

## RESEARCH ARTICLE

# Male Pseudo Hermaphroditism by Deficit in 5 Alpha Reductase : About A Case at Cnhu Hkm with Review of the Literature

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### ABSTRACT

**Introduction:** Male pseudohermaphroditisms are rare and include all anomalies in the masculinization of the external and/or internal genitalia occurring in a subject with a male karyotype. 5 alpha reductase type 2 deficiency (D5R) is a very rare condition, of autosomal recessive transmission, due to mutations in the gene coding for the enzyme 5 alpha reductase type 2 (SDR5A2) which transforms testosterone into dihydrotestosterone (THD). This deficit is manifested by an incomplete differentiation of the male genitalia which can be revealed at birth or at puberty. **Observation:** Patient 28 years old is referred to consultation for sexual ambiguity and psychological disturbance since puberty. The patient was declared female at birth and was raised as a girl. From the age of 12 he noticed the appearance of signs of male virilization. There is no consanguinity. At examination we find a patient of average height 1.65 m, TA 120/70mmHg, biacromial diameter is less than the bi-trochanteric diameter. The hairiness is gynoid, no gynecomastia. At the level of the external genital organs we have a micropenis of 3 cm in place of the clitoris and making about 6 cm in erection. The testicles are not palpated. The vulva is normal with a smooth surface, with well-developed labia majora and labia minora, a vagina of reduced diameter barely admitting 02 fingers, cervix untouched. On abdominopelvic ultrasound, the testicles are in abdominal position, a rudimentary prostate, a small uterus. The biology notes male 46XY karyotype with a high Testosterone/DHT ratio of 34.26 geared towards a male pseudohermaphroditism by enzymatic deficiency of 5alpha reductase type 2. **Conclusion:** Male pseudohermaphroditism by enzymatic deficiency of 5alpha reductase type 2 is difficult to manage. Its diagnosis is often late in our contexts.

**Key words:** Male pseudohermaphroditism, deficit in 5 alpha reductase type 2, CNHU-HKM.

## INTRODUCTION

Abnormalities of sexual differentiation, also called sexual ambiguities, are congenital anomalies in which the chromosome, the gonads of the anatomy of the sex are atypical [1]. They were first classified by Wright into four groups : female pseudohermaphroditism (XX with two ovaries), male pseudohermaphroditism (XY with two testicles mixed gonadal dysgenesis (one testicle and a remnant of gonad) or pure (presence of two hypoplastic gonads) and true hermaphroditism (presence of ovarian and testicular tissue) [1]. A careful clinical examination of any newborn will above all be of interest to define the type of sexual ambiguity, to know if there are gonads, if the genital anomaly is part of a

malformative context [1].

Male pseudohermaphroditisms are rare and include all anomalies in the masculinization of the external and/or internal genitalia occurring in a subject with a male karyotype [2,3].

5 alpha reductase type 2 deficiency (D5R) is a very rare condition, of autosomal recessive transmission, due to mutations in the gene coding for the enzyme 5 alpha reductase type 2 (SDR5A2) which transforms testosterone into dihydrotestosterone (THD) [4]. This deficit is manifested by an incomplete differentiation of the male genitalia which can be revealed at birth or at puberty [5]. The diagnostic and therapeutic approach remains uncoded [2]. Biologically, 5

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alpha reductase deficiency is defined by normal or even high levels of plasma testosterone contrasting with low levels of DHT and an increase in the plasma testosterone/DHT ratio [6].

The management of sexual ambiguity is difficult in our context and requires a multidisciplinary team including, among others, an endocrinologist, a geneticist, a urologist, a psychologist, and a radiologist.

We report a case of male pseudohermaphroditism due to 5 alpha reductase deficiency.

Our objective was to report the lived experience of the Urology Andrology department at the CNHU HKM of Cotonou in BENIN, describe the clinical and paraclinical profile of the patient, underline the difficulties encountered in our context, bring out the etiology, and underline the main features of patient care.

## OBSERVATION

Patient A. H., 28 years old, single, is referred to the CNHU HKM Urology consultation on November 17, 2022 for sexual ambiguity and psychological disturbance since puberty.

The patient with no significant history was declared female at birth and was raised as a girl. From the age of 12 he noticed the appearance of signs of male virilization with a hoarse voice, a micropenis, increased muscle growth. The medical consultation was late because of shame and trivialization. There is no consanguinity. He has a little brother who is growing normally.



**Figure 1** : Male pseudo hermaphrodite, Clinical case image.

The paraclinical examinations note :

- On abdominopelvic ultrasound :

The abdominal floor notes a liver of normal size and homogeneous echostructure, normal spleen, normal kidneys. The pelvic floor notes a normal bladder, testicles in abdominal position, a rudimentary prostate, a small uterus.

- Normal total testosterone at 7.2 nmol/l
- Dihydrotestosterone low at 0.21 ng/ml
- High Testosterone/DHT ratio of 34.26
- Normal FSH and LH
- Male 46XY karyotype

It is a male pseudohermaphroditism by enzymatic deficiency of 5alpha reductase type 2.

