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Gender Identity and Sex-of-rearing in Children with Disorders of Sexual Differentiation

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Abstract

Aim: To compare declared sexual identity to sex-of-rearing in individuals with disorders of sexual differentiation.

Methods: All 84 patients ≥5 years old in a pediatric psychosexual development clinic were assessed for sex-of-rearing and sexual identity. Diagnoses included 1) male-typical prenatal androgen effects but an absent or severely inadequate penis - 45 patients with cloacal exstrophy or aphallia; 2) inadequate prenatal androgens and a Y-chromosome - 28 patients with partial androgen insensitivity (pAIS) mixed gonadal dysgenesis (MGD), hermaphroditism, or craniofacial anomalies with genital ambiguity; 3) inappropriate prenatal androgen effects and a 46,XX karyotype - 11 patients with congenital adrenal hyperplasia (CAH).

Results: Of 73 patients with disordered sexual differentiation and a Y-chromosome, 60 were reared female 26 of the 60 (43%) declared female identity while 32 (53%) declared male identity including 18 (55%) with cloacal exstrophy, six (55%) with MGD, four (40%) with pAIS, one (50%) with aphallia, one (100%) with hermaphroditism, and two (67%) with craniofacial anomalies; two (3%) declined to discuss identity. Nine of 11 patients with CAH and a 46,XX karyotype were reared female and two reared male; six (55%) declared female identity and five (45%) declared male identity. Of 84 total patients, 69 were reared female, but only 32 lived as female, while 29 lived as male; four patients refused to discuss sex-of-living; parents of four patients rejected their declarations of male identity. All 15 patients reared male lived as male including two genetic females.

Conclusion: Active prenatal androgen effects appeared to dramatically increase the likelihood of recognition of male sexual identity independent of sex-of-rearing. Genetic males with maletypical prenatal androgen effects should be reared male.

Keywords

intersexuality; gender identity; androgens

INTRODUCTION

Disorders of sexual differentiation are a set of clinical entities typically including intersex conditions, such as androgen insensitivity syndrome in genetic males, as well as specific disorders of genital embryogenesis. such as cloacal exstrophy. Intersex is a generic term encompassing diverse neuro-endocrinopathies. These disorders include etiologies at the molecular, cellular, organ, and system levels, Central clinical questions must focus on the

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predictability of psychosexual development, especially sexual identity from infancy through adulthood. This report provides insight into the predictability of sexual identity based on neonatal sex-assignment and sex-of-rearing. It is a summary of outcomes in 84 patients ≥5 years old evaluated in a pediatric psychosexual development clinic over its 10-year history, including 50 patients not reported before: 34 of 84 patients have been previously reported[1-3].

METHODS

Ninety-four patients with disorders of sexual differentiation Who were ≥5 years old were evaluated in a pediatric psychosexual development clinic over a 10-year period. Patients with essentially no prenatal androgen effects - six genetic males with complete androgen insensitivity (cAIS) and four genetic females with vaginal atresia - were excluded from the study, Thus, 84 patients with some degree of prenatal androgen effect were evaluated for neonatal sex-assignment, sex-of-rearing. declared sexual identity, and sex-of-living. Diagnoses were available from medical records or accompanying doctors' notes or e-mails; molecular data was unavailable for patients with partial androgen insensitivity (pAIS). Diagnoses were diverse: of 11 patients with a 46.XX karyotype all had congenital adrenal hyperplasia (CAH); of 73 patients with a Y-chromosome, 42 had cloacal exstrophy or exstrophy or extrophy-variant, three had aphallia, 12 had pAIS, 11 had mixed gonadal dysgenesis (MGD), three had craniofacial-genital anomalies, and two had hermaphroditism (with ovotestes). Thirty-four patients reported previously[1-3] included 28 of the 45 with cloacal exstrophy and aphallia, three of the 11 with MGD, and three of the 12 with pAIS. Cloacal exstrophy and aphallia are errors of pelvic embryogenesis; phenotypical severe phallic inadequacy or absence is associated with male-typical prenatal androgen effects.

In this population sample 39 of 42 patients With cloacal exstrophy/exstrophy-variant and all three patients with aphallia were the total genetic male patient populations in the psychosexual development clinics (for children) at two pediatric urology centers, the University of Oklahoma Health Sciences Center and Johns Hopkins Medical Instutions. Seven of 11 patients with MGD, four of 12 with pAIS, nine of 11 with CAH, and the five with hermaphroditism or craniofacial anomalies were referred from outside centers. Thus, 56 patients were internally accrued while 28 were referred from outside centers.

