were absent (Figure 4).

Case 2: K. O. (V, 11) was a 4 3/12 years old child. He was a first degree cousin of Case I and was reared as a boy. His physical and mental development were normal. The right testis was palpable 3X2 cm. in the scrotum. On the left side gonadal tissue could not be palpated. The phallus was 1 cm. in lenght and was capable of erection. There was perineal hypospadias.

His buccal smear was negative and chromosomal analysis which was done from peripheral blood showed 46, XY karyotype. Unfortunately the family of the patient did not accept further investigations.

Discussion

There are 5 reported families with true hermaphroditism[1-6], to best of our knowledge our family will be the sixth.

The histological appearance of our first case indicated that the diagnosis was true hermaphroditism. The family of the second case did not accept the biopsy of the gonad or surgical exploration. Nevertheless,

previously there has never been an example of a family in which some members have true hermaphroditism and others have a familial male pseudohermaphroditism. In addition, it is difficult to believe that there are two different mutations in the same family which cause a defect in sexual differentiation. It is our opinion that these two children, although one was not completely investigated, are examples of true hermaphroditism.

Both patients showed XY karyotype but we were unable to find mosaicism in the peripheral blood, skin and gonad cultures of the first case. In familial true hermaphrodism both XX[3, 4, 5] and XY[2, 6] karyotypes have been reported. It is quite difficult to find an answer as to how ovarian tissue is produced in the XY individuals or vice versa. Theoretically undetected mosaicism is still possible, although we and other authors could not find evidence of this. It is also possible that there is undetected translocation of the male determining part of the Y chromosome on the X or that sex determining genes are located on an autosome can also be postulated. The first two possibilities are fairly improbable. The third posibility seems to be more feasible explanation. The existence of autosomal genes in goats and mice is well known.

Armandares[5] suggested as an explanation for this familial syndrome, an autosomal dominant mutation limited to the female; whereas Lowry et al[6] proposed an autosomal recessive inheritance. Our family is quite a good example of this type inheritance pattern. From the phenotypical difference between the reported cases, variable expression of the same mutant gene in a family is a more possible explanation than two or more different mutations in one family.

Summary

A large inbred family with 2 cases of ambiguous genitalia is presented.

One of the cases was operated, small island of ovary between immature testicular tubules was found in one gonad. The chromosome complement was XY in the peripheral blood, skin and gonad. No mosaicism was present.

Possibility of familial true hermaphroditism was discussed.

REFERENCES

1. Clayton, G. W., Smith, J. D., and Rosenberg, H. S.: Familial True Hermaphrodism in Pre-and Post-pubertal Genetic Females. Hormonal and Morphologic Studies. J. Clin. Endocr. and Metab., 18: 1349, 1958.

2. Milner, W. A., Garlick, W. B., Fink, A. J., and Stein, A. A.: True Hermaphrodite Siblings, J. Urology: 79, 1003, 1958.
3. Rosenberg, H. S., Clayton, G. W., and Hsu, T. C.: Familial True Hermaphrodism, J. Clin. Endocr. and Metab., 23: 203, 1963.
4. Mori, Y., Mizutani, S.: Familial True Hermaphrodism in Genetic Females, Jap. J. Urol., 59: 857, 1968.
5. Armandares, S., Salamanca, F., Cantu, J. M., del Castillo, V., Nava, S., Dominguez de la Piedra, E., Cortes-Gallegos, V., Callegos, A., Cervantes, C., and Parra, A.: Familial True Hermaphrodism in Three Siblings. (Clinical, Cytogenic, Histological and Hormonal Studies) Humangenetic, 29: 99, 1975.
6. Lowry, R. B., Honore, L. H., Arnold, W. I., Johnson, H. W., Kliman, M. R., and Marshall, R. H.: Familial True Hermaphroditism. Genetic forms of Hypogonadism. Birth Defects. Original Article Series. National Foundation March of Dimes Vol. XI, No: 4, 405, 1975.