



# A recurrence of advanced malignant sex cord tumor with annular tubules: case report

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**Abstract:** Sex cord tumor with annular tubules (SCTAT) is a rare special type of ovarian sex cord-stromal tumor, which has not achieved a standard treatment regimen currently. The aim of this report was to provide possible reference for treatment and supervision of recurrent advanced malignant SCTAT. A 33-year-old unmarried female with malignant SCTAT emerged recurrence after the cytoreductive surgery but preserved fertility and postoperative chemotherapy (3 cycles PEB regimens) 12 months. She was performed preoperative adjuvant chemotherapy (3 cycles, paclitaxel liposome and nedaplatin) before the third operation of secondary cytoreductive surgery, followed by platinum-based chemotherapy (7 cycles, TC regimens) timely because of dissatisfactory efficacy under the evaluation in combination with prior comprehensive treatment and PET/CT. The surgical stage was IIIB. She acquired complete remission after therapy and needed to regularly follow up every 3–6 months for 2 years and every 6–12 months after 2 years. There was no evidence of malignant SCTAT recurrence at the follow-up 24 months past the third surgery. No abnormality was found in other examination indexes, and menstruation was regular. The regular supervision of the patient was continually performed. The diagnosis of recurrent advanced malignant SCTAT was established on history and final pathology examination, whose prognosis mainly depended on the appropriate strategy of surgery and chemotherapy regimens. The classical TC regimens could be considered if the efficacy of other chemotherapy regimens were unsatisfactory. Regular follow-up was essential.

**Keywords:** Sex cord tumor with annular tubules (SCTAT); recurrence; malignant; therapy

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## Introduction

The morbidity of sex cord-stromal tumor may be only approximately 1.2–2% of primary ovarian cancer (1). However, sex cord tumor with annular tubules (SCTAT) is a rare special type of ovarian sex cord-stromal tumor, and accounts for approximately 6% (2,3), which histomorphology is considered as between a supportive cell tumor and a granulosa cell tumor. SCTAT is reported that about one third of patients experience Peutz-Jeghers syndrome (PJS) with mucocutaneous pigmentation in special locations and gastrointestinal tract polyposis,

whose form is usually benign and has excellent prognosis through surgery. However, SCTAT without PJS may have a 15–20% malignancy rate and malignant behavior with metastases might be examined in approximately 20% of patients (4), which is a most common phenomenon in women of reproductive age. The tumors both may express the hyperestrogenic manifestations, regardless of the clinical form.

Although SCTAT is a rare disease, it's not scary. The patient with SCTAT related to non-PJS is considered to emerge malignant behavior with recurrence and metastases, which also still has a good prognosis via excellent surgery

and chemotherapy (5,6). However, currently there is no standard treatment in advanced malignant SCTAT. Hence, we report a surgical stage IIIB recurrent case with SCTAT related to non-PJS, to provide possible reference for therapy and supervision. We present the following case in accordance with the CARE-Guideline (7).

