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A Case of Ambiguous Genitalia and Unaccustomed Sexual Behavior Depicted from the Margin Notes of a Byzantine Monk

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Abstract

A case of androgynism from Byzantine literature is presented. External genital ambiguity along with intense sexual behavior, both in the active and in the passive way is commented in the context of sexual ethics of Medieval Byzantine culture, compared to the ancient Greco-Roman approach. Male pseudohermaphroditism is excluded from the differential diagnosis, given that all male pseudohermaphroditisms are cases of insufficient masculinization due to insufficient androgen production and/or action. True hermaphroditism is also excluded from the differential diagnosis, due to gradual regression of testicular tissue. Consequently, female pseudohermaphroditism due to congenital adrenal hyperplasia is the most probable diagnosis. Differential diagnosis among the forms of congenital adrenal hyperplasia is further elucidated based on the features of sexual behavior. Insights in the variability of female sexual response emerge.

Keywords: Ambiguous genitalia; Sexual behavior; Female pseudohermaphroditism; Hyperandrogenemia; Congenital adrenal hyperplasias

Odds and Ends of Ancient Culture in the Context of Medieval Byzantine Christianism

Diodorus Siculus (Diodoros Sikeliotes) was a Greek historian, born in Agyrium (nowadays Agira) of Sicily around 80 B.C. He became famous for his “Bibliotheca Historica” (1) (Historical Library), in which all historical events from the time before the Trojan War until his own era were incorporated. This colossal work consists of forty books, of which less than half have survived to the present day. Fragments of the lost books are preserved in the Library of Patriach of Constantinople Photius (858/67-878/86 AD) and the excerpts of Constantine Porphyrogenitus. It is therefore of particular importance that Diodorus included in his work, among events of such a huge historical significance as the Persian Wars or the great battles of Alexander the Great, a testimony of cases of androgynism noted in his era.

While copying a manuscript by Diodoros Sikeliotes (Diodoros Siculus), stored in the Library of Photius and refering to androgynism, Theodore Skoutariotes, a monk and scholar of the 13th century, who served as an official during the royalty of Michael VIII Palaiologos (1259-1282 A.D.) noted: "A monster of this kind appeared in our times, rumored to possess simultaneously both sexes and exhibit both active and passive sexual behavior. It was reputed to be rampant in love, even in a passive role dictated by nature and not intentionally".

The note implicates semiology encountered in the literature of Ancient Era. In Antiquity, Androgynism was synonymous to Hermaphroditism and was strictly interpretated in simultaneous or alternate possession of both sexes by the same person [1]. When referring to the social level, maleness and femaleness were similarly clearly defined: Male was identified as warrior, while female as wife and mother. Therefore, active and passive roles in sexual activity were clearly distinguished. "Male" role in sexual relationship was synonymous to the active mode, as defined by sexual intercourse and accordingly, "female" role was equated with the passive mode. Refusal, dispute or inadequate accomplishment of these roles raised doubts concerning one's biological sex [2].

In Ancient culture, an androgynous creature, possessing both sexes could only be considered as a monster. According to Aristotle, "...the living creature which does not resemble its parents is, in a sense, a monster, as, in such cases, the nature deviates from the general formula..." [3].

In Antiquity, the presence of humans possessing both sexes could trigger tremendous liabilities, doubting social organization, threatening, therefore, survival of mankind [1]. Androgynous beings either considered as prodigies or regarded to suffer from anatomical dysplasia, had no position in Ancient societies and were consequently condemned to extermination. They were considered as divergencies from the natural sex differentiation which could provide sexual role diversity and subsequently sex-determined division in social duties [1].

Reactions to this crudeness against hermaphrodites were manifested early enough in human history. Diodoros Sikeliotes being a rationalist, frequently resorted to allegory in order to present the myths with less scandalous character, aiming to combat prejudices and superstition. Diodoros Sikeliotes interpretated androgynous creatures as mere faults of the nature, adopting thus a humanitarian view of the world [1].

Despite the humanitarian point of view of Diodoros Sikeliotes, Byzantine society remained reserved towards hermaphrodites considering them as abnormal creatures of paganistic origin, given that Hermaphrodite was acclaimed as a minor deity, while ambiguous genitalia were aesthetically acceptable in Ancient paganistic art [4]. Consequently, in the context of Medieval Byzantium, "Rampant in

love" is equivalent to heightened libido, to intense or unbridled sexual desire or to inordinate indulgence in sexual activity, all of which are other words for Lust, one of the Seven Deadly Sins that were used since early Christian times in order to classify inadmissible vices aiming to instruct Christians concerning humanity's tendency to sin [5,6].

