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Micropenis associated with testicular agenesis

In 1962 Bergada *et al.* described 4 boys who had small, dysgenetic testes associated with micropenis, but otherwise normal sexual differentiation. More recently, Najjar, Takla, and Nassar (1974) described a family in which 5 brothers had very small testes and micropenis. This paper describes 2 further, unrelated male infants with ambiguous external genitalia who showed features of this syndrome of 'micropenis with rudimentary testes'.

Patients

Case 1. The second child of unrelated parents, born after a normal term pregnancy. At birth it was difficult to decide the infant's sex. A minute penis consisting of a small prepuce-like skin tag devoid of palpable erectile tissue was present (Fig. 1). The urethral orifice could not be seen but urine was passed from this area. Testes could not be felt in the small, fleshy scrotum. Physical examination was otherwise normal.

FIG. 1.—External genitalia in Case 1.

The patient's buccal smear was chromatin negative, and chromosome analysis showed a normal male karyotype. At the age of 3 months, the urinary 17-oxosteroid excretion was 0.4 mg/24 h.

When the patient was 4 months old, surgical exploration was carried out (Mr. Innes Williams). A vas and epididymis were present in each groin. These structures were resected. Testes could not be identified at operation and histological examination of the surgical specimens showed no evidence of testicular tissue. In view of the extreme degree of micropenis and the operative findings, it was decided that the patient would be best raised as a girl and vulvoplasty was carried out at the age of 5 months.

Case 2. This patient is the fourth child of unrelated parents. 3 older sibs are normal but 2 further pregnancies had ended in spontaneous abortions during the first trimester. The patient was born after a term pregnancy complicated by an influenza-like illness at 10 weeks which was treated with an antibiotic. Further details of this illness are not available. The pregnancy was otherwise normal.

The patient was found to have ambiguous external genitalia after delivery (Fig. 2). The penis was represented by a small, fleshy swelling approximately 3 mm × 3 mm which was partly covered by a small prepuce. The urethra opened at the base of this structure. The scrotum was small and testes could not be felt. No other abnormalities were found on examination.

FIG. 2.—External genitalia in Case 2.

Buccal smear was chromatin negative and chromosome studies showed a male karyotype. Further investigations including intravenous pyelogram, plasma electrolytes, plasma 17-hydroxyprogesterone, and serum growth hormone were normal. The urine 11-oxygenation index was also normal. At the age of 3 weeks human chorionic gonadotrophin (HCG 5000 units) was given by intramuscular injection for 3 consecutive days. The plasma testosterone level was 21 ng/100 ml before HCG and 17 ng/100 ml 24 hours after the last HCG injection.

Surgical exploration and vulvoplasty were carried out (Mr. Innes Williams) at the age of 4 weeks. A small white fragment of tissue associated with a vas and epididymis was found in the left groin. A similar nodule was attached to the right epididymis which lay within the abdominal cavity. These presumptive dysplastic testes were removed, together with their ducts, but histological studies were not carried out on the tissues. No Mullerian structures were found at laparotomy.

Discussion

The findings reported above are similar to those described by Bergada *et al.* (1962) in 4 male children. These patients all had micropenis and the urethra opened at the tip of the penis in each case. Although the testes were very small, pre-Sertoli cells and Leydig cells were found in the 3 patients who had testicular biopsy. Wolffian structures (vas and epididymis) were present but there was no evidence of Mullerian remnants (Fallopian tubes and uterus). In the 3 patients who had chromosome analysis the pattern was male.

The abnormalities of the penis and testes in these patients were less marked than those found in our patients. In the first case described above the penis was represented by a small prepuce and in the second a minute glans and foreskin were present. Although fusion of the labioscrotal folds was complete in both cases, in one, the urethra opened at

the base of the minute glans. Testes could not be identified either at laparotomy or on microscopy in the first patient. Histological studies are not available in the second patient but the low testosterone levels found before and after HCG stimulation indicate that few functional Leydig cells were present. Like the patients described by Bergada *et al.* (1962), both cases had Wolffian structures but Mullerian derivatives were absent.

Although the aetiology of the testicular abnormality described above is not known, the clinical findings indicate that active testicular tissue had been present in early fetal life, leading to involution of the Mullerian ducts and persistence of Wolffian structures (Jost, 1953). Fusion of the labioscrotal folds was complete, suggesting that testicular failure occurred after the 12th week of fetal life and that the penile hypoplasia was related to absence of testicular androgen after this period.

Gross and Meeker (1955) have described the psychological difficulties encountered by adolescent males with marked micropenis, particularly if spontaneous virilization does not occur at the normal time of puberty. Although testosterone treatment in early infancy has been reported to increase the size of the penis in some cases (Guthrie, Smith, and Graham, 1973), it is widely accepted that some patients are best raised as females despite their male chromosomal sex. In the present cases, the decision to carry out vulvoplasty and later vaginoplasty was a relatively easy one as there seemed to be no prospect of useful penile development. The parents of both children agreed with this decision, understanding that further surgery and oestrogen therapy would be required at a later date to permit a satisfactory female sexual role. We hope that the psychological difficulties which can arise when gender reversal takes place in later infancy have been avoided as a result of this early surgery.

In less extreme cases of micropenis, decision as to the most appropriate gender for the child may be much more difficult. Present evidence suggests that plasma testosterone studies may be helpful in some of these difficult cases. Although the exact relation between plasma testosterone in early infancy and subsequent secondary sexual development is not known, Forest *et al.* (1974) have shown that plasma testosterone is raised in normal male infants and a finding of low testosterone levels which do not rise after HCG stimulation suggests that spontaneous virilization is unlikely to occur at the time of puberty. In a borderline case, such a finding would favour gender reversal as testosterone replacement therapy would probably be required if the patient were raised as a male.

Summary

This paper describes 2 male infants who were born with severe micropenis and in whom testicular tissue could not be identified at surgery. HCG stimulation in one infant was not followed by a rise in plasma testosterone. It was decided that both cases would be best raised as females, despite their male chromosomal sex.

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