all features of this disorder (Naftolin and Judd, 1973). The histological findings also are in favour of this diagnosis. The gonadal structure of an immature testis lacking spermatagonia and presenting with Leydig cell hyperplasia is consistent with the findings in testicular feminisation (Ferenczy and Richart, 1972).

The nature of the tissue resembling ovarian stroma is not clear. This feature has been described before (Stenchever et al., 1969). A Masson stain did not reveal any smooth muscle characteristics. The age of the patient precludes the presence of functional gonadal tissue. Ghosn et al. (1971), in a similar case of a 25-year-old woman, classified their patient as atypical testicular feminisation, hesitating to identify ovarian stroma as such when present without follicles. Pfeiffer (1974) prefers to classify cases without functional ovarian tissue as pseudohermaphrodites. Polani (1970), however, states that the absence of functional gonadal tissue does not eliminate true hermaphroditism.

The nodules of smooth muscle found in the inguinal canal could represent either remnants of Mullerian or Wolffian origin: cases of partial suppression of the Mullerian system have been described in testicular feminisation. The gonadal structure of an immature testis lacking spermatagonia and presenting with Leydig cell hyperplasia is also consistent with the findings in testicular feminisation.

Finally, normal levels, for an adult male, of testosterone and dehydrotestosterone in a perfectly female looking patient are hallmarks of testicular feminisation, where peripheral target organs are resistant to androgens. This finding correlated well with the well-developed Leydig cells in the testis and with the sparsity of pubic hair.

Inconsistent expression of both centromeres of a dicentric Y chromosome in a child with ambiguous external genitalia

SUMMARY A newborn child with ambiguous external genitalia had evidence of internal female development on the left and internal male development on the right. Blood chromosome analysis showed three cell types: 45,X; 46,XY with the Y being submetacentric and about twice the usual size with two 'centromeric' C bands; and 46,X, dic(Y). Chromosome studies from the skin, uterus, and Fallopian tube showed almost exclusively 45,X cells. This represents the second reported patient in whom two centromeres are inconsistently expressed though present as shown by two 'centromeric' C bands.

That human dicentric Y chromosomes are not rare is indicated by the review of 16 cases by Cohen and coworkers in 1973. However, none of these or

References


subsequently recorded cases showed an inconsistent expression of both centromeres until Buchanan et al. (1976) described a mitotically unstable dicentric Y chromosome in a patient with ambiguous external genitalia and male and female internal structures. We now report a second patient with cytogenetic and structural findings similar to those reported by Buchanan et al. (1976).

**Case report**

MB (15776) was referred to UCLA Medical Center at 1 day of age for evaluation of ambiguous external genitalia. The patient was the product of a full-term uncomplicated pregnancy of a 30-year-old primagravida and a 36-year-old man.

Physical examination described an infant weighing 2400 g, length 42.5 cm, and head circumference 33.5 cm. A fine petechial-like rash was noted over the face, arms, and upper torso. There were no other abnormal physical findings except in the external genitalia. A well-formed, darkly pigmented, and rugated scrotal sac was present on the right side containing a palpable mass estimated to have a volume of 1 ml. On the left side was a structure similar to a labia majora. No masses were palpable either within this structure or along the left inguinal canal. The phallus measured 2 cm in length and had a ventral opening situated at its junction with the scrotum. Bimanual abdomino-rectal examination did not disclose the presence of a uterus.

![image](http://jmg.bmj.com/)

**Fig. 1** Note left inguinal hernia, right hydrocele seen before surgery.

Voiding cystourethrogram showed a normal bladder without evidence of reflux or presence of a vaginal structure. An intravenous urogram was normal and a pelvic ultrasound delineated a mass that had the configuration of a small uterus. No ovarian structures were visualized. 17α-hydroxyprogesterone was 0.4 ng/ml (mean for infants 1 day to 6 weeks, 2.1 ng/ml ± 0.36 (Lippe et al., 1974) and excluded a possible diagnosis of congenital adrenal hyperplasia secondary to 21-hydroxylase deficiency. Haemagglutination inhibition antibodies to rubella were positive at a dilution of 1:256 and the IgM level was 60 mg/dl. No stigmata of congenital rubella were noted.

