Case Report
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BILATERAL ANORCHIA

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Abstract

Anorchia is a syndrome characterized by unilateral or bilateral absence of testicular tissue. At puberty, growth and development are normal but secondary sexual development fails to occur if anorchia is bilateral.

We present the case of a 21 year-old male with a late diagnosis of bilateral anorchia. The diagnosis was suggested by a bilateral empty scrotum, in a patient with male phenotype and poor secondary sexual development and established by karyotype analysis, hormonal profile and surgical exploration. The lack of testosterone response to hCG stimulation is the hormonal hallmark of bilateral congenital anorchia. In the absence of any information about germinal cell presence, bilateral excision of the testicular nubbins, implantation of testicular prostheses and hormonal replacement therapy were indicated.

Key words: bilateral anorchia, bilateral cryptorchidism.

INTRODUCTION

Anorchia is a syndrome characterized by unilateral or bilateral absence of the testicular tissue. Prevalence of bilateral anorchia is 1 in 20,000 males (1).

The etiology of the disease is yet incompletely understood. Traumatisms, vascular insufficiency, genetic factors, or infections were incriminated alongside other unknown factors (2). Whatever the cause, disappearance of testicular tissue occurs prenatally, after gestational week 16. The presence of Wolffian derivatives and the absence of mullerian derivatives certify the presence of some testicular tissue between 14 and 16 weeks of gestation (3).

In these patients, growth and development are quite normal until puberty when secondary sexual development fails to occur. In the absence of androgen replacement therapy, a eunuchoid pattern appears. Gynecomastia is absent (4).

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The hormonal profile involves markedly elevated gonadotropins, while serum testosterone concentration is quite low and does not rise after chorionic gonadotropin (hCG) stimulation (5). Chromosomal analysis reveals a 46XY karyotype and negative Barr test (6). Imaging studies show the absence of testicular tissue and normal Wolffian derivatives. Deferent ducts and testicular arteries end blindly, or in the conjunctive stroma of the scrotum or inguinal channel (7).

Bilateral anorchia must be differentiated from bilateral cryptorchidism. Normal serum gonadotrophins, and testosterone concentration that rise following the stimulation with chorionic gonadotrophin are indicative of bilateral cryptorchidism (8). The complications of bilateral anorchia are derived from androgen deficiency: infertility, difficult social insertion, or osteoporosis. Medical treatment consists of androgen replacement therapy which ensures the development and maintenance of secondary sex characteristics. Psychological support is frequently needed, so as testicular prosthesis.

CASE REPORT

The patient M.F., aged 21, originating from a rural area was diagnosed with bilateral anorchia when aged 20. He was the only child, born after a normal pregnancy at 39 weeks. The presence of genital external male organs, but the absence of scrotal testicular tissue was ascertained at birth. Similar or genetic diseases were not known to be present in any relatives. Urological examination was requested at the age of 16, because of bilateral absence of testicular tissue in the scrotum. Secondary sexual characteristics were also absent. An ultrasound examination established the diagnosis of bilateral cryptorchidism. Therefore, treatment with oral testosterone undecanoate 80 mg/day was initiated, and maintained for 1.5 years. Because of the absence of any significant clinical answer, the patient was referred to the department of Endocrinology.

Physical examination showed: height=170 cm, weight=62 kg, BMI=20 kg/m^2, pubis-to-floor height greater than crown-to-pubis height, underdeveloped muscular mass, absent facial and torso hair, sparse pubic and axillary hair, microphallus with stretched penile length 2 SD below the mean for age (Table 1). The scrotum was hypoplastic, without wrinkling, and testes were not palpable. The hormonal profile showed markedly elevated gonadotrophins, low testosterone with no response after the hCG stimulation test (hCG, 1000 UI, im daily for three days): basal testosterone was 0.394 nmol/L, while after hCG, 0.392 nmol/L. Prolactin and thyroid hormones were normal (Table 1).

Knee X-ray revealed the presence of active growth plates. Bone age was slightly delayed, -1.2 SD. An ultrasound examination confirmed the absence of the testes from the scrotum. At the upper pole of the scrotum, a hypoechogenic ovoid mass with a maximal diameter of 7 mm was seen adjoining bilaterally the tubular structures.

The diagnosis of bilateral anorchia was established. In the absence of clear

Table 1. Clinical and hormonal profile

Parameters	Achieved values	Normal ranges
Height (cm)	170	
Weight (kg)	62	
Pubis-to-floor height (cm)	92	
Crown-to-pubis height (cm)	78	
Testosterone (nmol/L)	0.394	9.9-27.8
FSH (UI/L)	78.6	1-10.5
LH (UI/L)	21.6	1-5.8
Prolactin (ng/mL)	8.7	2-12
TSH (μUI/mL)	2.4	0.5-4
FT4 (pmol/L)	13.6	12-22

information regarding the histology of the two masses, and taking into account aesthetical reasons, total ablation of the masses was performed and, concomitantly, testicular prostheses were placed in the scrotum.

The consequent macroscopic examination revealed the bilateral presence in the inferior portion of the inguinal duct, of a dense mass, 7/9 mm respectively 5/8 mm wide, distally to the ductus deferens and the testicular vessels. The microscopic examination revealed the presence of connective tissue containing some atrophic tubular structures, without Leydig or germinal cells (Figs 1 and 2).

