Case Study: Sex Reassignment in a Teenage Girl

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ABSTRACT

Neonatal genital ambiguity creates challenges for the parents and for health care professionals. In rare circumstances, the ambiguity may be missed until the child's adolescence. The purpose of this case study is to review as a child psychiatrist junior faculty member, such a child evaluated, treated, and followed for 5 years while I was a pediatric urologist.

Neonatal sexual differentiation depends on a complex series of molecular and anatomic events within the embryonic environment. Induced by the testis-determining factor on the Y chromosome, the embryonic testis elaborates two hormones critical to further male differentiation: testosterone (T) and Mullerian inhibiting substance. Directly and indirectly, these hormones induce the development of male external and internal genitalia and the atrophy of internal female ductal structures beginning about the eighth week of embryonic life. However, the hormonal effects extend into other organ systems as well, including the central nervous system.

The sexually dimorphic brain has been a topic of hypothesis and inquiry at least since the 1971 publication by Raisman and Field first demonstrated sexual dimorphism in the preoptic area of the rat. Subsequent studies have mapped sexual differences in certain brain nuclei and structures in both animals and humans (Allen and Gorski, 1992; LeVay, 1991). Behavioral and cognitive sexual differences have been variously ascribed to biological or environmental factors, with biological proponents exploring both prenatal and postnatal hormonal influences. Prenatal hormonal contributions to sexual behaviors are less well understood in humans than in laboratory animals.

Interest patients, with prenatal hormonal anomalies, and patients with genital malformations receive endocrinologic and urologic assessment and interventions that incorporate a current understanding of such dimorphism. Sex-of-rearing independence of a child's genotype is an important clinical consideration in cases where greatly inadequate genitalia exist at birth, such as in cases of pseudophallomorphim or cloacal exstrophy. In the case presented, somewhat unusual circumstances led to a delayed recognition of genital ambiguity and illustrate the challenge of sex-of-rearing assignment in light of our present understanding of sexual dimorphism of the brain.

CASE STUDY
History
At the age of 14 years, V.P., an adolescent female Hmong immigrant, was first evaluated after dropping out of school precipitously. When interviewed at home by the school nurse (an Asian-American), V.P. stated simply, "I am not a girl, I am a boy"; the child quit school after placement in girls' physical education and chorus classes. V.P.'s first statement about gender identity was this testimony to the nurse.

V.P. was born in the highlands of Laos. There were no problems in the pregnancy or delivery. The baby was healthy, and no questions were raised as to gender or phenotype, nor did the parents ever have reason

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to question the baby’s health or physical status. Two apparently normal brothers were born later. When V.P. was 5 years old, the family moved to the United States, where school enrollment physical examinations reported no abnormalities in the parents. All of her school-age friends were boys. She enjoyed rough-and-tumble play with her brothers and occasionally engaged in such play with peers. She never played house, never played with dolls, and preferred male roles in imaginary play but would be willing to take gender-neutral roles. She denied ever dressing up in adult male or female clothing.

At the age of approximately 8 years, V.P. recognized that “something was wrong,” although she could not pinpoint what was disturbing. She discussed three feelings with no one. By age 9, she knew she was not a girl and began to withdraw from required female activities around the house; an observation separately corroborated by her mother and father. V.P. told that at about age 10 she realized, “I am a boy.” She ceased wearing female clothing and wore unisex styles until age 11, when she began the exclusive use of boys’ clothing. Her haircut similarly was switched to a unisex style and later to a masucline style.

By the age of 12 years, V.P. felt increasingly isolated from family and “different” from peers. Although her parents had been only mildly upset by her behaviors as a younger, her mother denied her free participation in female roles within the home; her father directed her to obey her mother. At the time she was evaluated, a somewhat tense truce existed between parents and child. During this time the three siblings enjoyed fairly active interactions with occasional mild physical fighting. V.P.’s younger brothers looked up to her as the oldest but denied insight into her gender feelings.

Her few friends were all Hmong and were male. When she entered the seventh grade, she attended school but skipped girls’ physical education and chorus. When confronted by the principal, she quit school completely. V.P. was able to confide in the school nurse because “you are Asian.” The nurse referred the child for evaluation.

Evaluation

V.P. entered the office in male-typical clothes. She was quiet but assertive, cooperative, and attentive and spoke only when addressed. Although appearing somewhat anxious, she demonstrated a full range of affect.

Physical examination revealed a mid-to-late prepubertal child with lean body mass and moderate musculature. Brief urologic examination results were normal. There were no dysmorphic features. Shoulders were broad. There were no abdominal masses or inguinal masses. The penis was narrow and short. The female Tanner stage was P4B1. There was clinical hypotension with a stretched thigh-to-pubic phallic length of about 4 cm, or more than two standard deviations below the male mean for age (Schulzfeld and Beebe, 1942). Labioscrotal folds were separated by smooth, nonruptured perineal tissue plus a small urogenital sinus just inferior to the clitoris. No urinary meatus was visible.