It is noteworthy that despite these social beliefs of the Byzantine culture, Theodore Skoutariotes seemed to share the humanitarian point of view of Diodoros Sikeliotes by understanding and not condemning neither hermaphrodites nor any concurrent bizarre sexual behavior [2].

The aim of this study is to use this extremely limited information, namely the ambiguous genitalia and the unaccustomed sexual behavior as tools for a "modern" medical differential diagnosis of a case from the Medieval Byzantine literature. On this context, insights in the variability of female sexual response emerge.

Medical Interpretation

Given that the manuscript copied by Theodore Skoutariotes was dated in the Roman Era, it seems plausible that Androgynism was used in its original meaning. Therefore Theodore Skoutariotes seems to describe a case of Disorder of Sexual Differentiation (DSD), namely a case of hermaphroditism, either true or pseudohermaphroditism.

There is key evidence in the author's attest. Active or passive sexual behaviors are terms compatible only with the presence of penis. Given the external genitalial ambiguity, active or passive sexual behaviors presuppose the presence of a phallus-like structure, namely a juvenile penis or even an enlarged clitoris. Regardless of the penetrating potential of the phallus, motivational male copulatory pattern is exclusively testosterone-dependent [7]. In humans, male sexual behavior has been proved to be mediated by dihydrotestosterone (DHT), given that estrogen receptor antagonists and aromatase inhibitors have not been proved to affect male sexuality [8]. Furthermore, in cases of complete androgen insensitivity syndrome, sexual behavior pattern is completely feminized, whereas in males with estrogen receptor or aromatase gene mutations, male gender role and sexual behavior are intact [9]. Consequently, the described case represents the concurrence of ambiguous genitalia in the presence of, at least, adequate androgen action.

All male pseudohermaphroditisms are cases of insufficient masculinization due to insufficient androgen production and/or action. A major impairment of all parameters of sexual activity has also been reported in 46XY male adults with partial androgen insensitivity syndrome, due to partially decreased androgenic action [10]. Consequently, male pseudohermaphroditism should be excluded from the differential diagnosis.

In true hermaphroditism, the appearance of the external genitalia may simulate those of a male or female or may be ambiguous [11], while both ovarian and testicular issues are present, frequently in the same gonad, called ovotestis or separately. In most cases, while in infancy both follicles and seminiferous tubules are clearly recognized in histological incisions, testicular tissue gradually regresses while ovarian tissue remains intact becoming, therefore, functional at puberty [12]. Given the adequate androgenic action implied by the author, true hermaphroditism should also be excluded from the differential diagnosis.

We can therefore assume that the person described was a case of female pseudohermaphroditism, namely a virilised 46XX female. Virilization of 46XX females can be caused either by an androgen secreting tumor or by intrauterine exposure to androgens or by congenital adrenal hyperplasia (CAH). An androgen secreting tumor, which could cause a severely virilising effect in affected females, should be excluded from the diagnosis, as postnatal amounts of androgens cannot have an impact on the formation of the external genitalia, which differentiate towards the male or the female direction between the 7th and 10th week of gestation. Accordingly, intrauterine exposure to androgens is not adequate for establishing a permanent effect on male sexual behavior patterns reported in adult life. According to the revised Organizational/Activational Hypothesis (2009), there is one prolonged sensitive period of decreasing sensitivity that begins perinatally and ends late in puberty [13], during which structural organization of neural circuits, organizational remodeling of the previously organized neural circuits and hormone-induced facilitation (activation) of sex-typical behaviors induce permanent modifications in brain function establishing, thus, sex differences in human behavior. Prenatal/early postnatal transient rise in testosterone has been shown to masculinize and defeminize neural circuits in males, while the absence of this transient rise in testosterone, has been shown to induce a feminine neural phenotype [13].

Therefore, different forms of congenital adrenal hyperplasia (CAH) could be the most possible culprit of androgen exposure occurring both in utero and postnatally.

Our case was characterized as having an aggressive sexual behavior both in the male and female pattern. Could this described intense or unbridled sexual desire provide a further clue in elucidating the differential diagnosis of this case?

The differential diagnosis of the three forms of CAH (salt wasting, simple virilising and late onset) is based on the observation that women with salt-wasting form of CAH exhibit low levels of sexual interest and decreased libido. Certain psychosexual parametres have been reported to be influenced in females with CAH. Childhood play behavior (sex-typed toy, playmate preferences and activity level) [14,15], sexual orientation (homosexuality or bisexuality) [14,16,17] and core gender identity (sense of self as female or male) [14-18] have been clearly shown to gravitate towards the male pattern.