Medical treatment consisted of androgen replacement therapy with testosterone undecanoate, 1000 mg intramuscularly every three months. Before treatment, the patient complained about the relatively reduced exercise tolerance, lack of sexual arousal, and psychological discomfort, all of which substantially improved after 3 and 6 months of therapy. Unfortunately, infertility continues to be an important unsolvable issue.

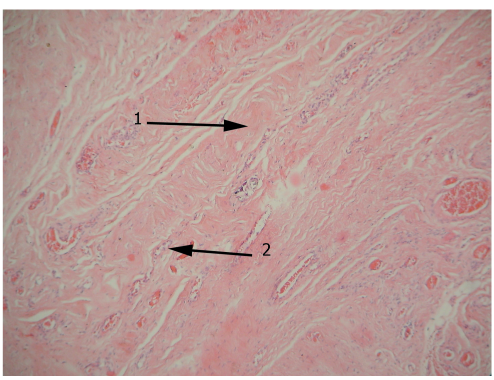

Figure 1. Haematoxylin-eosin (H-E) staining (objective 4X). Atrophy of testicular tissue, with presence of connective tissue (1) and vessels only (2).

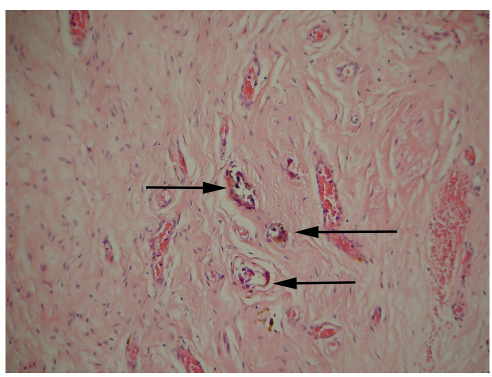

Figure 2. H-E staining (objective 20X). Presence of three tubular atrophic structures surrounded by haemosiderin pigmentation.

DISCUSSION

The presence of testicular tissue between the 12th and the 14th week of gestation, leads to the normal male development of internal and external genitalia. The absence of testicular function between the 8th and the 10th week of gestation leads to varying degrees of undervirilisation. If testicular tissue does not develop within 8 weeks of gestation, the differentiation of genital internal and external organs is shifted towards a female pattern (9). In our patient, loss of testicular function occurred probably after the 14th week of gestation. The responsible mechanism could not be established by anamnesis or after surgical intervention. Although there are some studies concerning the involvement of genetic factors in patients with congenital anorchia (10), other studies support the idea that genetic factors are probably not important in determining this condition. A recent study showed the absence of mutations of the SRY gene, of the INS*L3* gene –which is required for normal testicular descent–, and of the *INSL3* receptor gene (*LGR8*) in a cohort of 14 male patients with anorchia (11) but SF-1 haploinsufficiency was also recently reported. However, further genetic and molecular analysis is required, and it appears therefore important to take advantage of a very powerful tool, the DNA microarray analysis, in order to identify new genes and the molecular pathways related to congenital anorchia (12).

Impalpable testes at birth impose a complex medical assessment in order to ascertain the cause and the therapeutic schedule (13). Clinical findings, however, are not enough to establish the diagnosis, which must be confirmed by endocrine evaluation and stimulation tests such as the hCG test. In particular, this test is done to assess the presence and the secretory ability of testicular tissues, playing a pivotal role in the diagnostic of bilateral congenital anorchia. Measurements of inhibin B and AMH have also proven value in prepubertal patients, in which gonadotropin levels are low after the first six months of life (14). In our patient, the hCG test demonstrated a lack of testosterone response, confirming the absence of both testes. AMH would be irrelevant in this case considering the patients age. According to previous studies surgical exploration can be a convenient solution, and it is especially helpful in unilateral anorchia (15). In our patient, surgical exploration failed to find any testicular elements or mullerian structures, certifying once again the diagnosis of bilateral anorchia.

Although bilateral anorchia is frequently associated with the absence of secondary sexual development at puberty, occasional patients will undergo partial spontaneous virilisation at puberty. This phenomenon can be explained by the presence of functional Leydig cells in although they are not associated with testicular germinal epithelium or stroma in the mass of connective tissue adjacent to the ductus deferens and testicular vessels (16). Our histological examination of the tissue masses presumed to be testes failed to detect any stromal elements, seminiferous tubules or Leydig cells. According to update studies, the presence of functional Leydig cells in the testicular tissue in patients with anorchia varies between 0 and 16% (17). Therefore, it seems preferable to preserve the testicular tissue in completion to androgen replacement therapy when no germinal cells are present. In our case, we agreed on ablation of the testicular masses because of their convenient surgical approach and of the expressed patient option for testicular prosthesis.

CONCLUSIONS

Bilateral absence of testes in the scrotum at birth imposes a complex multidisciplinary evaluation. The hormonal profile, hCG stimulation test, ultrasonography and surgical exploration must be performed to confirm the diagnosis. Bilateral excision of nubbins and implantation of testicular prostheses associated to androgen replacement therapy is the most cautious decision in the absence of information concerning the presence of germinal cells in the testicular rests.

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