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# *A Case of Adolescent Ovarian Sertoli-Leydig Cell Tumor and Literature Review*

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***Abstract:*** Ovarian Sertoli-stromal cell tumor (SLCT) is a rare tumor. We report an adolescent SLCT patient and strengthen our understanding of the disease through literature review to understand its clinical manifestations, diagnostic methods and treatment, so as to avoid misdiagnosis, missed diagnosis and over-treatment.

## 1. Introduction

Ovarian Sertoli-Leydig cell tumor (Sertoli-Leydigcelltumor, SLCT), also known as male blastoma or testicular blastoma, is a rare type of ovarian sex cord-stromal tumor, accounting for 0. 2%-0. 5% of all primary ovarian tumors. It can occur in women of all ages, with an average age of 25 years [1]. Data show that infants can occur at least 5 months old [2]. SLCT usually occurs in unilateral, bilateral rare, only about 1. 5% occur in bilateral [3]. The disease is rare, the incidence is hidden, and there are few clinical reports. At present, the understanding of the tumor is not comprehensive enough, the rate of misdiagnosis and missed diagnosis is high, and its clinical features, prognosis and best treatment have not been unified, which is the difficulty of gynecological tumor. This paper reports a case of adolescent ovarian Sertoli-Leydig cell tumor and strengthens the understanding of the disease through literature review.

## 2. Clinical data

Patient, female, 13 years old, 8 months old, asexual life history. He was admitted to hospital for "finding pelvic mass for 2 days". Due to "not menarche" in the local hospital to check B-ultrasound: pelvic cystic mass; a small amount of fluid in the abdominal cavity. Past history and personal history are not special; family genetic history is unknown (adoption). Physical examination: the body hair of limbs and skin is dense, the upper lip is obvious, and the distribution of body hair can be seen in the neck. Breast: bilateral breast nucleus diameter 4cm, visible areola. Vulva: bilateral labia minora is asymmetrical, left large and right small, labia majoris develops normally, clitoris is large, pubic hair is dense, vulvar skin is pigmented; vagina, cervix, uterine body are not examined; anal and abdominal diagnosis: pelvic palpable mass of about 10cm × 10cm × 10cm, medium quality,