However, low levels of sexual interest along with decreased libido have been reported in women with CAH. More specifically, both masculinization of sexual behavior and impairment of normal psychosexual development have been noted in women with salt-wasting form of CAH [19]. Lower self-reported sexual arousability has been noted in women with CAH compared to their unaffected sisters. Therefore, women with CAH are characterized by a "masculine" pattern in sexual behavior, while their overall sexuality is rather atypical with markedly decreased sexual drive and evident delays in reaching psychosexual milestones [20]. The latter could be attributed to some degree of desensitization of the central nervous system in testosterone due to high androgen levels acting during the crucial neuro-organizational period of fetal development [19], which is a procedure normally occurring in men. Finally, among women with CAH, higher levels of sexual arousability have been reported in simple virilizers compared to salt-wasters [19].

Additionally, given the medical knowledge of the time, classical salt-wasting form of CAH could not be compatible with life, due to adrenal crisis occurring neonatally. Therefore, the classical salt wasting form of CAH should be excluded, as our case described an everlasting lust. Given that 46XX females with late onset CAH do not exhibit

ambiguous genitalia, the case described by Theodore Skoutariotes should be a case of simple virilizing form of CAH.

The case stemming from Byzantine literature shed light to highly controversial substrates of female sexuality. In females, the experience of orgasm is not only estrogen but also androgen dependent. Actually, arousal is predominantly estrogen dependent, while orgasm itself mainly androgen dependent [21]. Indeed, androgens play an important role in female sexuality. A large body of evidence support androgen-induced enhancement of female sexual behavior: higher levels of sexual interest and desire, increased number of sexual partners, less sexual avoidance, more erotic fantasies, increased rate of initiation of sexual activity and vaginal vasocongestion [20,22-26]. Testosterone is considered to affect the dopaminergic, serotoninergic and norepinephric systems, which mediate female sexual behaviour [27-30].

Based on the Desensitization Hypothesis for testosterone effects in central nervous system [23], a substantial difference in the responsiveness to androgens between men and women could be suggested. Given that testosterone levels are less crucial for reproduction compared to men, there is no desensitization process of the central nervous system normally occurring in women. Consequently, subtle differences in androgen receptor activity due to polymorphic sites in androgen receptor gene are permitted to be expressed in evolutionary terms, suggesting variability in the sensitivity to testosterone signalling in women [25,31].

Experimental data suggest an "upper threshold" of testosterone levels above which no change in sexual response can be reported in males: No alteration in frequency of sexual activity and sexual interest was reported after administration of testosterone in eugonadal men [32,33]. Furthermore, no correlation between sexual activity, sexual interest or nocturnal penile tumescence (NPT) and upper or lower testosterone levels within normal limits has been noted [34]. On the other hand, no such "upper threshold" of testosterone levels has been noted in females, given that administration of testosterone in eugonadal women with normal sexual activity resulted in an increase in self-reported sexual arousal and vaginal vasocongestion [35].

In conclusion, female sexuality is highly complicated, with multiple factors implicated: previous sexual experiences, self-esteem, emotions, cognitive interpretation of the situation, age. Although there is no unifying hypothesis concerning female sexuality, androgens seem to play an important role in its inner experience, as females escape both the central desensitization and the upper threshold of androgenic action. Lust without androgens cannot be experienced. In the presence of androgens female orgasm presents a higher variability and diversity of in contrast to male orgasm. Furthermore, multiple orgasms of women [32] are unattainable by males, given their post-orgasmic refractory period. been characterized as linear, in contrast to non-linear female ones [36].

Therefore, in any case of DSD, all non undervirilized males can experience increased sexual behavior. On the other hand, certain degrees of virilization could be compatible with intense sexual response in females with DSD, such as the simple virilising form of congenital adrenal hyperplasia (CAH) which is the most likely diagnosis for the case described by Theodore Skoutariotes.

Theodore Skoutariotes as a humanitarian scholar deviates from the general ethical beliefs of his era which condemns female sexuality as “diabolic” by pointing out that the sexual behaviour of the case he describes was “dictated by nature and not intentionally." He, therefore, rediscovers the ancient acknowledgment of female sexual diversity and pleasure, so nicely expressed in the ancient “paganistic” myth of Tiresias.

When clairvoyant Tiresias saw two snakes mating, he killed the female and immediately was transformed to a woman, living as a prostitute for seven years. When the episode recurred, he killed the male and turned back into a man. When Zeus and Hera had a disagreement about which one, the male or the female, has more pleasure in sexual activity, Tiresias was asked and he quoted: «Of ten parts, a man enjoys one only». Hera was deeply displeased. Women’s secret was revealed.

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