Assessment questions for patients included, “Are you a boy or a girl? ...Would you rather be a boy or girl? ...Do you now live as a boy or a girl (call yourself a boy or a girl with your friends, at school, etc.)?” Questions for parents or adult patients included, “was your child (were you) raised as a boy or a girl?” Declared sexual identity was defined by patients' persistent and unwavering declarations of identity for >3 months, as reported by patients and parents. Refusal to declare sexual identity was defined by patients' persistent declining to discuss the topic for at least 1 year, with parents and others.

Data were obtained by personal interview except for one patient with exstrophy and two with MGD (<13 years old), with data obtained by parent interview only. Three adults with CAH Were interviewed by telephone. Follow-up ranged from 1 year to 12 years.

RESULTS

Of 84 patients with disordered sexual differentiation 69 were sex-assigned and reared female from birth (One died at 16 years of uncertain causes). Of 73 patients with a Y-chromosome, 60 were reared female. Of 11 patients with a 46,XX karyotype and inappropriate androgen exposure due to CAH, nine were reared female, and two were reared male, both Prader stage 5. Of 73 patients with a Y-chromosome, 45 experienced male-typical prenatal androegen effects - 42 with cloacal exstrophy and three with aphallia. Twenty-eight patients with a Y-

chromosome experienced incomplete androgen effects (ambiguous genitalia) - 11 with MGD, 12 with pAIS, two with ovotestes, and three with craniofacial/genital anomalies. All 11 46,XX patients had genital virilization abnormalities.

Sexual identity was unpredictable except that all patients reared male declared male identity, independent of karyotype. Of 60 patients with a Y-chromosome but reared female, 26 (43%) declared female sexual identity, 32 (53%) declared female sexual identity, and two (3%) persistently declined to discuss sexual identity with anyone for >1 year, after being informed by parents at about 12 years old that they were “born a boy” (see Table 1). Of those genetic male patients reared female but declaring male identity, 18 (55%) had cloacal exstrophy and one (50%) had aphallia that is, those with male-typical prenatal androgen effects - while six (55%) had MGD, four (40%) had pAIS. One (100%) had hermaphroditism, and two (67%) had craniofacial anomalies. Of 11 46,XX patients with CAH, six declared female identity, while five persistently declared male identity - one of whom declined to discuss sex-of-living status after attemapts to change sexual identity status socially at school and church were reportedly severely rebuffed (see Table 2). Eight of these genetic females were Prader stages 3 to 5; four of five, declaring male identity were Prader stage 5.

Ten patients reared female spontaneously declared male sexual identity at ages 4½ years in one patient, 7 years in two patients, 8 years in one patient, 9 years in one patient, 12 years in three patients, and 13 years in two patients, sometimes even after parents persistently rejected their declarations. Four of the five patients ≥12 years had begun estrogen administration; the fifth, a genetic female with CAH, was Tanner stage 1. Twenty-four patients with a Y-chromosome transitioned to male identity after parents informed them that they were “born a boy”. Patiets spontaneously declaring male identity already had a chosen male-typical name. All but two whose parents disclosed their birth status chose a male name within a day of parental announcement; one of these two was only 2 years old (and was reassigned male by the parents), and one, a 5 year-old, transitioned and chose a male name 3 weeks later. Clinically important, suicidal ideation has not been present in any patients while living as male.

Of 69 patients reared female, 32 lived as female, while 29 lived as male. For eight patients sex-of-living was unsettled: four refused to discuss sex-of-living, and parents of four refused their persistent declarations of male identity. All 15 patients reared male lived as male. No patient declared intermediate or indeterminate sex, although the four above who refused to declare identity also refused to identify a sex-of-living status.

DISCUSSION

Sexual differentiation disorders include intersex condition and primary problems of genital embryogenesis. A central clinical issue in neonates with major genital anomalies is assigning sex-of-rearing. Such assignation determines or dictates myriad postnatal and subsequent social dynamics, including parenting implications, social trajectories, surgical interventions, and, often, lifelong sex-hormone administration - not to mention the psychsocial and psychosexual developmental ramifications for the child. Historical clinical approaches tended to advocate fairly narrow guidelines for sex-assignment, and assumed sex-assignment would determine a child's later declared sexual identity. However, a protocol-driven standard of care has been largely impeached in recent years by the recognition of:

1. the paucity of outcome data for evidence-based approaches to these rare disorders;
2. conflicting reports when outcome data are presented[1,3-6];
3. the complexities of neurobiological and psychosexual developmental implications[3,7-9].