Laboratory results included a peripheral blood cell karyotype of 46, XX. A random T level was 135 ng/dL (laboratory normal range = 360 to 990 for adult male, 17 to 50 for adult female); after 4 weeks of twice-weekly injections of 1,000 units of h-chorionic, clomiphene citrate, and estradiol, serum T level was 107 ng/dL. One week later, serum T was 135 ng/dL with a dipheresestosterone concentration of 15 ng/dL and free T of 6.5 ng/dL, both comparable with the normal T level. Electrolyte levels were normal; cortisol levels were 10 µg/dL, dipheresestosterone 211 ng/dL, and prolactin 5.7 ng/dL, all in the normal range.

Magnetic resonance imaging of the brain showed no abnormalities; computed tomographic scan of the abdomen and pelvis revealed no abnormalities but a questionable small gonad at the left internal inguinal ring. Ultrasound of the pelvis revealed a probable small vagina and hypoplastic uterus with no visible gonads. Cystoscopy with a pediatric cystoscope revealed a moderate-sized urogenital sinus and a long urethra opening into the bladder with a broad bladder neck. No prostatic tissue, circulatory ducts, or vermiciform were visible. Inferiorly and inferiorly was a prepubic female glans (but without a normal prepuce, vestibule, or clitoris) and a small urogenital sinus. The phallic structure with an artificially induced erection demonstrated marked clitoral hypoplasia. Biopsy of the left gonad revealed immature testes with sparse seminiferous tubules lined by Sertoli cells and sparse Leydig cells. Laboratory,
Sex Reassignment in a Teenage Girl

Surgically, the labioscrotal folds were united, the left testis was placed in the new scrotum, the right streak gonad was excised, the phallus was straightened, and a penile urethra was constructed. Endocrine approach was testosterone therapy, due to the inad- equate response of the patient's gonad to β-human chorionic gonadotropin. Over the 2 following years V.P. voice changed, minimal axillary and linea alba hair developed, and the penis grew rapidly to a stretched phallic length of nearly 7.0 cm, with a 2.5-cm midshaft breadth while erect. Erections were of full rigidity, and masturbatory activity led to orgasm with a dry ejaculation.

Clinical Course

V.P.'s psychosexual development was progressive, if delayed from that of his peers. The child made a firm decision that he was a male and was to be referred to as "he." However, his psychosocial progress and his psychological state were somewhat unstable for a period of time. He was quite frustrated over the need for two corrective repairs for postoperative complications and, over the Medicaid program's refusal to pay for a right testicular prosthesis.

V.P.'s parents, although initially agreeing to the surgeries, subsequently were unsupportive. They felt they had lost their only daughter; with time this was accentuated. At the completion of all surgeries, V.P. was facing his medical plight alone—excluding transportation, injections, and office visits. Communication with his parents continued to be problematic. School counselors were in close contact with the child, but mental health agencies had been woefully inadequate from the beginning. Three months after his final surgery, V.P. expressed disappointment that his penis was small; he showed signs and symptoms of major depression. Attempts at enlisting psychiatric consultation at this time were difficult and were successful only after he expressed some passive suicidal ideation.

Within 6 weeks his mood had improved, and he began a series of somewhat regular though spontaneous visits for "psychosocial counseling." While his friends remained nearly all males, V.P. expressed an interest (at age 16) in a Hawaiian-American girl in his high school class. He asked for suggestions for appropriate content of conversation with a girl. Six months later he asked for guidance in how to ask a girl for a date. At age 17 he sought counsel in how to kiss and pet, and at age 18 he noted he was quite serious about a girl in his class and wished to know whether sexual intercourse was feasible. Being counseled not only in technique and positions for intercourse (in terms of his anatomical deficiency), V.P. was additionally counseled about the need for open communication with his partner about such intimate matters prior to initiating sexual contact. V.P. was "still dating the same girl" and was sexually active when seen for a visit 6 months later (age 19), after which time I received from surgical practice. His mood remained stable, his outlook was expectant, and he had never again raised questions about his gender identity.

Discussion

M.G.D. is a syndrome of variable phenotype whose presentation in any single patient most likely relates through some as yet unknown mechanisms to the mosaic cellular nature within the gonads of 45, X0 to 46, XY cells (Ménédex et al., 1995). The patient in this case presented with a fairly typical M.G.D. phenotype. He displayed prenataal asyndrymal local lateralization of production of T and of Müllerian inhibiting substance as demonstrated by the asymmetry of his internal and external genitalia. His laboratory and anatomic profile similarly reflect M.G.D. and rule out other diagnoses of interest. The creating of only 21 blood leukocyte metaphases in this patient was inadequate for establishing peripheral mosaicism (Meyers-Seifer and Chardes, 1992), but the clinical picture is consistent with gonadal mosaicism (Winters et al., 1979). What was appralling in this case was the absolute commitment of his family and social environment to seeing and raising this child as a female possibly the cross-cultural barriers and spending his early years in Laos played a significant role in maintaining an incorrect posture about this child's genotypic and phenotypic for so many years.

