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CASE REPORT

COEXISTENCE OF LEYDIG CELL TUMOUR AND SERTOLI CELL-ONLY SYNDROME WITH AN INCOMPATIBLE HORMONE PROFILE AND AZOOSPERMIA

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Abstract

Leydig Cell Tumor (LCT) is very rare in adults. It constitutes only 1% of total testicular tumors. LCTs can produce steroid hormones such as estrogen, progesterone, and testosterone. Sertoli cells are found in seminiferous tubules, they are part of the blood-testis barrier. Sertoli Cells Only Syndrome (SCOS) also known as germ cell aplasia is characterized by azoospermia in which the seminiferous tubules of testicular biopsy are lined only with Sertoli cells. The expected hormone profile in SCOS is increased FSH with normal T and LH. The expected hormone profile in LCT is increased/normal FSH and LH with increased T or E2. A patient presented to our clinic with a well-circumscribed mass in his right testicle and underwent radical orchiectomy. Tumor markers were negative. Azoospermia was detected in the spermiogram. T and E2 were normal, FSH, and LH were high. Right radical orchiectomy was performed. A combination of LCT and SCOS were reported in pathology results. Azoospermia cases secondary to high androgen levels are frequently encountered in LCTs. As in the case we have presented, two different testicular pathologies may present at the same time and create an unexpected hormonal picture. Such situations can cause the laboratory to mask the clinical truth.

Keywords: Leydig Cell Tumour, Sertoli Cell-Only Syndrome, Testicular tumors, Azoospermia, Hormone Profile.

INTRODUCTION

Testicular tumors constitute 1-1.5% of adult tumors. Leydig Cell Tumours (LCT) is seen in 1% of testicular tumors (1). Although the majority of LCTs are benign, 10-20% of them are malignant and have the potential for metastasis. Eighty percent of the cases are seen in adults (2). LCTs originate from Leydig cells and are included in the class of sex cord-stromal tumors. They are usually unilateral.

In 20% of cases, endocrine anomalies secondary to the steroid hormones produced from Leydig cells are observed. Changes can be seen in secondary sex characteristics such as precocious puberty, hirsutism, and gynecomastia in children. In adults, erectile dysfunction, infertility, and testicular atrophy are changes due to hormonal anomalies.

LCTs are neither radiosensitive nor chemosensitive. Although the current treatment is orchiectomy in general, there are recent publications that TSS is a safe treatment in selected patients. TSS can be applied especially in children, infertile and bilateral tumors. In our clinic, since almost all testicular tumors are treated as potentially malignant, orchiectomy is mostly applied to obtain the best oncological result.

Sertoli cells are found in seminiferous tubules, they are part of the blood-testis barrier. SCOS is also known as Del Castillo syndrome and germ cell aplasia. It is an important cause of infertility. Spermatogenesis is completely absent or severely reduced. Most patients have normal testicles and hormone levels. The diagnosis can only be made by testicular biopsy.

We present a case with LCT accompanied by SCOS.

CASE PRESENTATION

A 23-year-old single, sexually active male applied to our clinic when he noticed a painless swelling in his right testicle 1 day ago. Except for swelling, there was no redness or sensitivity in the scrotum. He did not describe erectile dysfunction. No gynecomastia was observed. The examination of the circumcised penis was normal. The left testicle and appendages were normal, and there was a palpable, irregularly demarcated stiffness 2.5 cm-in-diameter at the upper

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pole of the right testicle.

On testicular ultrasonography, the left testis was reported as 12 cc and normal, the right testis was reported as 16 cc with a 27x20x19 mm hypoechogenic solid mass with lobulated contours in the upper pole. On Doppler examination, the mass was found to be moderately hypervascular. Testicular tumour markers are displayed in Table 1. No anomaly or pathological lymph node was detected in the lower and upper abdominal computed tomography. Orchiectomy was planned for the patient. Before the procedure, it was decided to perform sperm cryopreservation so that the patient was single and not to affect prospective fertility. Azoospermia was detected according to the patient's sperm test. Hormone levels are shown in Table 1. There were no detected abnormalities in chromosomes and azoospermia factor in the region of chromosome Y.

Right radical orchiectomy was performed. No complications occurred during or after the operation. On macroscopic examination; a nodular gray-white, well-circumscribed tumoural mass with a diameter of 2.5 cm was observed in the upper part of the testicular specimen. Microscopically, in neoplastic testicular tissue, polygonal cells with eosinophilic cytoplasm and uniform nuclei were seen. Sertoli cells with germ cell aplasia were observed in the neighboring testicular parenchyma and the basement membrane was thickened (Figs 1-5). The patient was diagnosed as a coexistence of benign LCT and SCOS with the results of clinical, hormonal, and histopathological studies.

Physical examination of the patient in the 1st month control was normal, and erection quality was good. Hormone levels are seen in Table 1. Azoospermia persisted in the 4th month control spermiogram.

