The XY Female Child

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It has been known for some years that apparently female patients are sometimes found to have an XY sex chromosome complement. Morris (1953) focused attention upon the syndrome of testicular feminization in which, despite the presence of XY sex chromosomes and testes, the phenotype and secondary sexual development are female. Harnden and Stewart (1959) applied the term pure gonadal dysgenesis to an XY patient of female phenotype, without secondary sexual development; many others have since been described; a condition with some similarities has been described in association with an XY karyotype and gonadal absence (agonadism (Overzier, 1963)). A further category constitutes those patients who have predominantly female genitalia but with some degree of masculinization and who show male manifestations at puberty (partial testicular failure).

If the patient is seen for the first time about 16 or 17 years of age or more, the distinction between these conditions will not be difficult to draw from the presence or absence, nature and extent of the secondary sexual changes. If, however, the patient shown to be XY is a child with female, or predominantly female, external genitalia it becomes a matter of considerable importance to decide if secondary sexual development will occur and if it will be female or male in type. If a male type puberty seems likely, it must be prevented, since it can hardly fail to have important psychological effects upon a child who has been brought up in the female sex.

This article deals with the management of such a problem.

Clinical Features of Syndromes

A brief consideration of the clinical features of the different conditions as seen in the adult reveals differences between them which are important to the management of the child. The significant features are italicized.

Testicular feminization. The features of this syndrome in its typical form are these (Fig. 1):

- (1) Female bodily configuration.
- (2) Excellent breast development.
- (3) Absent or very scanty pubic or axillary hair.
- (4) *A normal vulva.*
- (5) *A short blind vagina with absent cervix.*
- (6) *An absent uterus.*
- (7) Testes which are abdominal, inguinal, or rarely labial in position.
- (8) A high incidence of inguinal herniae.
- (9) *A positive family history of sisters, aunts, or great aunts with similar features.*

These features are remarkably consistent, though occasionally small variations are noted. The principal variants concern the pubic hair which

FIG. 1.—An XY patient with typical features of testicular feminization.

may be moderate in extent, the length of the vagina which can vary from very short indeed to almost normal, and the positive family history which may not be obtainable.

Pure gonadal dysgenesis. This condition is more common in XY than in XX patients, but either may be affected. The patients are of normal height, or tall, with absent secondary sexual development and primary amenorrhoea (Fig. 2). The vulva is hypoplastic but otherwise normal and there is a *vagina, a uterus, and tubes*. The gonads are whitish streaks of tissue occupying the normal position of ovaries; histologically their nature cannot positively be identified.

Agonadism has similar features but there is minimal evidence of androgenic activity at some time giving rise to absence of uterus and vagina and to excessive fusion of labial folds: despite this no sign of any gonadal tissue is to be found on operation (Schoen *et al.*, 1955; Overzier and Linden, 1956; Philipp, 1956; Dewhurst, Paine, and Blank, 1963; Burns *et al.*, 1963).

XY females with masculinizing puberty (partial testicular failure). The clinical features of patients in this category are more variable than those in other groups. The external genitalia show

FIG. 2.—Pure gonadal dysgenesis in an XY patient.

evidence of masculinization in one or more of the following features (Fig. 3), *phallic enlargement, and excessive fusion of labio-scrotal folds which are pigmented and rugose*. The internal genital organs are also variable. The uterus and tubes may be present or absent. The testes vary in appearance from the near normal to the rudimentary; or one only may be recognized as a definitive structure, the other being represented by a whitish streak of tissue or being absent.

Two XY patients have been described with both ovarian and testicular tissue (hermaphrodites) (Sandberg *et al.*, 1960; Shearman *et al.*, 1964). This contingency, however, is clearly a very rare one indeed.

The significant features in the context of subsequent secondary sexual development are:

- (1) The presence of masculinization of the external genitalia.
- (2) The normality of the vulva.
- (3) The presence of a cervix and uterus.
- (4) A positive family history.

