

The Preferred Approach to a Male Pseudohermaphroditic Patient with 17-Hydroxylase Deficiency

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ABSTRACT

17-hydroxylase deficiency is the rarest variant of congenital adrenal hyperplasia, which causes male pseudohermaphroditism (MPH). MPH is a type of intersex in which the testes are present and cryptorchid, with 46, XY, and the patient has male genotype and female phenotype, with widely varying degrees of feminization. Gonadal evaluation and resection are important in order to rule out malignancy. When gonadal evaluation by radiologic imaging with pelvic ultrasonography, computed tomography or magnetic resonance fails, laparoscopy could be the appropriate and safe route for evaluation and also treatment. In recent years, laparoscopy has been used for the evaluation and resection of the gonads in patients with pseudohermaphroditism. It is advantageous because it is a minimally invasive approach and has better cosmetic results. Herein, we present a pseudohermaphroditism case in which evaluation and management was done by laparoscopic route.

Key words: Gonads, Pseudohermaphroditism, Laparoscopy

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ÖZET

17 hidroksilaz eksikliği konjenital adrenal hiperplazinin en nadir şekli olup, erkek psödohermafroditizmine (MPH) neden olur. MPH bir interseks tipi olup testisler mevcut ve kriptosidiktir; hasta 46 XY erkek genotiplidir ama değişken derecede feminizasyon gösteren kadın fenotiplidir. Malignansiyi ekarte etmek için gonadların değerlendirilmesi ve rezeksiyonu önemlidir. Gonadların değerlendirilmesinde pelvik ultrasonografi, bilgisayarlı tomografi veya manyetik rezonans ile radyolojik görüntüleme yöntemleri yetersiz kalırsa laparaskopi hem değerlendirme hem de tedavi için doğru ve güvenilir yöntem olabilir. Günümüzde laparaskopi psödohermafroditizmlili hastaların gonadlarını değerlendirme ve gonadların rezeksiyonu için laparaskopi kullanılmaktadır. Laparaskopi minimal invaziv bir yöntem olduğu ve daha iyi kozmetik sonuçları olduğu için avantajlıdır. Bu makalede, değerlendirme ve yönetimi laparaskopiyle yapılan bir psödohermafroditizm olgusu sunuyoruz.

Anahtar kelimeler: Gonadlar, Psödohermafroditizm, Laparaskopi

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INTRODUCTION

Male pseudohermaphroditism (MPH) is a type of intersex in which the testes are present and cryptorchid, with 46, XY, and the patient has male genotype and female phenotype, with widely varying degrees of feminization. There are several causes, such as inborn errors of testosterone biosynthesis; Leydig cell aplasia/hypoplasia, androgen insensitivity syndrome (AIS), congenital adrenal hyperplasia (CAH), and persistent Müllerian duct structures (PMDS). CAH is an autosomal recessive inherited disorder characterized by loss of activity of one of the enzymes necessary for adrenal steroidogenesis. 21-hydroxylase (21-OHD) deficiency accounts for more than 90% of all cases and may be complete or partial, causing virilization of the fetuses^[1,2]. 11-beta-hydroxylase deficiency accounts for 5 to 8% of cases of CAH, also causing virilization of external genitalia^[3].

The last and the rarest variant of CAH is 17-hydroxylase deficiency described in the 1960s in patients with sexual infantilism and hypertension, and also in the setting of MPH^[4,5]. In 17-hydroxylase deficiency, there are alterations in the CYP17 gene, encoding the P450C17 enzyme, which plays a central role in steroidogenesis^[6].

Patients with 17-hydroxylase deficiency have reduced plasma levels of cortisol, androgen and estrogen, with impairment in adrenal and gonadal steroidogenesis. Although patients with 17-hydroxylase deficiency have decreased cortisol production, they do not have signs or symptoms of adrenal insufficiency due to elevations of corticosterone and glucocorticosteroids.

In recent years, laparoscopy has been used for the evaluation and resection of the gonads in patients with PH. It is advantageous because it is a minimally invasive approach and has better cosmetic results^[7-9].

Herein, we present a case with 17-hydroxylase deficiency, in whom gonadal evaluation and resection were done by the laparoscopic route; the gonads could not be located with radiologic imaging.

CASE REPORT

A 17-year-old female patient applied to our clinic with primary amenorrhea and weakness. On the routine physical examination, it was detected that she had only breast buds, but no breast tissue formation, and axillary and pubic hairs were absent. The labia majora were present, but fused on the anterior side.

The clitoris and the labia minora were absent, and the vagina was a blind pouch. The serum levels of sex hormones are shown in Table 1. The serum levels of estrogen, testosterone, cortisol, dehydroepiandrosterone sulfate (DHEAS), and 17-hydroxyprogesterone (17-OHP) were all decreased, but follicle stimulating hormone (FSH), luteinizing hormone (LH) and progesterone were increased. The serum level of adrenocorticotropin hormone (ACTH) was marginally elevated. The serum level of aldosterone was also elevated. The patient had hypokalemia (2.9 mmol/L) and metabolic alkalosis. During the adrenocorticotropin stimulation test (250 µg ACTH), there was no increase in the serum levels of cortisol, testosterone, 17-OHP, or DHEAS. X-rays of the patient assessed a 10-year-old bone age, which was also compatible with hypogonadism. Since the patient applied with amenorrhea, genetic karyotyping was also ordered. The result was as 46, XY, but the patient had been reared as female. The pelvic ultrasonography revealed neither uterus nor gonads. Then, abdominal computed tomography (CT) was done, but no gonadal tissue could be determined. In magnetic resonance imaging (MRI) of the patient, neither uterus and cervix nor ovaries or testes were determined. Therefore, for further evaluation of the anatomy of the internal genitalia and to confirm the existence of the gonads, laparoscopic evaluation was done. Under general anesthesia with endotracheal and nasogastric intubation, the external genitalia was re-evaluated, and the entire abdomen and the external genitalia of the patient were cleansed. The classical steps for laparoscopic surgery were followed, i.e. insufflation with a Veress needle inserted infraumbilically, and insertion of a 10 mm umbilical trocar for laparoscopic evaluation, and one 5 mm suprapubic trocar and one 5 mm left lumbar trocar for therapeutic procedures. On the laparoscopic view of the patient, bilat-