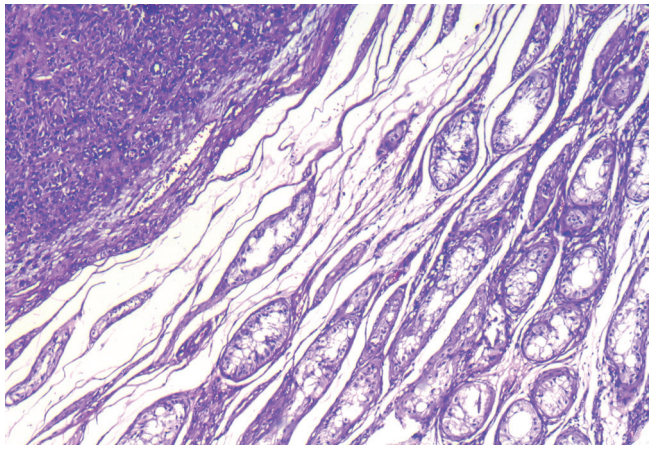

Figure 1. LCT and SCOS combination (H&E, x50).

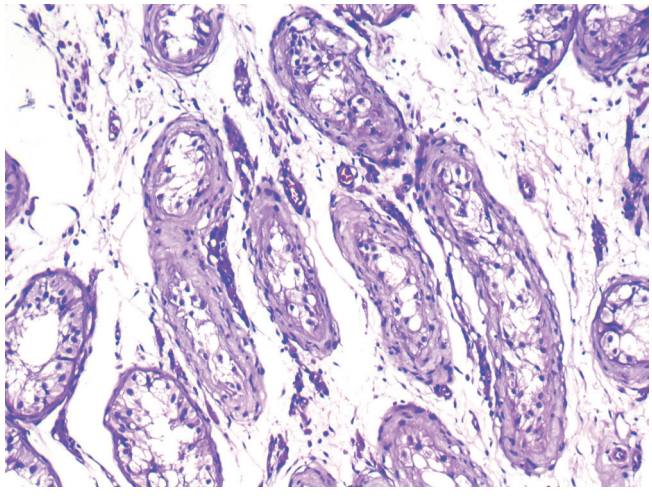

Figure 2. In non-neoplastic testicular tissue, seminiferous tubules are lined only with Sertoli cells. Lack of spermatozoa and a thickened basement membrane is noticed (H&E, x100).

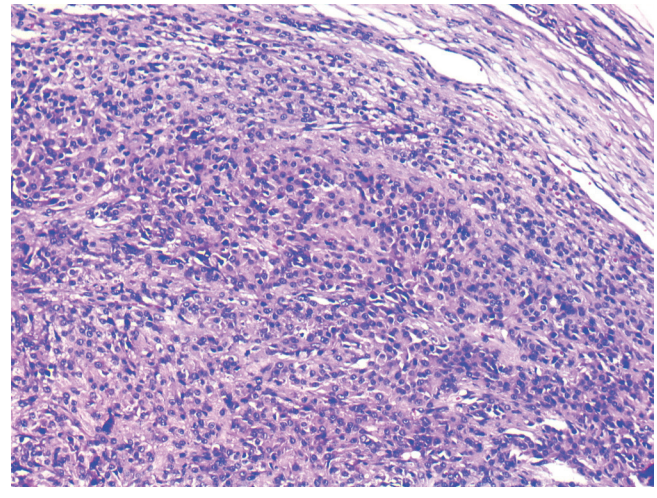

Figure 3. LCT of the testis. The tumour showed a solid growth pattern (H&E, x100).

Table 1. Pre and postoperative results

Parameter	β-HCG	α-FP	LDH	T	FSH	LH	E_2	PRL
Preoperative	1.2	3.84	184	741	14.75	10.42	37	14.94
Postoperative				689	17.7	7.33	33	11.46
Reference values	0-2.67	0-13.4	125-220	240-836	*	*	25.8-60.7	1.9-17.2
Unit	mIU/mL	ng/mL	U/L	ng/mL	mIU/mL	mIU/mL	pg/mL	ng/mL

*: There is no clear reference range defined for FSH and LH in men in the literature. However, previous studies point-out that FSH above 8 mIU/mL or LH above 6 mIU/mL indicates impaired spermatogenesis (11).