Masculinization of external genitalia in an XY individual is very strong evidence in favour of a male type puberty developing later. Clitoral enlargement of mild to moderate degree has been reported in very few examples of testicular feminization (Greenblatt, 1958; De la Harpe, 1959; Teter and Boczkowski, 1966; Dewhurst, 1967), and when it has been present the vulva has been otherwise normal. The presence of a *uterus and cervix* may similarly be taken to eliminate the likelihood of secondary feminization, and pubertal changes can be expected to be absent or male. A *positive family history* provides strong evidence of the likely type of puberty to be expected. If feminization has been noted in other members of the family with similar clinical features typical of testicular feminization, it is likely that feminization will occur again. Male secondary development in sibs with partial testicular failure is sometimes seen but a family history is less common than with testicular feminization. The type of puberty would again tell us what to expect.

Aetiology. The differences between these various conditions can probably be explained on a basis of their aetiology. This is not yet fully elucidated, but sufficient is known to suggest that it is predominantly concerned with the functions of the testis in the early embryo (Jost, 1953). These functions are apparently two:

- (1) to promote male organ (Wolffian) development (the male organizing function);
- (2) to inhibit female organ (Müllerian) development.

If testicular function fails totally in the early

FIG. 3.

FIG. 4.

FIG. 3.—External genital appearances in an XY patient aged 20. The clitoris is enlarged and the labio-scrotal folds excessively fused creating a urogenital sinus with a single external opening. Testes are in the groins. The patient was disturbed by hirsutes, deepening of the voice, and vague 'masculine' feelings and she was confused about her sexual identity. She responded well to orchidectomy and replacement oestrogen therapy.

FIG. 4.—External genital appearances in a 7-year-old XY child from whom a testis was removed at hernia repair. The resemblance to the appearances in Fig. 3 is close. The remaining testis was removed to prevent similar masculine changes and consequent mental distress at puberty.

embryo, as appears to be the case in pure gonadal dysgenesis, there is no male organ development and the child is born with normal female pelvic organs; there is no secondary sexual development at puberty because there is no functioning gonadal tissue present. If testicular function fails in part, there may be imperfect male organ formation while the vagina, uterus, and tubes are permitted to develop as well; partial intrauterine testicular failure of this kind is none the less compatible with some testicular activity at puberty, and the male type puberty may occur at least in part. Why in some such cases the uterus and the vagina are permitted to develop and in others not is not fully understood; it may be concerned with the timing of the intrauterine testicular failure or there may be some other explanation which need not be speculated on here. Testicular feminization appears to have a different explanation concerned with insensitivity to normal or near normal levels of testosterone produced by the testes. The normal male amounts of oestrogens produced by the testes, being unopposed in their action, probably bring about secondary female changes at puberty.

Presentation in the Child

The discovery of the XY karyotype in a child being reared as a female may be made in various

circumstances. A testis may be found at an operation for the repair of an inguinal hernia; sometimes the operation is an abdominal procedure which may either reveal the presence of the testis or the absence of the uterus. Masculinization of the external genitalia may be the presenting feature and should, therefore, be noted at birth, but its significance may not be appreciated and nothing may be done. If a female patient with an XY karyotype has younger or older sisters, buccal smear and chromosomal analysis are indicated which may reveal other XY females in the family. It is a theoretical possibility that a routine survey in the newborn may lead to the discovery of a chromatin negative female child who is later shown to be XY. The frequency of this must be very small indeed, for MacLean, Harnden, and Court Brown, 1961; MacLean *et al.*, 1964) found no XY child in 13,046 female babies surveyed in Edinburgh. Rarely inguinal or labial swellings may be discovered at routine examination leading to the disclosure of the XY sex chromosome arrangement.

Management

Careful examination of the external genitalia is always required. Particular attention must be paid to the presence or absence of clitoral enlargement, fusion of the labial folds, their pigmentation or

rugosity, and whether the urethra and vagina are distinguishable as separate openings. Palpation of the groins and labio-scrotal tissue should be carried out for any possible gonadal swelling. A rectal bimanual examination may be sufficient to establish the likely presence or absence of a uterus, but if this is in doubt the same examination carried out under anaesthesia may be more informative. At this examination under anaesthesia inspection of the vagina should be performed to see if it is short and blind or if a cervix is present. Inquiry should always be made of a possible family history.