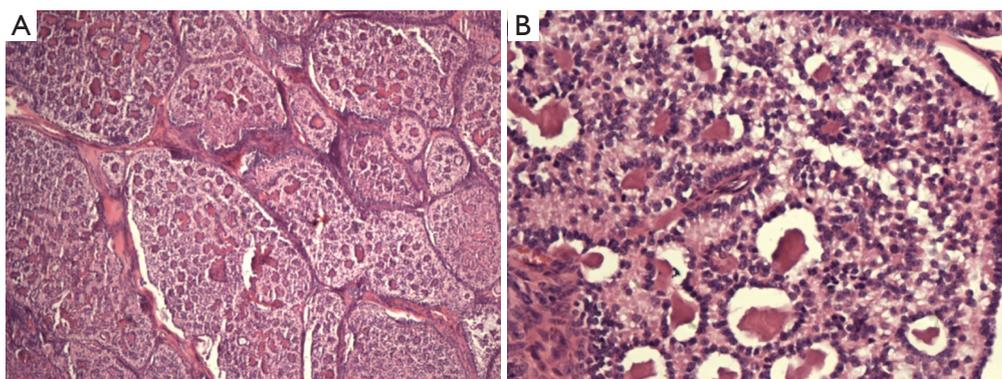
### Case presentation

An unmarried female, 33-year-old, gravida-1-para-0, without a history of ovarian and uterine tumors, emerged menstrual disorder for 6 months, presenting with irregular menstrual cycles (cycle is 15–40 days, used to be 30 days) and heavy menstrual bleeding, without abdominal pain and mucocutaneous pigmentation visually. The patient was discovered a cyst sized approximately 4 cm × 5 cm in right ovary by transvaginal ultrasonography. Finally, she received a laparoscopic ovarian cystectomy on account of the ovarian cyst achieved the surgical requirements. Postoperative pathology reported ovarian granulosa cell tumor. There was no adjuvant therapy such as postoperative chemotherapy. During the follow-up 8 months after the first surgery, the right ovary was recurred a 5 cm × 6 cm mass by pelvic ultrasonography, which suggested cystic solid and rich blood flow sign, but without the hyperestrogenic manifestations. This recurrence of cyst was considered as the malignant tumor. Hence, the second surgery was made to perform with laparoscopic right salpingo-oophorectomy and greater omentectomy and bilateral pelvic and para-aortic lymphadenectomy and left appendix and suspicious lymph nodes resection. Intraoperatively, a mass with sized about 5 cm × 5 cm was seen in the right ovary, several vesicles were seen outside the right fallopian tube, multiple small lesions were found on the intestinal tube surface, but the anatomy of the left fallopian tube and ovary was normal. The lesions were removed completely. Postoperative pathology evaluation of the tumor demonstrated the neoplasm was ovary SCTAT, additionally, 27 lymph nodes from pelvic and partial omentum were not metastasized by the tumor. The surgical stage was IIIB after operation, then 100 mg of nedaplatin intraperitoneal chemotherapy was performed. Subsequently adjuvant regimens including 3 cycles PEB (cisplatin, etoposide and bleomycin) intravenous chemotherapy was received. The treatment process was successful and the side effects were controllable. Thereafter, she followed up regularly every 3 months. The above treatment was conducted in the local hospital of this patient.

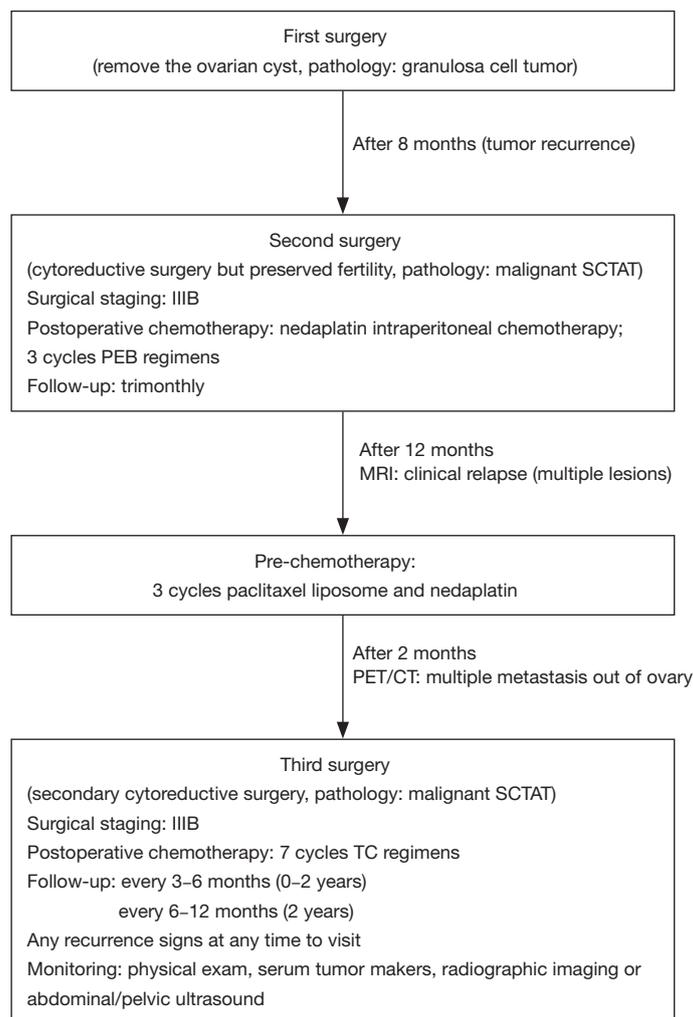
One year after the second operation, she returned to the

hospital for examination because the emergence a symptom of irregular vaginal bleeding. Serological examinations showed the serum levels of estradiol reached 164 pg/mL, but levels of other hormones including progesterone, androgen, luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin were in the normal range. Then, the multiple little lesions on the surface of pelvic and abdominal viscera were recurred by MRI examination, which were considered clinical relapse. Hence, the pre-chemotherapy including 3 cycles paclitaxel liposome and nedaplatin was decided by the professors from department of gynecological oncology in Peking Union Medical College Hospital (PUMCH). After the pre-chemotherapy, she was recommended to detect PET-CT examination, in order to further measure the disease and followed therapy. The result exhibited that the right posterior lobe of the liver was occupied, and the metabolism was increased, and left pelvic soft tissue lesion, increased metabolism, which strongly supported metastasizing lesions. The third operation, secondary cytoreductive surgery, was planned through the evaluation in combination with prior comprehensive treatment and PET-CT. This time the aim of this surgery was to remove the visible tumors of the pelvic and abdominal cavity completely. Postsurgical pathology reported that these lesions, including left abdominal wall, upper uterine wall, posterior uterine wall, left broad ligament, colonic surface, subhepatic retroperitoneal, retroperitoneal space, retroperitoneal surface, rectal surface, mesentery surface, anterior abdominal wall, were consistent with the diagnosis of malignant SCTAT (see the *Figure 1*). She received 7 cycles postoperative chemotherapy of TC (paclitaxel and carboplatin) regimens. The patient acquired complete remission after therapy during follow-up stage. The whole treatment process flow was shown in *Figure 2*.

