

Hermaphroditism: Cytogenetics, Gonadal Pathology and Gender Assignment A Case Report

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ABSTRACT

True hermaphroditism is a rare intersex disorder in which individuals possess both testicular and ovarian gonadal tissue. A case of true unilateral hermaphroditism presenting with ambiguous external genitalia, right scrotal testis and left pelvic ovotestis is herein outlined. Phallic, gonadal and genetic factors were considered before male gender was assigned. Gender assignment procedures have been questioned by intersex activists opposed to early genital surgery. Western societies have a binary perspective on gender and this leads to a stigma being placed on intersex cases. A multidisciplinary approach to this problem involving paediatric specialists in the field of endocrinology, surgery and psychiatry is necessary, along with educational programmes that promote tolerance in society to variations in gender.

Hermafroditismo: Citogenética, Patología Gonadal y Asignación de Género

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RESUMEN

El verdadero hermafroditismo es un trastorno intersexual raro en el cual los individuos poseen tejido gonadal tanto testicular como ovárico. Aquí se describe en rasgos generales el caso de un verdadero hermafroditismo unilateral con genitales externos ambiguos, un testículo escrotal derecho y un ovo-testículo pélvico izquierdo. Los factores fállicos, gonadales y genéticos fueron considerados antes de asignar el género masculino. Los procedimientos de asignación de género han sido cuestionados por activistas intersexuales que se oponen a la cirugía genital temprana. Las sociedades occidentales poseen una perspectiva binaria sobre el género y esto conduce a la estigmatización de los casos intersexuales. Se requiere un enfoque multidisciplinario de este problema, que involucre a pediatras especialistas en el campo de la endocrinología, la cirugía y la psiquiatría, simultáneamente con programas educacionales que promuevan la tolerancia de la sociedad frente a las variaciones de género.

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INTRODUCTION

True hermaphrodites are unique individuals with both testicular and ovarian gonadal tissue (1). The term hermaphrodite is derived from the Greek mythological god Hermaphroditos, son of Hermes and Aphrodite, whose body, after being merged with the nymph Salmakis, assumed a

more perfect form with both male and female attributes (2). True hermaphroditism falls within the spectrum of intersex disorders, manifesting discordance between genetic, gonadal and phenotypic sex. This spectrum includes masculinized genetic females (female pseudohermaphrodites), androgen deficient genetic males (male pseudohermaphrodites) and gonadal dysgenetics (2).

True hermaphrodites are categorized based on the type of gonadal asymmetry exhibited: true lateral hermaphrodites have one ovary and one testicle (27% of cases), bilateral hermaphrodites have both gonads as ovotestes (35% of cases) and unilateral hermaphrodites have one gonad as an ovotestis and the other as either an ovary or a testis (38% of cases) (3).

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Those entrusted with the care of hermaphrodites know that gender assignment has become an increasingly controversial subject (4, 5). In this report, the management of a case of true unilateral hermaphroditism and a review of the literature on hermaphroditism as it relates to cytogenetics, gonadal pathology and gender assignment are presented.

CASE REPORT

A newborn with ambiguous genitalia was referred to the paediatric endocrinology service at the University Hospital of the West Indies, Kingston, Jamaica. Physical examination of the external genitalia revealed a 2.8 cm phallus (normal length 2.7 cm to 5.7 cm) with severe chordee and penoscrotal hypospadias (Fig. 1). The right hemiscrotum appeared



Fig 1: External genitalia showing phallic hypospadias and hypoplastic left scrotum.

normal and contained a normally descended gonad, but the left hemiscrotum was hypoplastic with ipsilateral cryptorchidism. Pelvic ultrasonography revealed a 2.6 cm x 1.4 cm x 1.7 cm homogenous mass lying posterior to the urinary bladder, with a 1.5 cm superior cystic component. These findings pointed to possible hermaphroditism.

Chromosomal analysis revealed a 46XX karyotype, despite the phallic structure and right scrotal gonad. No signal for the *sry* male-determining gene locus was detected. Groin exploration and laparotomy were performed to facilitate gonadal biopsies. The right scrotal gonad was biopsied via an inguinal approach. During this exploration, the left fallopian tube and attached gonad were noticed protruding through the right deep inguinal ring and therefore accessible through the same wound. Through the laparotomy incision, the left fallopian tube could be seen to be connected to a rudimentary left hemi-uterus. Pole to pole biopsies of both scrotal and prolapsed left adnexal gonads were performed.