If the child has entirely normal female external genitalia, a short blind vagina, and a positive family history of relatives with testicular feminization it is likely that this diagnosis can be made. Laparotomy is unnecessary. If a child has similar clinical features but no positive family history, the diagnosis of testicular feminization cannot be made with quite such confidence, but the clinical features of the normal vulva, short blind vagina, and absent uterus make this presumptive diagnosis entirely reasonable. Under these circumstances, the most satisfactory form of management is to leave the testes entirely alone and await feminization at puberty. It should be stressed that if the testes are removed, no secondary sexual development at puberty will occur. A recent personal survey of 85 patients with testicular feminization disclosed 4 examples of children destined to feminize at puberty had testes not been removed; in all, after orchidectomy in childhood, no secondary sexual development took place. Only in rare instances of testicular feminization need consideration be given to removing testes in childhood; their unusual prominence in the groins or labia rendering them liable to trauma may be such a circumstance. It may then be wise to remove them and to give substitution oestrogen therapy around the normal age of puberty; the alternative is to replace them within the abdomen and await spontaneous female pubertal development; since it will probably be necessary to perform a further operation after puberty to remove the testes (*see below*), removal and substitution therapy appears preferable.

Once secondary sexual development is complete, consideration must then be given to the advisability of orchidectomy in view of the raised cancer potential such ectopic testes are believed to possess. The likelihood of this contingency has been variously computed by different authors (Morris, 1953; Hauser, 1963; Jones and Scott, 1958), but the evidence suggests a frequency of 5% or less at some time; the risk of malignant change at a comparatively young age is likely to be far smaller.

In all other types of case, removal of testes or of testicular remnants during childhood must be seriously considered. If a uterus is present feminization alone cannot be expected; absence of secondary development or masculinization is likely depending on the extent of testicular formation in the individual case. It has been mentioned already and is worthy of re-emphasis that masculine changes at puberty must be prevented, and, therefore, unless this risk can confidently be excluded removal of the gonadal tissue is desirable. Similar considerations apply to the management of a child with masculinization of the external genitalia (Fig. 4). In such a case, however, masculinization at puberty is more likely still, since the changes which have already taken place in the genital organs are evidence of some testicular function during intrauterine life. As mentioned already there are rare instances of clitoral enlargement in patients with testicular feminization, but these are associated with an otherwise normal vulva and are in any case rare. Unless a positive family history of feminization can be obtained in a child showing such a feature, testicular removal in childhood seems wise.

The unexpected discovery of a possible testis or testes in a female child undergoing some form of surgical procedure is a difficult problem. In most instances removal of the gonad at the time is probably unwise, for its nature cannot be known for certain unless an immediate frozen section of satisfactory quality is obtained. The nature of the other gonad remains unknown if, as is generally the case, the discovery is made during the repair of an inguinal hernia. A preferable procedure appears to be biopsy of the disclosed gonad and, if it is situated in the groin, its temporary replacement in the abdomen; immediate consideration should be given to inspecting the internal pelvic organs and to biopsy of the opposite gonad if this can be located. Further operation will, of course, be required later, but the rational management of the case will be greatly facilitated by the information obtained while the original operation is in progress.

Conclusions

A child being brought up in the female sex may be shown to have XY sex chromosomes in several circumstances. The diagnosis may be testicular feminization with normal breast growth and female bodily configuration at puberty. The diagnosis may be pure gonadal dysgenesis with normal primary female development but absent secondary development at puberty; complete absence of gonads may resemble pure gonadal dysgenesis, and again there is no secondary development at puberty. Partial

intrauterine testicular failure may give rise to external genitalia which are predominantly female with a degree of masculinization as well; here, secondary development at puberty may be male in type. Features in the child which are helpful in the distinction between these conditions and which permit a reasonable assessment of the type of puberty to be expected are: the absence of the uterus, the normality of the vulva, the short blind vagina, and sometimes a positive family history which suggests a diagnosis of testicular feminization. The presence of a uterus virtually excludes female secondary sexual development alone at puberty; pubertal development is more likely to be absent or male in type depending on the degree of development of the testicular tissue present. The presence of masculinization of the external genitalia indicates that there is a distinct likelihood of male type puberty appearing.

Unless female secondary development alone can be expected with confidence, removal of the testes or testicular remains is indicated during childhood. If female puberty can be expected the testes may be left alone until after puberty when removal can be reconsidered in view of some increase in the risk of malignant change.

The accidental discovery of a testis at an unrelated surgical procedure is better not dealt with by a removal but by biopsy and, if necessary, abdominal replacement; biopsy of the other gonad may be taken also, and the nature of the internal genital organs established.

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