Case Reports


Presumptive 46,XX/46,XY/47,XXY Mosaicism in a Hermaphrodite

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Contrary to the expected XX/XY sex chromosome complements in hermaphrodism, a variety of karyotypes have been reported instead. Dewhurst et al. (1965) summarized from published reports the karyotypic findings in 27 patients with convincing evidence of hermaphroditism, as follows: 46,XX (17); 46,XY (2); 46,XX/47,XXX (1); 46,XX/46,XX + Frag (1); 46,XX/46,XY (3); 46,XX/47,XXY/49,XXYY (1); 46,XX/47,XXY (1); 46,XX/48,XXYY (1); 46,XY/45,X (1); and also described a patient of theirs with 46,XX + Frag/45,X mosaicism. Ribas-Mundó and Prats (1965) reported a hermaphrodite with mosaicism consisting of 3 cell lines, 46,XX/46,XY/47,XXY. The present paper reports the second case.

Case Report

Baby M., who was referred to one of us (S.C.) because of ambiguous external genitalia, was born normally 3 weeks before term in March 1968 to an 18-year-old mother and 24-year-old father, at the Ramakrishna Mission Seva Pratisthan. Both parents were healthy and this was their first child. The birthweight was 2.75 kg, and the length was 48 cm. The family history was non-contributory.

The neonate was normal in all respects except for the external genitalia which were obviously ambiguous (Fig. 1). The external genitalia consisted of a phallus intermediate in size with a single opening at its base. The gonads could not be felt in the sac-like vulva surrounding the phallus. Instillation of dye through the opening did not reveal female internal genitalia.

At the age of 2 weeks the baby was referred to one of us (A.C.) for cytogenetic investigations, and was discharged from the hospital after the collection of blood and buccal mucosa samples, to be readmitted for diagnostic exploration and further cytogenetic studies at the age of 6 months. Apparently, the parents were either unable or unwilling to look after a baby of indeterminate sex and the baby was brought back to the hospital in June 1968 weighing only 2 kg. and in a moribund condition. The infant expired on the following day and a necropsy was performed.

There were normal female genitalia in the pelvic cavity but the vagina had terminated high up on the back of the urethra; and there was thus a single external opening (Fig. 2). All the other organs appeared to be normal. The ovaries were macroscopically normal in appearance.

Histological findings. The histopathological sections of both gonads showed a preponderance of ovarian elements (Fig. 3). The cortical portions of the gonad showed a large number of primordial follicles. Occasional follicles were in the growing phase. Polynuclear ova and multiovular follicles could be seen. The interstitial tissue showed the characteristic pattern of ovarian stroma. However, the tunica albuginea was significantly more thickened than in postnatal ovaries. Atretic follicles could be seen as well. The deeper part of the gonad showed tubular structures in the loose connective tissue. These tubules were solid and lined with multilayered cells. Some of the nuclei showed chromatin grooving as is seen in Sertoli cells. These structures resembled seminiferous tubules but their identity as germ cells could not be ascertained with certainty. Cells bearing a morphological resemblance to Leydig cells could be seen lying scattered or in small groups. The suprarenal gland did not show any abnormality.

Cytogenetic investigations

Sex chromatin. Buccal mucosa smears from both sides of the cheeks were stained with 2% aceto-orcein and were examined for sex chromatin masses. In 400 cells, 14% contained a single chromatin body, normal in size, and in contact with the nuclear membrane. The range for normal adult females in this laboratory is 25–55%.

Chromosomal analysis. Leucocyte culture from capillary blood was carried out by our modification of Arakaki and Sparkes' method (Chaudhuri, 1967; Chaudhuri and Roy, 1967). A total of 90 cells was counted. Strict criteria were observed in the choice of cells for analysis, only unbroken cells having been selected for examination. Cells with 3 different chromosome numbers were found, 78 cells with 46, 9 cells with 45, and 3 cells with 47 chromosomes. No cells were seen with less than 45 or with more than 47 chromosomes.

