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Case Report

Simultaneous Sertoli Cell-Only Syndrome and Leydig Cell Tumor in a Patient with Azoospermia: A Rare Case Report

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Keywords
Sertoli cell-only syndrome · Leydig cell tumor · Infertility · Testicular tumor

Abstract
Testicular cancers comprise 1–1.5% of entire cancers in men, and sex cord-stromal tumors include 5% of testicular cancers. This study aims to report a simultaneous Sertoli cell-only syndrome and Leydig cell tumor in the same patient. A 32-year-old man presented with a history of primary infertility for 3 years. Physical examination revealed normal secondary sexual characteristics. Two successive seminal fluid analyses revealed azoospermia. A scrotal ultrasound scan showed a 28 × 27 mm hypoechoic and hypervascular right testicular mass. Right radical orchiectomy and simultaneous left testicular biopsy were conducted. The histopathological examination revealed Sertoli cell-only syndrome and Leydig cell tumor with focal Leydig cell hyperplasia. Reversing fertility following the management of Leydig cell tumor is rarely mentioned in the literature. A study revealed that fertility recovered following 4 months of management in a primary infertile male. However, infertile men with nonobstructive azoospermia due to SCOS can only have a child by testicular sperm extraction technique. Despite the rare occurrence of Leydig cell tumor, it could be seen in association with Sertoli cell-only syndrome in infertile men with azoospermia. Clinical examination and imaging studies are important in these patients as the possibility of having a testicular mass is high among them.

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Introduction

In recent decades, infertility has been regarded as one of the main public health issues encountered by almost 15% of couples [1]. Testicular cancers comprise only 1–1.5% of entire cancers in men. They can be germ cell tumors, which are the most common type and comprise 95% of all the cases, or sex cord-stromal tumors which include only 5% of the testicular cancers [2]. Leydig cell tumors (LCTs) belong to nongerm cell tumors that account for 1–3% of all testicular neoplasms [2]. It can be present alone or associated with germ cell tumors. It mostly affects the prepubertal males and men in the third to sixth decades of life. This tumor is usually identified as a benign tumor, but malignancy is possible in 10% of adult patients with a poor prognosis [3]. The clinical presentations are variable ranging from asymptomatic to feminization, pubic hair growth, enlargement of the genital organ, and voice change in the prepubertal stage while gynecomastia, undesired sexual behavior, infertility, and impotence may be the presenting symptoms in adult patients [4]. Sertoli cell-only syndrome (SCOS) was initially described by Del Castillo in 1947 which is defined as the complete absence of germ cells in the seminiferous tubules with normal secondary sexual characteristics and decreased size of testicles [5]. Its prevalence in azoospermic men is approximately 26.3–57.8% [1]. The prevalence of testicular nodules, various germ cell, and nongerm cell tumors is very high in SCOS; however, due to the rare occurrence of LCTs, few simultaneous of both conditions have been reported in the literature [6]. This study aims to report a simultaneous SCOS and LCT in a young patient with azoospermia.

Case Presentation

Patient Information

A 32-year-old man presented with a history of primary infertility for 3 years. His wife was a 26-year-old female with regular menstrual cycles and having no apparent female factor of infertility.

Clinical Findings

Physical examination revealed normal secondary sexual characteristics with no signs of gynecomastia. The right testis was larger than the left one and had no apparent testicular mass, nor palpable inguinal lymph nodes.

Diagnostic Assessment

Two successive seminal fluid analyses revealed azoospermia. Scrotal ultrasound (U/S) scan showed a 28 × 27 mm hypoechoic and hypervascular right testicular mass and a normal left testis (Fig. 1). No para-aortic lymph nodes were seen on the abdominal US scan. Tumor markers were within normal ranges. Estradiol was normal, while both serum LH and FSH were elevated.

Therapeutic Intervention

Under spinal anesthesia, right radical orchiectomy and simultaneous left testicular biopsy, for the possibility of retrieving sperms to proceed, intracytoplasmic sperm injection and in vitro fertilization were done. The gross appearance of the specimen showed a 3 cm well-defined, firm, brown mass in the upper and mid part of the testis, without gross invasion to the tunica albuginea and testicular hilum. Histopathological examination of the mass was consistent with LCT (Fig. 2). The histological findings of the remaining part of the testicular tissue of the right testis and the left testicular biopsy showed Sertoli cell-only syndrome with