smooth surface, poor activity, no tenderness. Abdominal ultrasound: pelvic cavity: uterine-like echo of 1.5 × 2.5 × 5.4cm was seen behind the bladder, and the thickness of endometrium was about 0. 3cm. Several cystic masses can be seen behind it, which is about 6.3 × 7.5 × 7.7cm. The boundary is clear, the light insulating zone can be seen inside, and the echo is enhanced. Lying in the hepatorenal space, the liquid dark area of 0. 6cm can be seen in the anterior and posterior path. As seen at the back of the bladder, more consideration was given to the uterine and pelvic cystic mass and a small amount of effusion in the abdominal cavity. Mr pelvic cavity: a cystic-solid abnormal signal shadow was seen behind the uterus in the pelvic cavity. Most of the cysts showed low signal intensity on T1WI, high signal intensity on T2WI and fat compression sequence, patchy, layered short T1 and long T2 signal intensity on some cysts, uneven thickening of cyst wall and septum, patchy, banded and nodular changes, high signal intensity on T1WI, low signal intensity on T2WI and fat compression sequence, high signal intensity on DWI sequence diffusion limitation, and low signal intensity on ADC. The uterus was obviously compressed, small in size, regular in shape, and no clear abnormal signal was seen in the uterine wall. The attachment on the right seems to be seen, while the attachment on the left is not clearly shown. No abnormal signal was found in the uterine cavity. The bladder could be filled, the wall was not locally thickened, and there was no clear abnormal signal in the cavity. Fluid signal was seen in the pelvic cavity, but no major lymph nodes were seen. Hint: 1. The cystic and solid space at the back of the uterus is more likely to originate from the left adnexa. Pelvic effusion. Enhanced MRI: a large 10.8cm × 8.3cm × 10.5cm cystic-solid mixed signal focus was seen in the left posterior part of the pelvic uterus. On contrast-enhanced scan, multiple obvious enhanced nodules of different sizes were seen, the cyst wall and septum were slightly enhanced, and the boundary of the focus was clear. It is suggested that the cystic and solid space in the posterior part of the uterus is likely to come from the left adnexa. Laboratory examination: TSTO testosterone: 2.79ng/mL hormone; androstenedione: 12.17nmol/mL hormone; AFP:37.6ng/mL hormone; TSH thyrotropin 5.510uIU/mL hormone; karyotype: 46XX; dehydroepiandrosterone sulfate, adrenocorticotropin, cortisol, 17 α-hydroxyprogesterone and other related tests showed no abnormality. On September 5, 2022, laparoscopic exploration was transferred to abdominal left adnexectomy, right ovarian biopsy and pelvic abdominal multi-point biopsy. During the operation, the celiac effusion was about 400ml, the uterus was slightly smaller and the surface was smooth, and the left ovary was enlarged to form a 10cm × 10cm × 10cm mass with intact capsule. During the operation, the tumor was removed and sectioned: cystic and solid, and the solid part was bad and brittle. Intraoperative freezing: malignant tumor. Postoperative pathological examination: (1) (left) differentiated Sertoli-Leydig cell tumor in the ovary, no tumor tissue was found in the left fallopian tube. (2) (bilateral pelvic wall, mesentery, greater omentum, Douglas fossa peritoneum, right para-colonic biopsy, right ovary) no tumor tissue was found. (3) (peritoneal lavage fluid) no tumor cells were found. Immunohistochemistry: CK (pan) (Sertoli cell +), Ki-67 (+, 20%), p53 (+), WTI (Sertoli cell +), EMA (focal +), CD56 (+), Inbbin-a (+), CD99 (+), CR (interstitial cell +), Melan-A (-). Pathological consultation in the first affiliated Hospital of Xi'an Jiaotong University: "left" ovarian moderate-poorly differentiated mixed cord-interstitial tumor (Sertoli-Leydig cell tumor) infiltrated the left fallopian tube. Considering that the patient is young, infertile and communicate with his family members during the operation, if it is germ cell or sex cord stromal cell malignant tumor, it is feasible to remove the adnexal tumor on the affected side + contralateral ovarian biopsy + pelvic abdominal multi-point biopsy, and if it is epithelial ovarian tumor, comprehensive staging exploration is required. After family communication, it is decided that temporary left adnexal resection + right ovarian biopsy + pelvic abdominal multi-point biopsy. Postoperative diagnosis: Sertoli-Leydig cell tumor stage II a. Paclitaxel / carboplatin chemotherapy was given according to NCCN guidelines. 10 days after surgery, Testosterone:0. 19ng/mL. Two months after operation, menarche. During the follow-up for 7 months, the body hair disappeared

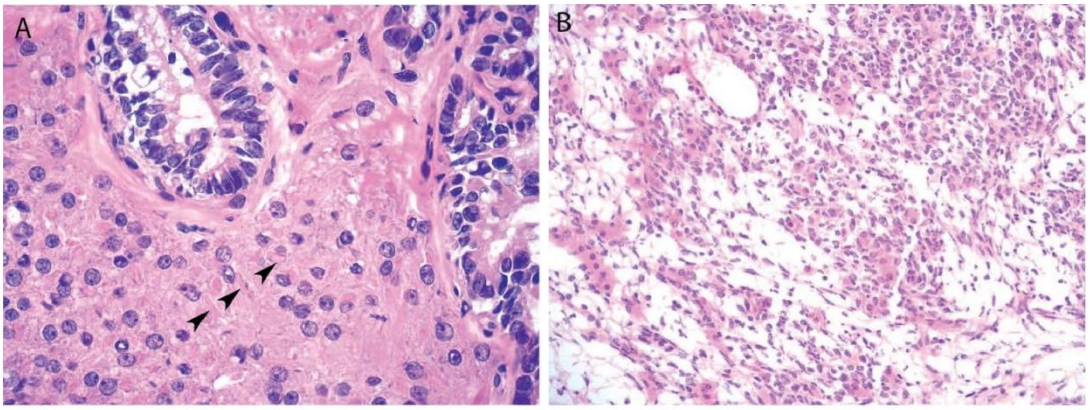
obviously and there was no recurrence.