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117
Microscopical inspection revealed that 5 of the cells with 46 chromosomes carried 5 G's, the remaining cells having 4 G chromosomes (Table). Of the 9 cells with 45 chromosomes, inspection showed that 2 of them had 5 and 7 had 4 G chromosomes. All the 3 cells containing 47 chromosomes had 5 G's. It is, perhaps, noteworthy that in 7 of the 10 cells which carried an extra G, one of the G chromosomes was always located at the periphery. In one of these 10 cells a member of the G group was morphologically similar to the Y chromosome. In view of the patient's phenotype and the presence of presumably male elements in the gonads, it was felt that the possibility of the extra G being a Y was not unlikely.

**TABLE**

**CELL TYPES AND THEIR SEX CHROMOSOME CONSTITUTION**

<table>
<thead>
<tr>
<th>Chromosome No.</th>
<th>No. of Cells Counted</th>
<th>No. of Cells Analysed</th>
<th>Sex Chromosome Constitution</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>9</td>
<td>9</td>
<td>XX XY (7)* (2)</td>
</tr>
<tr>
<td>46</td>
<td>78</td>
<td>19</td>
<td>XX XY XXY (14) (4) (1)</td>
</tr>
<tr>
<td>47</td>
<td>3</td>
<td>3</td>
<td>XXY (3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>90</strong></td>
<td><strong>31</strong></td>
<td></td>
</tr>
</tbody>
</table>

* Figures in brackets indicate the number of cells.
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Fig. 3. Low Power view of left gonad showing primordial follicles and immature testicular tubules. (x 120.)

though, of course, it could also be the centric fragment of an X, or for that matter, of an autosome.

Thirty-one of the 90 cells examined were karyotyped, the details of which are shown in the Table. There were 14 46,XX cells, 4 presumptive 46,XY cells, and 3 presumptive 47,XXY cells. In addition to this, 2 of the cells with 45 chromosomes were considered to be XY and one of the cells with 46 a presumptive XXY cell. The remaining cells with 45 chromosomes were all XX, with random loss of a chromosome in 4, and an unexplained consistent loss of a G in 3 of them. Thus, of 31 cells analysed, there were 21 XX, 6 XY, and 4 XXY cells (Fig. 4, 5, 6).

Discussion

The term 'hermaphrodite' in the strictest sense indicates functioning testicular and ovarian structures in the same individual. However, of the reasonably fair number of cases reported (Gudernatsch, 1944; Stirling, 1946; Jones and Scott, 1958; Jones and Heller, 1965) only a few (Stojalowski and Debski, 1933; Masson, 1952) showed evidence of functioning gonads. Gonads containing ovarian and testicular structures are termed 'ovotestes'. About 18 cases of bilateral ovotestes have been reported (Jones and Heller, 1966) and none of these was in the neonatal age-group.

In the identification of sex, some of the parameters which should be considered, according to Jones and Heller (1966), are (1) sex chromatin and sex chromosomes, (2) the appearance of the external genitalia, (3) the morphology of the internal genitalia, and (4) the microscopical composition of the gonads. In female neonates the percentage of Barr bodies, according to some workers, is less than that of adult females. Robinson and Puck (1965), however, found 26 ± 5% chromatin positive cells in the buccal mucosa of babies within 48 hours of birth. The low percentage (14%) in the newborn under
FIG. 4. Karyotype of cultured leucocytes with XX sex chromosome constitution from hermaphrodite.

FIG. 5. Presumptive 46,XY cell from blood of same patient.
Fig. 6. Karyotype of 1 of the 4 cells with XXY sex chromosome complement.

Report may be due to sex chromosomal mosaicism, approximately 7% of the cells in a leucocyte culture carrying only a single X chromosome. In the reported cases of hermaphroditism in which chromosomal studies were carried out (Jones, Ferguson-Smith, and Heller, 1965), the presence of the Y chromosome was always associated with testicular structures. The phallus in the present case was intermediate in size. Seven out of ten cases of true hermaphroditism with bilateral ovotestes showed masculinization of the external genitalia and were reared as males (Jones and Scott, 1958).