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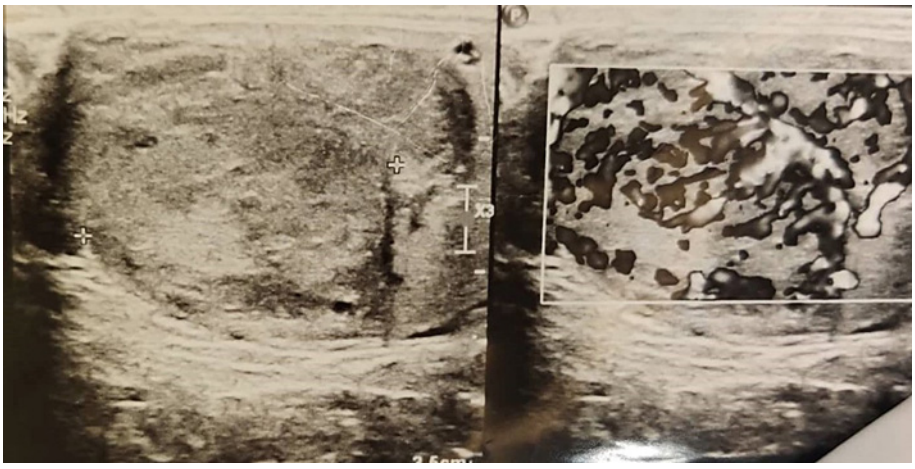

Fig. 1. A U/S scan of the left testis showing hypoechoic and hypervascular mass.

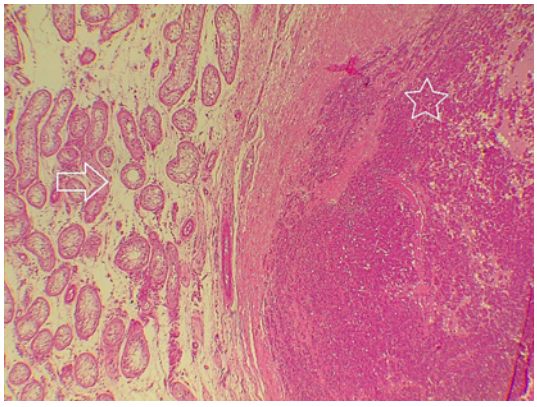

Fig. 2. Diffuse polygonal cells with abundant eosinophilic cytoplasm (white arrow). Absence of germ cell in the seminiferous tubules with only Sertoli cells (star).

complete germ cell aplasia and focal Leydig cell hyperplasia. The immunohistochemistry result was consistent with LCT (Fig. 3).

Follow-Up

The postoperative period was uneventful, and the patient is on regular follow-up concerning his fertility status.

Discussion

Azoospermia happens in 10–15% of infertile male patients which may be obstructive or nonobstructive. SCOS is one of the nonobstructive causes of azoospermia with a prevalence of 26.3–57.8% in these patients [1]. The major risk factors include genetic disorders, viral infection, undescended testis, radiation, environmental factors, hormonal treatment, and Klinefelter syndrome [1]. Two types of SCOS have been reported in the literature: focal SCOS, where there are residual spermatogenesis areas in the testis, and complete SCOS, which is characterized by false migration of gonocytes on their way to embryonic gonads and absence

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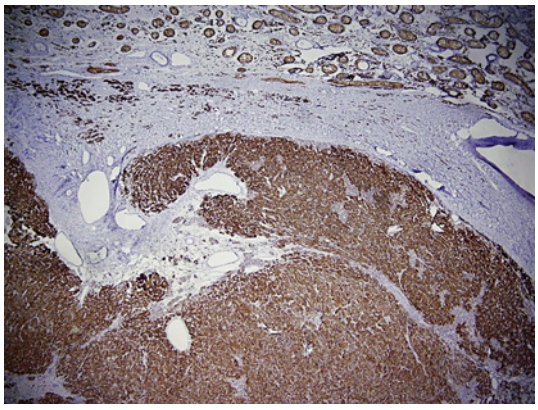

Fig. 3. Diffuse positive reaction of tumor cells to inhibin stain.

of germinal epithelium layer [5]. LCT is a rare non-germ cell tumor that may be solitary tumor or associated with different types of germ cell tumors. It develops in prepubertal age and third to sixth decades of life [3]. Feminization, infertility, undesired sexual behavior, testicle degeneration, and many other factors aggregate with LCT [4]. The current case was a 32-year-old male who presented with primary infertility for 3 years with normal secondary sex characteristics and no signs of gynecomastia.