Table 1. Serum hormone levels of the patient

Testosterone	19.13 ng/dL (14-76)
Cortisol	1.46 µg/dL
DHEA-SO ₄	< 15 µg/dL (10-391)
Growth Hormone	1.89 ng/mL (0.014-5.21)
Somatomedin C	28 ng/mL (49-550)
FSH	64.5 IU/mL
LH	52.62 IU/mL
PRL	3.28 ng/mL
E2	19.64 pg/mL
P	6.09 ng/mL
Dihydro testosterone	68 pg/mL

eral undescended testes, the atrophic seminiferous tubules and the ductus deferens were seen on the proximal part of the inguinal canal (Figure 1); both were removed laparoscopically and the specimen was sent to pathology. The pathologic evaluation of the specimen was compatible with testes (Figure 2,3).

DISCUSSION

Phenotypic female patients with XY karyotype are known to be at increased risk of developing gonadal malignancies, which may increase up to 25% for dysgenetic gonads.

Furthermore, in the presence of a uterus, the risk of endometrium carcinoma also increases; therefore, gonadectomy and hysterectomy are surely indicated for patients with 46, XY karyotype and female phenotype^[10,11]. When detected earlier, especially in the childhood period, gonadectomy is also indicated to prevent virilization^[12].

For years, the traditional means of determining the gonadal localization was laparotomy, but in the last decade, laparoscopic evaluation and treatment have been used more frequently in place of laparotomy and other surgical approaches^[13].

The gonadal visualization can be made by radiologic imaging via pelvic ultrasonography, CT or MRI. Then, the gonadal exploration should be done by laparotomic or laparoscopic route to prevent malignant transformation. In our case, the gonads could not be visualized radiologically, and laparoscopy was preferred for further evaluation. The advantages of laparoscopy over laparotomy and open surgery are rapid recovery, minimal blood loss, shorter hospital stay, and minimum psychological trauma. Localization of the gonads was also found to be easier and faster by laparoscopy when compared to gonadal laparotomy due to the better visualization of the abdomen and pelvis. This makes the laparoscopic route a good alternative to the traditional laparotomy and gonadectomy^[14]. The localization of the gonads is important for choosing the surgical route. Generally, gonads located in the inguinal canal are removed by laparotomic route, but if the localization of the gonads is in the proximal part of the canal, as in our case, the laparoscopic route may also be helpful.

Yu et al. stated that laparoscopy has an important role in defining the internal ductal and gonadal structures to confirm the diagnosis, and that it serves as an efficient method for gonadectomy and removing structures contrary to the assigned gender^[8].



Figure 1. Laparoscopic view of testes, the atrophic seminiferous tubules and the ductus deferens on the proximal part of the inguinal canal.

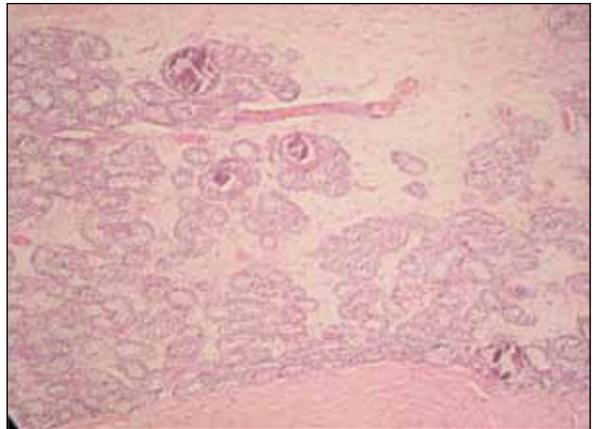


Figure 2. Atrophic seminiferous tubules surrounded with Sertoli cells and calcifications in the lumen [hematoxylin & eosin (HE), X40].

In conclusion, we present a male PH patient with 17-hydroxylase deficiency, which is a very rarely seen endocrine disorder, in which the gonads were visualized only by laparoscopy. Laparoscopy was used both for diagnosis and surgical gonad resection. We advise clinicians to keep in mind that radiology can fail in the localization of the gonads. Laparoscopy can be used as a safe approach for diagnosis and management.

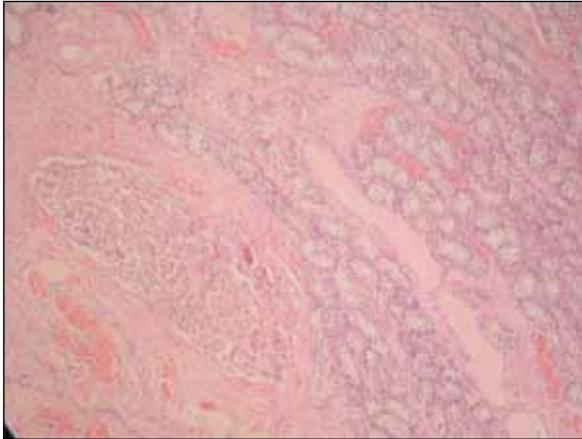


Figure 3. Proliferation of the Leydig cells (HE, X40).

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