This child's development does, however, suggest a formulation of hypothetical mechanisms in the etiology of gender identity in a way quite compelling in light of present day neuroscientific inquiry and controversy.
Neonatal genital ambiguity is fairly prevalent in tertiary care centers, including, for example, severe hypospadias, pseudohemaphroditism, and clitoral hypertrophy. However, as evidenced by this case, gender identity has been difficult to predict in these children (Money and Nomann, 1986). Many have argued that the test masculinized a 46, XY child with ambiguous genitalia is, in the more important is it to reassign his sex of rearing to female surgically, hormonally, and socially, although Money worries about a dichotomy between gender identity and sex of rearing due to the risks that the child will learn of and be stigmatized about the test genotype. Money suggests that no child should have a sex-of-rearing assignment after the toddler age if at all possible (Money, 1994).

It is clear that gender identity in the human involves complex biological and psychosocial developmental processes, some of which take place during prenatal developmental periods and some postnatally. Controversy about the roles of the various components persists between psychological and biological schools of thought. However, this case implies that the morphic areas of the brain in these children are induced by prenatal hormonal mechanisms even when such hormonal levels may be too inadequate that only ambiguity of the genitalia is induced.

Requiring urgent consultation among pediatrics, endocrinology, surgery, and the parents, decisions about the sex-of-rearing of these newborns generally have been based on projected genital appearance, sexual function, fertility, and the desires of the family (McGillivray, 1992; Meyers-Selzer and Charette, 1991; Winstead et al., 1988). Initial interactions between the parents and the treatment team usually center on these very considerations. Yet perhaps striving to understand the etiology of gender as a long-range implication for these children should be central. V.P. maintained his recognition of male gender in spite of being raised as a girl, requiring numerous surgical adventures and enduring ongoing opposition from his family. In addition, the child's gender identity developed apparently independently of stigmatization or insights, as the parents as well as the patient denied that any suggestion was ever made to them that this child had ambiguity. A number of studies have examined children whose phenotypic gender changes at puberty, as in the case of 5α-reductase deficiency (Imperato-McGinley et al., 1979, 1991; Menerv, 1994). These studies demonstrate a similarity to this case. Yet, although this case demonstrates some of the clinical feature typical of gender problems in other interest patients (Meyer-Bahlburg, 1994), it does not fit the hypotheses of these reports. That is, social factors appear to have been strong in favor of maintaining the assigned sex, and prepubertal anatomical discordance was not recognized by family or the child. Although this child technically meets DSM-IV criteria for gender identity disorder in adolescence (GID) (American Psychiatric Association, 1994), his case is not strictly comparable to noninterest children with GID (see Meyer-Bahlburg, 1994). This case supports the notion that in spite of the effects of sociocultural factors, gender identity may be determined by prenatal hormonal influences, even though the prenatal hormonal milieu may be inadequate for full genital differentiation. In other words, this case gives evidence supporting the concept of prenatal organizational effects of sex hormones on the neurons (Barzack and Coffley, 1982), leading to gender identity and sexual orientation: prenatal T levels in this child were likely to have been very low.

Far from being a single question of the assignment of sex-of-rearing at birth, then, interest syndromes imply the need for a greater understanding by the treatment team of psychosocial as well as psychosocial implications of decision making in the neonatal period. The treatment team for these children needs to include a psychiatrist (McGillivray, 1992), but this case underscores the need for a knowledgeable child psychiatrist to assist the parents and the team at the time of their decision making. The psychiatrist can underscore the psychosocial developmental hurdles these children will face while reviewing the literature available at the time. He or she can provide consultation to the team about the mechanisms of sexual dimorphism of the brain and should be able to provide insight into the likelihood of dimorphic effects on the brain given the apparent degree of differentiation of internal and external genitalia.

During the child's psychosocial development, the child psychiatrist can offer counseling and important insights into behavioral and attitudinal phenomena of the child. He or she can be an important resource to the parents, the treatment team, and the child when questions of abnormal development or unusual behavioral reactions arise. The child psychiatrist may need to interact directly with the family incrementally or
regularly, asking in questions of parental acceptance and guilt, sibling effects, parental expectations, social interactions, and the child’s physical function and self-image and body image. Gender identity is an important issue for the child, and acceptance of the child is an important issue for the family. These concerns are child psychiatry concerns.

REFERENCES