In an infertile male patient, finding Sertoli cell-only tubules in the testes can be caused by the following factors: an abnormality during embryogenesis causing Del Castillo's syndrome, postnatal germ cell renewal failure, and X-radiation exposure that destroys the germ cells [7]. Detecting only immature Sertoli cells within the tubules suggests hypogonadotropic hypogonadism due to gonadotropin insufficiency, which prevents maturation of the cells, while the presence of mature Sertoli cells in the Sertoli cell-only tubules reveals infertility with the clinical manifestation of Del Castillo's syndrome [7]. It has been reported that 15–20% of male infertility is caused by genetic abnormalities such as microdeletions on the Y chromosome, mutation, and polymorphism. A study investigated the role of genetic abnormality in SCOS, the outcome revealed the involvement of genetics (sex chromosomes) in more than 23% of the patients, and Klinefelter syndrome was found in most of the cases [8] A study by Mancini et al. [6] revealed that the presence of SCOS in the azoospermic patients increases the chance of testicular nodule and carcinoma development. Due to that reason, conducting clinical screening has been suggested in azoospermic patients to establish certainty [6]. Another study reported that azoospermia was detected in most of the individuals with SCOS and oligozoospermia has been confirmed in some of the patients. The testicular size was normal in almost half of the cases [9]. In contrast to the previous studies, the patient in this study had normal secondary sexual characteristics with no chance of Klinefelter syndrome, and the right testis was larger than the left one. The presence of azoospermia in this patient correlated with the literature. Furthermore, the patient refused genetic analysis, so the involvement of the heredity, in this case, has remained unknown.

Regarding the prognosis of LCT, it is divided into two groups with different clinical characteristics and outcomes. The tumors that occur in older patients are more susceptible to malignant transformation with few symptoms, while those affecting young individuals are usually benign and allied with dysplastic syndromes [10]. A cohort study on 3,518 Klinefelter patients showed that there is no significant difference in the prevalence of gonadal tumors in Klinefelter patients and normal populations, although another study recorded 20 cases of LCT in 4,000 patients with Klinefelter syndrome [11, 12]. Due to controversy in the involvement of Klinefelter syndrome in arising testicular tumors, two hypotheses have been proposed. The

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first one believes that Klinefelter patients are spared from these tumors by an unidentified immunologic response. The second theory postulates that the variation in the phenotype of Klinefelter syndrome makes it undetectable in most patients with testicular tumors [13]. LCTs are commonly unilateral. Bilateral LCTs have been approximated to be 3–10%, and the tumor may spread beyond the testis in 15% of the cases [14]. In the current case, the LC tumor in the right testis was benign, and SCOS was found in both testes.

Scrotal U/S is defined as a crucial modality in detecting testicular tumors, but it is insufficient to segregate a benign from a malignant tumor. Tumor markers like AFP, beta hCG, and lactate dehydrogenase are always negative in patients with LCT [2]. In the current case, scrotal U/S showed a 28 × 27 mm hypoechoic and hypervascular right testicular mass. No para-aortic lymph nodes were seen on the abdominal U/S scan. Tumor markers were within normal ranges. Histopathological examination of the mass was consistent with LCT, and the histological findings of the remaining part of the testicular tissue of the right testis and the left testicular biopsy showed Sertoli cell-only syndrome.

Radical orchiectomy is suggested as the major treatment to prevent malignant transformation. Moreover, partial orchiectomy can be done whenever the patient is young, fertile, and the size of the tumors is small [15]. Reversing fertility following the management of LCT is rarely mentioned in the literature. A study by Markou et al. [16] revealed that fertility recovered following 4 months of management in a primary infertile male. However, infertile men with nonobstructive azoospermia due to SCOS can only have a child by testicular sperm extraction technique [1]. In this case, under spinal anesthesia, a right inguinal orchiectomy with a left testicular biopsy was performed. The postoperative period was uneventful.

Conclusion

Despite the rare occurrence of LCT, it could be seen in association with SOCS in infertile men with azoospermia. Clinical examination and imaging studies are important in these patients as the possibility of having a testicular mass is high among them.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Rawa Bapir and Bana Shapoor: major contribution, diagnosing the entity, manuscript revising, and final approval of the manuscript. Rawezh Q. Salih, Abdulwahid M. Salih, Fattah H. Fattah, and Shvan H. Mohammed: literature review, manuscript revising, and final approval of the manuscript. Fahmi H. Kakamad, Karzan M. Salih, and Hiwa O. Abdullah: literature review, writing the manuscript, and final approval of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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