Histological examination of the right scrotal gonad showed typical features of a testis with seminiferous tubules filled with Sertoli cells and spermatogonia, all lying within loose lamina propria containing Leydig cells (Fig. 2). The

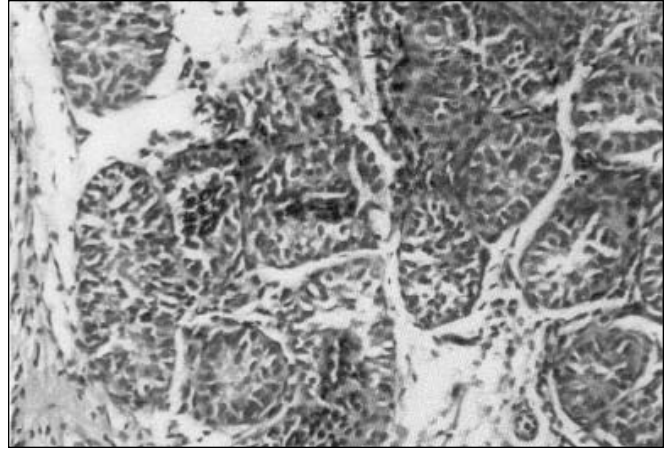


Fig. 2: Histological section from right scrotal gonad showing testicular tissue with closely packed seminiferous tubules within loose lamina propria.

left adnexal gonad however was an ovotestis composed predominantly of primordial follicles in a spindle cell stroma with a solitary focus of testicular tissue at one pole (Fig. 3). A diagnosis of true unilateral hermaphroditism was made

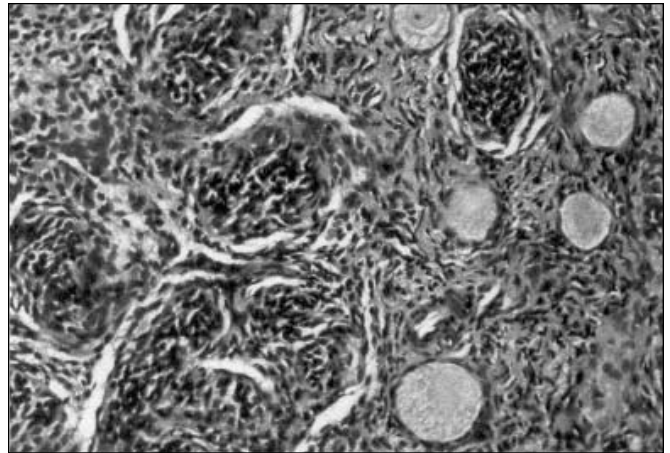


Fig. 3: Histological section from the left internal adnexal gonad showing ovotestis with seminiferous tubules (left) and primordial follicles (right).

since both a right testis and a contralateral ovotestis were confirmed on histology.

The phallic length of 2.8 cm allowed for assignment of male sex of rearing in keeping with the parents' wishes. A beta human chorionic gonadotropin stimulation test done after the gonadal biopsy showed a rise in serum testosterone level from 50 ng/dL to 235 ng/dL reflecting testicular function sufficient to sustain a male phenotype. The rudimentary uterus, left fallopian tube and left ovotestis were excised, in keeping with the recommended practice of removing contradictory gonads and internal genitalia (6). The penile hypospadias will be corrected by urethroplasty at age one year and arrangement will be made for follow-up by hospital social workers and a child psychiatrist.

DISCUSSION

The diagnosis of true hermaphroditism requires histological proof of both testicular and ovarian tissue occurring in the same individual (1, 6, 7). Ovotestes are the gonads most commonly detected in hermaphrodites, with ovaries and testes following in order of prevalence (8).

The appearance of the external genitalia ranges from normal male to normal female but many have ambiguous genitalia, manifesting phallic chordee, hypospadias and cryptorchidism (6, 7). The non-specific appearance of external genitalia results in many cases of hermaphroditism being missed at birth, only to come to light at puberty when amenorrhoea presents in patients raised as girls or breast development causes alarm in patients raised as boys (3, 6). A high index of suspicion is necessary to reduce the frequency of late diagnosis. To this end, patients with hypospadias and cryptorchidism should be subjected to early laparotomy and biopsy of gonads (6).

The distribution of ovarian and testicular tissue within ovotestes varies from case to case with one moiety predominating and the other assuming a polar or hilar distribution (8). Gonadal biopsies should therefore be performed from pole to pole extending deep into the hilum of the gonad (1, 8).