## 3. Discussion

### 3.1. Clinical features

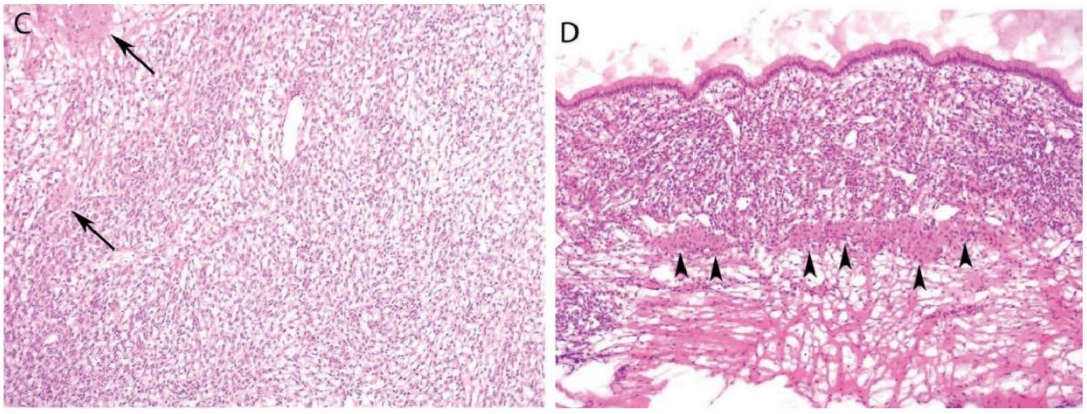
According to the classification of female reproductive organ tumors by WHO (2020), SLCT can be divided into high, medium, low differentiation and reticular type, medium, low differentiation and reticular type may be accompanied with heterogenous components, may have the biological behavior of malignant tumor, moderate and low differentiation is more common, high differentiation is relatively rare. Microscopically, SLCT is composed of Sertoli and Leydig cells with different proportions and different degrees of differentiation, about 20% of which contain heterologous components [4], as shown in Figure 1. Except for Sertoli cells, Leydig cells and primitive cord components in the tumor, the other components are heterologous components, and the most common is gastrointestinal mucous epithelium [5]. Sertoli cells are arranged in strips, glandular tubes or solid nests, with oval or short fusiform nuclei, lightly stained cytoplasm, weakly eosinophilic or transparent, shaped like sunflower seeds. Leydig cells are often distributed singly or in clusters in the tumor fibrous stroma and around the nests of Sertoli cells, with small round nuclei and rich eosinophilic cytoplasm [4]. Highly differentiated Sertoli cells are hollow tubules or solid tubules under light microscope, without obvious atypia, surrounded by scattered or clustered Leydig cells; moderately differentiated cells are "lobular" under light microscope. Under light microscope, poorly differentiated patients are composed of dense fusiform cells, mitotic phase is more common, reticular type can be seen consistent with each other or large irregular reticular space or cystic cavity, and sometimes papillary structure can be seen. Patients with heterologous components contain non-funicular stromal components, including epithelial and mesenchymal tissue components [6]. Reticular structures and heterologous elements can be found in undifferentiated or moderately differentiated forms [1].

Naked eye view, SLCT has a complete capsule, mostly solid, cystic solid mass, the section can be gray, gray red, gray yellow, can also be dark red or brown, soft texture, fleshy feeling, part of the solid part shows cauliflower pattern. When the tumor is large, it often has multilocular cystic components, containing transparent fluid [7].




Highly differentiated SLCT shows open Sertoli tubules mixed with abundant clusters of Leydig cells, with Reinke crystals visible in the cytoplasm (arrow)

Moderately differentiated SLCT shows compressed alkaline Sertoli cell cords scattered in eosinophilic Leydig cells




Low differentiated SLCT shows diffuse patchy distribution of immature Sertoli cells, with a small number of Leydig cell clusters visible around the tumor (arrow)

Low differentiation SLCT accompanied by heterologous components. At the top of the image, gastric mucinous epithelium can be seen, surrounded by immature Sertoli cells and Leydig cells (arrow)