Before scheduled exploratory laparotomy could be carried out, the infant was found to have a left inguinal hernia and a right hydrocele at the age of 2 months (Fig. 1). At operation the hernial sac on the left was found to contain a small hemi-uterus and Fallopian tube. A left-sided gonad or streak was not seen at the time of operation but the area of the left gonadal ridge was removed. There was no vaginal structure. On the right side there was a small testicle (microscopical structure confirmed by examination of a frozen section), epididymis, and vas deferens. The right hernial sac, right hydrocele, left hernial sac with uterus, and Fallopian tube were removed.

Histological examination of the removed structures was consistent with their gross appearance. In addition, an embryonic ovary was detected imbedded posterior to the Fallopian tube in the broad ligament on the left side. It contained numerous structures which were interpreted to be primordial germ cells within the ovarian stroma. On further histological review of this specimen, it was difficult to determine with certainty whether these structures contained follicular elements which, if present, would thus classify this patient as a true hermaphrodite.

The infant is alive and healthy at the age of 13 months. Surgical reconstruction of the penis is planned for the future.

**Cytogenetic studies**

Leucocytes were cultured using a whole blood micro-technique. Fibroblast cultures were established from skin, uterus, and Fallopian tube using the technique of Harnden (1974). Chromosomes were examined using conventional Giemsa staining, Q-banding with quinacrine mustard (Caspersson et al., 1970), G-banding with trypsin-Giemsa stain (Seabright, 1971), and C-banding as described by Sumner (1972).

G-banding analysis on the blood of both parents showed no abnormality. The results of the chromosome analyses on the infant are summarised in the Table. Figure 2 shows a G-banding analysis in which
Table  Chromosome results on patient

<table>
<thead>
<tr>
<th>Type of analysis</th>
<th>46,XY</th>
<th>46,X, dic(Y)</th>
<th>Total cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood, Giemsa</td>
<td>13</td>
<td>79</td>
<td>100</td>
</tr>
<tr>
<td>Blood T-G</td>
<td>6</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>Skin</td>
<td>14</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>Uterus</td>
<td>47</td>
<td>3</td>
<td>50</td>
</tr>
<tr>
<td>Fallopian tube</td>
<td>59</td>
<td>1</td>
<td>60</td>
</tr>
</tbody>
</table>

*These 46,XY cells have a large metacentric Y with only one primary constriction.

The variability of phenotypic expression in patients with a dicentric Y chromosome, as well as possible mechanisms of formation, have previously been reviewed (Cohen et al., 1973; Siebers and Vogel, 1973). The majority of patients with this abnormality show varying degrees of mosaicism. Phenotypic expression apparently depends partly on the degree of the mosaicism and partly on the extent of structural deletions of specific areas of either the long or short arms of the dicentric Y chromosome (Siebers and Vogel, 1973). Dicentric Y chromosomes are unstable and the presence of a dic(Y) is suggestive but not clearly seen. Figure 3 shows the varying appearance of the Y chromosome as shown by Q-banding and conventional staining. One centromere is present in some and 2 centromeres are present in other Y chromosomes. The Q-banding stain shows the brightly fluorescent ends of the Y chromosome. The instability of the Y chromosome is manifested by the number which have primary constrictions and the large proportion of cells which lack Y chromosomes.

Discussion

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and it is this property that contributes to variation in degree of mosaicism and hence ultimate phenotype (Cohen et al., 1973; Tuncbilek et al., 1976).

Although we cannot be certain, it seems likely that our patient was conceived as a 46, X, dic(Y) and that instability of the dic(Y) chromosome led to its loss in some cells resulting in 45, X karyotypes. If the chromosomal material between the centromeres represents only that present in short arms, it appears that very little Y chromosome material has been lost in formation of the dic(Y) when a comparison is made between the Y chromosomes of infant and father. Therefore, the expression of gonadal structure on the right probably reflects a male determining dic(Y).