Rational decision-making requires evidence. Evidence-gathering requires outcome research. Outcome research has been spotty. Studies that compare outcomes across disorders of sexual differentiation may obscure what we do understand about sexual differentiation[1,3,5-8,10,11]. For example, female sexual identity might be expected in patients With cAlS. Similarly, male sexual identity might be expected in genetic males with highly virilized external genitalia. Lumping these two populations into a single outcome study or measurement would be counterintuitive - and the results not likely to benefit patients or clinicians. Interpreting data statistically across these disorders might also tend to overstate - or understate - clinically important disease-.specific characteristics or outcomes.

Additionally, study bias or methodological problems are frequently encountered. Studies may experience poor patient participation or low numbers because these disorders are so rare. Selection bias is likely to be problematic because of the rare prevalence of the conditions or of the complexities of accruing research subjects, Thus, CAH studies may lack: higly virilized patients, or MGD studies may attract behaviorally masculinized patients. Additionally, mediating and moderating facotrs may be difficult to evaluate. Such biases are difficult to eliminate.

This paper provides a large volume of sexual identity outcome data that should be clinically useful even if suffering from many of the biases mentioned above. For example, the CAH data are indeed limited but unusually skewed towards highly virilized patients. Data from patients with Y-chromosome conditions are also likely skewed, towards more behaviorally masculinized patients, although the cloacal exstrophy data were largely from the total clinic population. It is likely that many individuals with intersex were referred to the clinic precisely because of problems of psychosexual development - an important selection bias in subject accrual. However, considering diagnosis-rarity, these data are clinically relevant even if they tend to over-represent one end of the outcome range. In other words, it is important for parental and clinical decision-markers to know all potential outcomes[13].

The data presented here imply potential clinical problems if we attempt to interpret the impact or intensity of prenatal androgen effects on inadequate or incomplete genital virlization or on sexual identity in such conditions. We do not know whether there is a correlation between the degree of inadequate prenatal genital virilization and neurodevelopment - precisely because we do not know the prenatal timing, dosage, or duration of exposure to prenatal androgens in any given newborn even in normal boys or girls, although we can predict psychosexual outcomes with fairly high accuracy in the normal child Although Hines[8] as well as Berenbaum and Bailey[9] relate that female identity is the rule in genetic females with CAH, at least with mild to moderate degrees of virlization, individualds exposed to inadequate or inappropriat prenatal androgen effets in this Study demonstrated unpredictability in psychosexual outcome if they were assigned female at birth. Those few assigned male at birth and most learning of their birth status declared male identity. That two patients discovering their birth status declined to discuss sexual identity at all speaks to an added clinical risk in assigning some virilized children to female sex-of-rearing. Preventing access to medical records does not appear to be feasible.

That genetic males with male-typical prenatal androgen effects had a high likelihood of recognizing male sexual identity apparently independent of sex-of-rearing implies that absence of the penis - or the presence of a vulva - does not appear to account for sexual identity declarations. Converting such individuals to female did not appear to have relieved problematic psychosexual outcomes. Additionally, female sex-assignment of genetic males requires lifelong administration of exogenous hormones, while precluding potential fertility.

CONCLUSIONS

Genetic males exposed to male-typical prenatal androgen effects have a high likelihood of declaring male sexual identity when reared as female. Assigning them female prevents any potential fertility, requires lifelong exogenous hormone administration, and risks their transitioning to male at various ages. Female sex-assignment appears to be contraindicated in such children. Genetic males experiencing inadequate prenatal androgen effects or genetic females experiencing inappropriate androgen eftects (from CAH) had unpredictable sexual identity outcomes in this population sample, although the sample was likely skewed towards more behaviorally virlized individuals, All those reared male declared male identity. Especially if prenatal virilization is moderate to severe, childhood recognition of and transition to male identity is a possible outcome. Thus, feminizing surgery in moderately to severely virilized children may present unacceptable long-term clinical risks. It should be approached with great caution and only after parents and clinicians have carefully reviewed and applied all relevant and up-to-date research data.

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Table 1

Declared gender identity in genetic males sex-assigned female at birth*

Diagnosis	Reared female	Declared female (%)	Declared male (%)	Refused to declare (%)
Cloacal exstrophy	33	14 (42)	18 (55)	1 (3)
Mixed gonadal dysgenesis	11	5 (45)	6 (55)	-
Partial androgen insensitivity	10	6 (60)	4 (40)	-
Aphallia	2	0 (0)	1 (50)	1 (50)
Hermaphroditism	1	0 (0)	1 (100)	-
Craniofacial anomalies	3	1 (33)	2 (67)	-
Total	60	26 (43)	32 (53)	2 (3)

* All 13 patients sex-assigned male at birth declared male gender identity.

Table 2

Declared gender identity in genetic females with congenital adrenal hyperplasia

n	Reared female	Declared female (%)	Declared male (%)	Refused to declare (%)
11	9	6 (55)	5 (45)	0 (0)