Figure 1: Different histological features of SLCT

### 3.2. Pathogenesis

The pathogenesis of SLCT is not clear at present. Some studies have shown that about 32% to 97% of SLCT may be accompanied by somatic mutations of DICER1 [8]. Some studies have also found that some other related genes have higher mutation frequencies in ovarian SLCT, such as PMS2, FOXL2 [9,10] and PALB2 [11]. The conclusions drawn from the case studies of these small samples need to be confirmed by further studies. Karnezis et al. [12] have found that DICER1 gene mutations and FOXL2 mutations are mutually exclusive. According to WHO's classification of female reproductive organ tumors in 2020, gene mutations divide SLCT into three subtypes. DICER1 mutant, the patient is younger, and the tumor is usually moderately-poorly differentiated, which may be accompanied by reticular structure or source heterogeneity, and the clinical manifestations are mainly increased androgen symptoms such as masculinization or defeminization. Patients with FOXL2 mutations are usually older and often occur in postmenopausal women. Their tumors are usually moderately-poorly differentiated and generally do not contain reticular or heterogenous components. Clinically, these patients often show symptoms of increased estrogen, such as postmenopausal vaginal bleeding or abnormal uterine bleeding. DIC-ER1/FOXL2 wild type usually occurs in young and middle-aged patients. Tumors usually have good differentiation, no reticular or heterogenous components, and no obvious hormone-related symptoms. The findings of Karnezis et al are consistent with this classification.

DICER1 syndrome is a familial tumor susceptibility syndrome, which is mainly caused by DICER1 gene mutation. In addition to ovarian reserve oocyte tumors, there are also common diseases such as cystic nephroma, pleuropneumoblastoma, multiple nodular goiter and cervical embryonal rhabdomyosarcoma. A report on the frequency of DICER1 mutations in SLCT of Chinese SLCT patients shows that germ line and somatic DICER1 mutations are more common in younger SLCT patients, suggesting that genetic detection may have important clinical significance for SLCT patients, especially young patients. DICER1 gene detection, if there are mutations in hot spots of DICER1, can be used to predict and evaluate patients and their close relatives in clinical genetics [13]. Ovarian SLCT patients with DICER1 gene mutations need to be vigilant against the occurrence of other systemic symptoms and need multi-disciplinary follow-up, and annual multi-system evaluation and physical examination, including respiratory system, digestive system,

urinary system, motor system, central nervous system and endocrine system, etc. [14]. Further detection of DICER1 gene in young patients is of great significance not only for gene detection and genetic counseling of patients and their families, but also for a better understanding of the potential molecular pathogenesis of SLCT can help improve tumor classification and disease prognosis, and may lead to the discovery of more effective treatment strategies. In this report, although we provide detailed information about the DICER1 mutation, the patient refuses to test for DICER1 for some reason.

The typical clinical characteristics of SLCT are mainly related to the steroid secretion function and tumor components of the tumor. Sertoli cells mainly produce estrogens and Leydig cells mainly produce androgens. Most of the clinical manifestations are masculinization caused by excessive androgen, Such as clitoris hypertrophy, acne, beard growth, hairy, etc. The level of reproductive hormone showed an increase in serum testosterone, accounting for about 1/3 of patients with ovarian SLCT [15]. There are also some patients with SLCT caused by excessive estrogen, such as dysfunctional uterine bleeding, postmenopausal vaginal bleeding and so on. It has been reported that hyperandrogenism is more common in young women and high estrogen in older women [16]. About 50% of the patients had no hormone-related symptoms, only abdominal pain, abdominal distension and abdominal masses [14]. Some studies have also suggested that most of the SLCT with elevated serum AFP are moderately and poorly differentiated or accompanied with heterogenous components, which should be vigilant [17], but there are only sporadic cases reported in the literature, whether it indicates that the patients with elevated AFP are malignant need to be further studied. Part of the results show that the older the onset of ovarian SLCT, the higher the degree of differentiation and the lower degree of malignancy; on the contrary, the youngest age of onset is moderately differentiated and accompanied with reticular components, and the degree of malignancy is relatively higher [6]. The biological behavior of SLCT is diverse and difficult to predict, and the reasons for seeing a doctor are various. As a result, the early clinical manifestations of most patients are easy to be ignored or misdiagnosed.

### 3.3. Diagnosis

At present, imaging examination can be used as a preoperative auxiliary diagnosis of ovarian SLCT, especially MRI is a good preoperative examination method (Figure 2), most of which are cystic or solid masses, complete solid masses or multilocular solid masses with multiple cysts, and most of the masses show medium-large blood flow, the boundary is clear, the solid component T1WI shows equal or slightly low signal intensity, and the signal intensity is different on T2WI, which can be low, equal or slightly high signal. It mainly depends on the number of fibrous stroma, the cystic part usually shows high signal on T2WI, and most of the components on DWI images show high signal intensity, while ADC shows low signal intensity, indicating that the tumor diffusion is limited, enhanced solid components or septum, and the cyst wall is moderately or obviously enhanced [18]. If the cystic lesions show a wide basal parenchyma growing along the cyst wall or septum, it suggests that SLCT may be [19]. SLCT should be differentiated from ovarian Sertoli cell tumor, ovarian granulosa cell tumor, ovarian carcinoid, ovarian endometrioid carcinoma and so on. The diagnosis mainly depends on pathological examination. The gold standard for the diagnosis of ovarian SLCT is histopathology and immunohistochemistry.