Our patient is also unusual in that the full expression of two centromeres in the dic(Y) is inconsistent. However, as suggested by C-banding analysis, two heterochromatic centromeric C-bands are observed not only in the Y chromosomes with two obvious centromeres, but also in those large submetacentric Y chromosomes with only one apparent functioning Y centromere. The significance of the phenotypic effect of this instability and its influence on mitosis is not evident. Since previously reported patients with dic(Y) or large metacentric Y chromosomes did not have C-banding performed and because only a small proportion of the cells in our patient had the dic(Y), it is not clear if instability of the dic(Y) is responsible for variation in expression of the male determining portion of the chromosome. We have found only one other reported case with similar cytogenetic and phenotypic findings. Our case is similar to that reported by Buchanan et al. (1976) who showed premature disjunction of one of the centromeres of the dicentric Y using the C-bandng technique. Premature disjunction was noted in a majority of lymphocyte metaphases studied in both patients. Though it seems logical to suspect that internal instability of the dicentric Y chromosome contributes to the overall mitotic instability and thus the degree of mosaicism, it remains difficult to correlate the degree of this instability with phenotypic expression. Our case showed external asymmetry of genital organs as compared with symmetrical but ambiguous structures in the case of Buchanan et al. (1976). Internally, greater similarity could be appreciated between the two cases.

It is believed that only a small part of the Y chromosome contains the genes necessary for male differentiation and maturation (Siebers and Vogel, 1973; Tuncbilek et al., 1976) and that this locus codes for the H-Y antigen (Gerald, 1975; Silvers and Wachtel, 1977). The exact location has been in doubt and evidence has been produced to suggest that it may be located either on the short arm (Dosik et al., 1976) or the long arm (Wachtel et al., 1975). Recently Silvers and Wachtel (1977) made reference to unpublished studies by Koo, which show that the H-Y antigen is situated in regions known to be male determining on both the long and short arms of the Y chromosome and near the centromere. It would be of great interest to determine the H-Y antigenicity in both patients with dicentric Y long arms and dicentric Y short arms as an additional means of localising that portion of the Y chromosome essential for testicular formation and maturation.

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References


Deletion 14q and pericentric inversion 14

SUMMARY A woman with deletion 14q as well as inversion 14 is presented, and physical signs are compared with those of patients with deletion long arm 13. No previous case of deletion long arm 14 has been published.

Deletion Dq has been described in a number of cases. In most where banding was performed, it has, however, been found to be deletion 13q (Allerdice et al., 1969; Wilson et al., 1969; Gey, 1970; Orbeli et al., 1971; Grosse and Schwanitz, 1973; Wilson et al., 1973; Adâmek and Kašpárková, 1974; Ikeuchi et al., 1974; Orye et al., 1974; Kučerová et al., 1975; Noel et al., 1976) (Table). Against the background of these findings and the findings of partial trisomy 13, Lewandowski and Yunis (1975) have produced a phenotypic map of chromosome 13.

Wilson et al. (1969) described a presumptive case of deletion 14q, but later found that it was actually deletion 13q (Wilson et al., 1973).

Very few cases of pericentric inversion D have been described previously; 4 cases of pericentric inversion 13 (Hauksdóttir et al., 1972; Taysi et al., 1973; McDermott and Farrington, 1975), and 2 cases of pericentric inversion 15 (Cohen et al., 1967; Crandall and Sparkes, 1970) have been described, but no cases of chromosome 14 pericentric inversion.

We wish to report one case of pericentric inversion 14 as well as deletion 14q.

Subjects and methods

The proband was found in the prevalence study of all cases of mental retardation in the Århus County with a population of approximately 560 000. Chromosome examination was made on 48-hour lymphocyte cultures, and staining was done with the BUDR-acridine-orange method.
Inconsistent expression of both centromeres of a dicentric Y chromosome in a child with ambiguous external genitalia.

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