## AT EXAMINATION

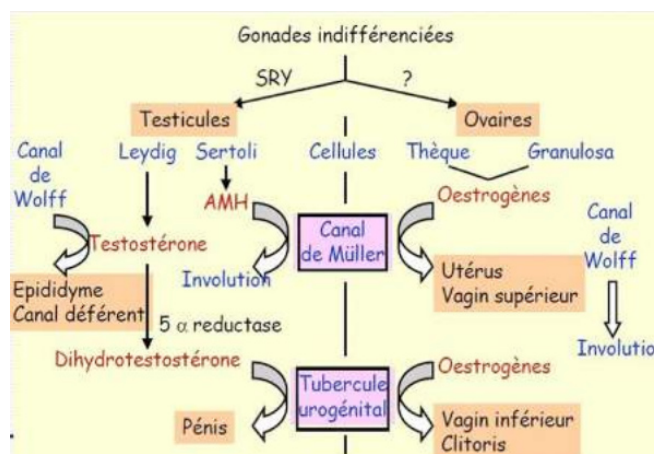
We find a patient of average height 1.65 m, TA 120/70mmHg, biacromial diameter is less than the bi-trochanteric diameter. The hairiness is gynoid, no gynecomastia.

- On the urological level, at the level of the external genital organs we have a micropenis of 3 cm in place of the clitoris and making about 6 cm in erection. The testicles are not palpated.
- Gynecologically, the vulva is normal with a smooth surface, with well-developed labia majora and labia minora.
- On vaginal examination we have a vagina of reduced diameter barely admitting 02 fingers, cervix untouched. These signs are also seen on the figure 1, our clinical case image.

## DISCUSSION

Male pseudohermaphroditism poses a diagnostic and therapeutic problem. Diagnosis is based on physical examination, hormonal assay, pelvic ultrasound (2). There are cases where laparotomy with gonadal biopsy is used for diagnostic confirmation [7].

Discovery at birth is rare. Most patients are declared female at birth and have a 46XY karyotype [6,8]. The observation is often made at puberty by signs of virilization with growth of the testicles and penis [9]. Patients generally consult a few years after puberty for sexual ambiguity and/or primary amenorrhea. At the prepubertal age the syndrome can be discovered on the occasion of an inguinal hernia, hypospadias and/or micropenis [4]. The notion of consanguinity is variable. It was absent in our patient. Nestor Gislain et al. described a case of 46XYY male pseudohermaphroditism with micropenis. The sexual differentiation is controlled by hormonal factors like on the figure 2.



**Figure 2:** Hormonal factors controlling sexual differentiation [10]

Disorders of androgen action is the main cause of male pseudohermaphroditism and includes androgen insensitivity, 5 alpha reductase (D5R) deficiency, enzyme block mainly 17beta HCG [9,11]. The other causes are represented by mixed gonadal dysgenesis (PRADER 4 or 5), Leydig cell agenesis, testicular hormone synthesis defects (Leydigian insensitivity to LH, testicular steroidogenesis disorder, antiMüllerian hormone deficiency), the feminizing testis which is the complete form of androgen insensitivity [3]. Y chromosome micro deletions have also been reported, as well as amino acid substitutions [12].

The Testosterone/dihydrotestosterone ratio is helpful in strongly suggesting the diagnosis of D5R. In our case, this ratio was high, greater than 20, guiding the diagnosis of 5 alpha reductase deficiency. These Disorders of Sex Development (DSD) 46XY result from mutations in the SRD5A2 gene, located on chromosome 2p23, which codes for the steroid 5alpha reductase 2 [13,14]. 5 alpha reductase is an enzyme that transforms testosterone into dihydrotestosterone essential for the development of male genitalia including the prostate during embryonic life [4]. This deficit is characterized by female genitalia with a certain degree of masculinization, clitoromegaly and a bifid scrotum corresponding to pseudovaginal perineoscrotal hypospadias. Its prevalence is rare [5]. Our patient presented with a micropenis with a well-developed vulva and intra-abdominal testicles.

FSH and LH levels were normal.

The abdominopelvic ultrasound is the first-line examination for the exploration of the internal genital organs. Genitography still has limited indications today, in particular the detection of fistulas. MRI makes it possible to take stock of the male or

female genital organs present or absent, to specify their seat (non-palpable gonads), their shape, size, contours as well as their signal and the impact on the organs in this vicinity [1]. Our patient had not had an MRI because of the cost in our context.

The management is difficult and a discussion must be made between the medical staff and the patient for the maintenance of a sex [5,14]. The treatment is both hormonal and surgical with phenotypic improvement [2,8,6,15]. Psychological follow-up is necessary [11,16]. But the analysis raises the negligence, the ignorance or the ignorance of the parents vis-a-vis a sexual ambiguity or the arbitrary choice of the social sex according to the will of the parents without medical approach poses heavy problems for the insertion of this individual in the company [17].

Patients rarely choose the female sex because of the virilization of the male genitalia which takes over. Patients not subjected to orchiectomy in childhood choose the male sexual phenotype. Patients who chose the male sex adapt better socially and sexually than those who chose the female sex, but their main problem was the micropenis, which is a source of significant psychological impact [13].

In our patient who chose the male sex, we initiated a treatment with Dihydrotestosterone. Surgical correction of masculinization is considered. Psychological support is provided.

## CONCLUSION

Male pseudohermaphroditism is a rare pathology and difficult to manage. Its diagnosis is often late in our contexts. It often goes unnoticed at birth. Pseudohermaphroditisms often pose diagnostic and therapeutic problems. Steroid 5 alpha reductase deficiency should be considered not only in sexreversed patients with female or ambiguous phenotypes, but also in those with mild symptoms of undermasculinization, such as those seen in patients with hypospadias and/or micropenis [12]. MRI provides the most accurate anatomical assessment possible. Treatment decisions are made by a multidisciplinary team and depend on the anatomy of the external genitalia and the possibility of surgical repair.

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