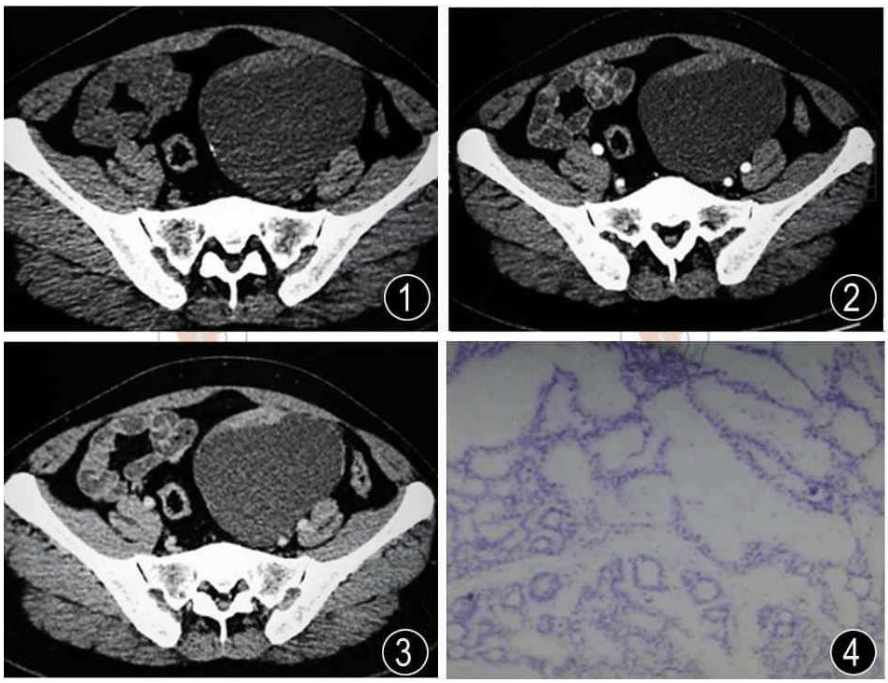



Figure 2: MRI of SLCT

### 3.4. Treatment

SLCT is rare in clinic, and there is no standardized treatment at present, so surgery is the main method for the treatment of SLCT. Surgical recommendations are based on NCCN guidelines. Surgery can be performed on patients who want to retain fertility. It is recommended to perform a comprehensive and standard staging operation for patients who do not need to give birth. Lymph node metastasis is rare, mainly through implantation and blood transmission. Therefore, there is no need for lymph node dissection during SLCT surgery to avoid possible complications. The role of adjuvant chemotherapy after SLCT is still controversial. Most scholars believe that clinical stage is the most meaningful indicator of postoperative supplementary chemotherapy. At present, there is no best treatment for recurrent patients, surgical treatment is the basis for the treatment of recurrent patients, tumor cell reduction surgery should be performed as soon as possible [14], this kind of tumor should be closely followed up after operation. Ultrasound and MRI examination are important auxiliary examinations. Patients with hyperandrogen clinical manifestations and elevated serum markers can be combined with serum tumor markers and testosterone levels to comprehensively judge whether the tumor is recurrent or not. It can also be used as an important index to assist in diagnosis, monitoring recurrence and prognosis. It is suggested that postoperative multidisciplinary follow-up is recommended, and more large sample studies are needed in order to formulate the optimal standardized treatment plan and improve the prognosis of patients.

## 4. Summary

To sum up, although SLCT is a very rare disease, and the number of reports in this field is limited, by studying this case, we can sum up the experience, that is, for women of any age, once the serum testosterone level increases and is accompanied by female masculinity, clinicians should be vigilant to avoid misdiagnosis, missed diagnosis and over-treatment. The treatment of SLCT needs to be individualized, and follow-up after surgery can assess the prognosis and risk of recurrence, which is very important. Further detection of DICER1 gene in young patients is not

only of great significance for gene detection and genetic counseling of patients and their families, but also can better understand the potential molecular pathogenesis of SLCT, help to improve tumor classification and disease prognosis, and may find more effective treatment strategies.

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