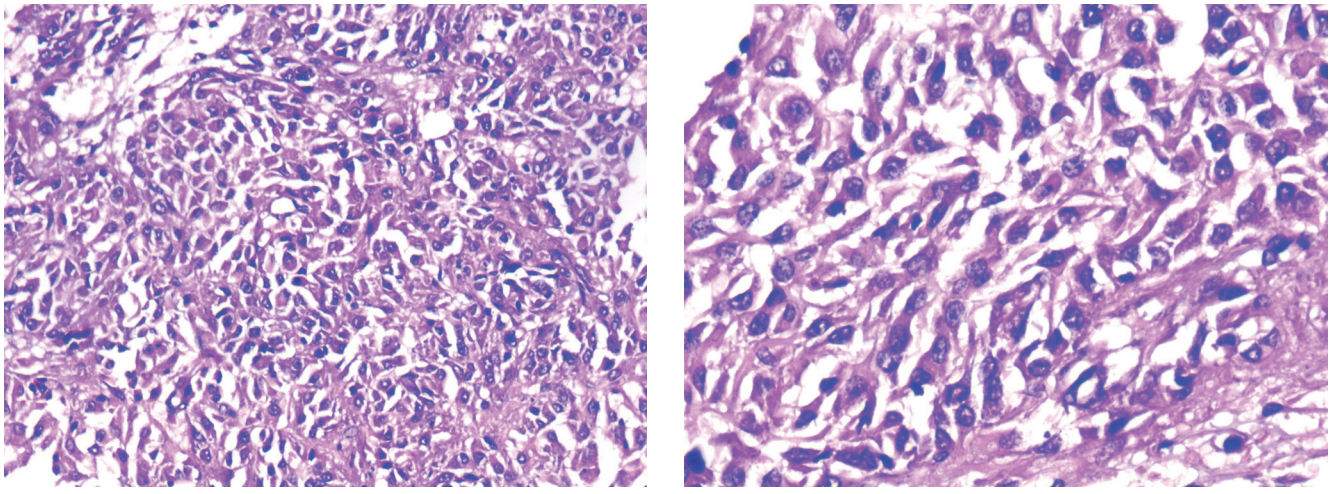

Figure 4, 5. The tumour cells were polygonal, large with eosinophilic cytoplasm and regular round nuclei, some with visible nucleoli (H&E, x 200; H&E, x 400).

DISCUSSION

LCTs are very rare testicular tumors of gonadal stromal origin. LCTs constitute 1-3% of testicular tumors in adults and %4 before puberty. In 20% of the patients, tumors can secrete androgen that can convert into T and E2. Different clinical features may be observed in patients due to increased androgen levels. Gynecomastia, hirsutism, and pubery precox are common endocrinological disorders (3). Suardi *et al.* found 8% for gynecomastia, 8% for testicular pain, 11% for infertility and 5% for isosexual pseudo-puberty in a wide range LCTs study (4). The patient's height was 178 cm and his weight was 75 kg. His development at male phenotype had been normal and he had been in puberty in expected time.

Azoospermia in adult males is a condition that can be seen as isolated. Suppression of FSH and LH levels due to increased T and E2 is observed, which impairs spermatogenesis. There are many cases of LCT with azoospermia in the literature (5). In the presented case, testicular volumes are low and FSH and LH levels are high. TT is normal, which is not expected from testicular size. Increased FSH and LH levels are consistent with impaired spermatogenesis (6).

Orchiectomy for the treatment of LCT or TSS in small and possibly benign tumors is recommended. All definitive diagnoses interpreted the neoplasia as benign LCTs using the criteria originally proposed by Kim *et al.*, which included dimensions (maximum neoplasia diameter), the presence of infiltrative margins and extratesticular extension, nuclear atypia, the presence of necrosis and of angioinvasion, and high mitotic index (7). Benign histopathological features are no capsular invasion, less mitotic count and nuclear pleomorphism. Successful oncological results of TSS similar to radical orchiectomy in small tumors have been reported (8). In the presented case, tumour size and localization were suitable for TSS, but radical orchiectomy was deemed appropriate due to the malignant potential of the tumour.

In our clinic, sperm cryopreservation is definitely recommended for single or married men who want to have children before orchiectomy. This routine procedure was recommended to our patient either and azoospermia was detected in the spermiogram.

There have been cases where improvement in sperm quality was reported after TSS or orchiectomy (9). In our case, the usual azoospermia condition accompanying LCT is observed. In our case, Sertoli cell syndrome is present together with LCT which has been reported very rarely before.

Sertoli cells are an important part of spermatogenesis, which functions under the effect of FSH. It has a place in the formation of the blood-testis barrier. Leydig cells also synthesize T, which acts as a paracrine regulator on Sertoli cells and stimulates spermatogenesis (10). SCOS is a multifactorial idiopathic condition that causes germ cell aplasia. Patients have abnormal spermotegenesis with normal sexual development. It is one of the common causes of azoospermia. Today, there is still no clearly defined treatment. In some patients, sperm can be found by TESE. Fertilization can be achieved by ICSI after TESE.

One month after the orchiectomy, there was no change in the hormonal parameters. The patient's erection quality remained same. Again, no sperm

was seen in the spermiogram. In the genetic research, karyotype analysis result was normal.

In conclusion, it is an accepted fact that testicular tumour risk is higher in infertile men compared to the normal population. Epidemiological studies have shown many common risk factors for azoospermia and testicular tumour. As in the case we have presented, two different testicular pathology may present at the same time and create an unexpected hormonal picture.

Conflict of interest

The authors declare that they have no conflict of interest.

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