Having determined hermaphroditism, assignment of an appropriate gender becomes urgent. Traditionally, a multidisciplinary team of healthcare professionals comprised of paediatrician, paediatric endocrinologist, paediatric surgeon and paediatric psychiatrist meet with parents and assign a sex of rearing based on genital, gonadal and genetic factors (5). Phallic size and its potential to develop into a sexually functional organ have long been held to be the most important factors in the choice of male sex of rearing (8–10). Female sex of rearing is the likely choice when phallic length is below 1.5 cm because an adequate and functional vagina can be more reliably constructed in that setting than a functional penis (8).

Gonadal factors are also important in the choice of sex of rearing. Whatever decision is made, there must be adequate functioning gonadal tissue present to sustain the sex of rearing, and gonads producing contradictory hormones should be excised (6). This guided the decision to excise the left ovotestis while preserving the right testis. Malignant gonadal tumours occur in 1.91% of true hermaphrodites, most commonly arising in patients with a 46XY karyotype and in dysgenetic or undescended testes (1, 8, 10). Though the right testis was shown to be histologically normal and descended, the decision to preserve the gonad in this patient mandates long-term follow-up and screening for testicular neoplasms.

A patient's genetic sex, as determined by karyotype studies, is not always the appropriate choice for sex of rearing in hermaphrodites. The 46XX karyotype occurs in 60% to 70% of hermaphrodites (1, 2, 8), while 46XX/46XY mosaicism and 46XY genetic males are seen less commonly.

Although the Y chromosome predisposes to a male phenotype in 46XY karyotypes, a 46XX karyotype does not necessarily promote a female sex of rearing. This is because the testis-inducing *sry* locus, normally located on the short arm of the Y chromosome, can sometimes become transferred to an X chromosome during meiotic division of a primary spermatocyte (1,6). Thus 46XX patients may have not only a testis, but also normal testosterone production. Despite evident testosterone production, the *sry* gene locus was not found in this case, suggesting that subtler gene translocations may suffice to cause development of male characteristics. Mosaic karyotypes such as 46XX/46XY are thought to result from chimerism, possibly from double fertilization (involving two spermatocytes—one X and one Y) of either a bi-nucleate ovum or of an ovum and its polar body.

The process by which healthcare professionals and parents have consultations to assign gender to intersex cases is called the paternalistic approach (11). This approach is based on the concept that children are gender neutral at birth and can be made to assume male or female characteristics through a combination of psychosocial rearing and “normalizing genital surgery” in infancy (12). Patients are generally not told about their intersex status during childhood to avoid mental trauma and psychosexual conflicts (13).

Vehement opposition to the paternalistic approach has come from intersex activists led by The Intersex Society of North America (ISNA), a group constituted largely of intersex adult patients who have become disappointed with their assigned gender (12–14). These intersex activists have challenged many of the time-honoured practices of gender practitioners, including early genital surgery, which they say damages sexual sensation and disrupts intimacy in adult life (14). Applying standard ethical principles, they propose that genital surgery be delayed until when patients are able to give informed consent (13, 14). They also plead for patients to receive age appropriate medical disclosure, aggressive mental counselling and peer support therapy (14, 15). They dismiss as flawed, emphasis on phallic length and functionality in the determination of male sex of rearing (12). The merit of positions adopted by these intersex activists has been affirmed by the British Association of Paediatric Surgeons Working Party on the Surgical Management of Children born with Ambiguous Genitalia. This group, while recognizing standard protocols on gender assignment, proposed that parents be allowed to consider the option of non-operative management with psychosocial support before consenting to early genital surgery (15).

Newer concepts on the genesis of gender, focus on gender as the product of genetic and endocrine influences on the brain during intrauterine life (13, 16, 17). Workers have come to view gender as an innate quality with three aspects to it: gender role (which relates to dress, speech and gestures), gender identity (the gender of one's self image) and psychosexual preference (homosexuality, heterosexuality or

bisexuality) (13) and variation occurs on each level leading to many possibilities (11, 13). Because western societies have a binary perspective on sex and gender (13), bizarre labels are placed on anyone not viewed to be a normal male or normal female. This leads to stigmatization of intersex patients and their families (11). While it is clear that a multidisciplinary approach to clinical care is best for intersex cases, educational programmes that increase tolerance to variations in gender are also necessary.

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