The present case revealed at necropsy normal female internal genitalia. However, the vagina terminated high up on the back of the urethra and there was thus a single external opening. In the cases of bilateral ovotestes reported, 2 subjects out of 11 had a normal uterus in one series and 1 out of 6 in another series (Jones and Heller, 1966). The Fallopian tubes were present bilaterally in 5 cases out of 6 (Jones and Heller, 1966). In a series of 21 reported cases by Jones et al. (1965), 16 subjects had ovotestes in combination with ovotestes (6), ovary (6), and testes (4) i.e. there were 22 ovotestes. Sixteen Fallopian tubes were present in this series. No Fallopian tube could be detected on the side where testicular tissue alone was present. It thus appears from the cases reported in the literature, that the testes can supress Müllerian development but the ovotestis is likely to behave as an ovary concerning the suppression of Müllerian development. In one of our cases being reported in detail elsewhere, there was an ovotestis and an ovary, a unicornuate uterus, and a normal tube on the side of the ovary, and complete suppression of Müllerian elements on the side of the ovotestis.

In the present case, the gonads consisted principally of ovarian tissue with a reasonably good number of primordial follicles and characteristic ovarian stroma. Growing follicles and atretic follicles were present as well. Atretic follicles are encountered in the ovaries of the newborn at times. Polynuclear ova and multiovular follicles were present. Their occurrence, though infrequent, has also been reported. The tunica albuginea was, however, definitely thick and simulated that of the testes. Within the depths of the gonads were tubular structures simulating poorly developed testes. There was aplasia of the germinal cells. The testicular tissue was not as florid as in some of the reported cases whose age range was from several years to a few decades, and none was in the newborn period. The karyotype in these cases, however, did not include complicated 3-cell line mosaics, as the present case. In the 46,XX/46,XY/47,XXY hermaphrodite reported by Ribas-Mundó
and Prats (1965) the description of the testicular tissue was similar to the findings in the present case. The human ovary is potentially an ovotestis and male elements may be remnant in the hilum. Potter (1952) considers the occurrence of ovotestes in the newborn to be a rarity and she failed to find any authentic report. She stated that the mere development of tubules, though remarkable, in a newborn should not be considered as evidence of ovotestes.

The present case showed a number of cells resembling Leydig cells and the tunica albuginea showed male development. The external genitalia were somewhat masculine in type though the adrenal glands were histologically normal, and there was no history of hormone or drug therapy. The mother had no clinical features of androgenic activity. The poor development of the tubules and the germinal aplasia may be due to the mosaic condition, only a few cells carrying what appeared to be a Y chromosome. Hence it appears that the tubules in this patient should be regarded as poorly developed male sex elements rather than as developmental relics.

Summary

A 2·75 kg. neonate had a moderately sized phallus surrounded by a sac-like vulva. The infant died at 2 months of age and necropsy revealed normal internal female genitalia, with the vagina terminating high up on the back of the urethra, resulting in a single external opening.

Histological examination of both gonads revealed a preponderance of ovarian elements. The tunica albuginea, however, was abnormally thickened and solid testicular tubules lined with multilayered cells were seen in the deeper parts of the gonad. Some of the cells resembled Sartoli and Leydig cells.

There were 14% chromatin-positive cells in buccal mucosa. Cells having 46 and 47 chro-

omes, respectively, were found in a leucocyte culture. On karyotypic analysis an extra G was found in a proportion of these cells.

The clinical, pathological, and cytogenetic findings were interpreted as presumptive 46,XX/46,XY/47,XXY mosaicism in a hermaphrodite.

Addendum

Since submission of this paper for publication, Barreiro et al. (1969) have described a 3-month-old true hermaphrodite with similar cytogenetic findings.

References


Chaudhuri, Amala (1967). Bean extract from Phaseolus vulgaris in the culture of capillary blood for chromosome analysis. Indian Journal of Medical Research, 58, 47–50.


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A Chaudhuri, S K Chatterjee and S Sarkar

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