The patient would be re-examined in Gynecological Oncology Outpatient Department after end chemotherapy 1 month. The serum levels of estradiol had decreased to the normal range value. The abdominal and pelvic Ultrasound examination also found no abnormalities. Subsequent supervision should be followed every 3–6 months for 2 years and every 6–12 months after 2 years. Now the patient has been followed up 2 years, who would be monitored long-term. The monitoring involved physical exam including pelvic exam, serum tumor makers (e.g., estrogen), and radiographic imaging (e.g., chest X-ray) or abdominal and pelvic ultrasound for evaluating the mass recurrence. The examinations of chest/abdominal/pelvic CT, MRI, PET/CT



**Figure 1** Sex cord tumor with annular tubules (A: HE, x40; B: HE, x200).



**Figure 2** The therapeutic process flow. SCTAT, sex cord tumor with annular tubules.

or PET would be performed when a suspicious abnormality was found in the previous basic inspection.

Over the follow-up 24 months past the third surgery, there was no evidence of malignant SCTAT recurrence. No abnormality was found in other test indexes, and menstruation was regular.

## Discussion

Clinical presentations of sex cord tumors with annular tubules include irregular vaginal bleeding or menstrual disorder, hyperestrinism symptoms, and the presence of an abdominal or pelvic mass (5,8,9). Childbearing female was a vulnerable population to suffer SCTAT, however the young girl was reported only in sporadic cases (10,11), usually presenting malignant behaviors and causing precocious puberty because of secreting estrogen-progesterone (10,12,13). The form with PJS or without PJS was identified as two characteristic manifestations. SCTAT with PJS was usually benign and had a genetic predisposition. Surgical resection of the lesion or could result in good remission and a good prognosis. SCTAT without PJS had a malignant tendency, approximately 22%, which seemed to spread mainly through the lymphatics with typical locations of tumor metastasis being the pelvic tissues, particularly in high-order lymph nodes, such as para-aortic and supraclavicular lymph nodes (14). The peritoneum, omentum majus, kidney, liver, lung and other organs might be prone to metastasis and recurrence. In spite of metastasis, the fertility could be retained (15). Though the serum tumor markers such as inhibin, CD99, MIS, estrogen receptor, progesterone receptor have been studied as diagnostic moleculars and supervision of clinical prognosis of the tumor post-operation (16), these laboratory examinations were still nonspecific. This disease should be differentiated from granulosa cell tumor and other endocrine tumors of ovary. Pelvic ultrasound examination could be used as an auxiliary detection tool. This case first diagnosis was classified as ovarian granulosa cell tumor in her local hospital because of similar secretory hormone characteristics to SCTAT and pelvic mass. Hence the final diagnosis still depended on pathology characterized by simple or complex annular tubes (17) (see Figure 1A,B), even providing a disease history might be necessary.

Surgical staging and treatment were similar to other malignant sex cord-stromal tumors and epithelial ovarian cancer. Patients with stage II to IV tumor were recommended cisplatin, etoposide and bleomycin as

postoperative chemotherapy, which resulted in pathological complete remission (18). Recurrence treatment included docetaxel, paclitaxel/ifosamide, and paclitaxel/carboplatin. Hormone recurrence therapy included aromatase inhibitors, leuprolide, and tamoxifen. Secondary cytoreductive surgery might also be considered (19). In our case, this patient appeared multiple recurrent and metastatic lesions in the abdominal and pelvic cavity via MRI examination no more than 12 months after the second operation and PEB regimens. Hence, switch to paclitaxel liposome and nedaplatin (3 cycles) as the adjuvant chemotherapy. However, the multiple lesions were not decreased by PET/CT evaluation, considering the unsatisfactory effect of the chemotherapy regimens. Therefore, the secondary cytoreductive surgery was decided through negotiations by the gynecologic oncologists. Subsequently, postoperative adjuvant chemotherapy was switched to the classical TC regimens, without hormone therapy. Ultimately, our patient acquired complete remission and disease-free status after 7 cycles of chemotherapy, indicating that the current therapy was suitable for this patient. Therefore, we believed that the classical TC regimens could be considered if the efficacy of other chemotherapy regimens were unsatisfactory in recurrent advanced malignant SCTAT.

Malignant SCTAT has a long-term risk of recurrence. Kulkarni (20) has reported the time of first recurrence in patients with malignant SCTAT ranges from 3 months to 20 years. Shen *et al.* (3) also reported the relapse and metastasis rate at first surgery was 20%. In our case, she appeared multiple metastasis lesions, which located in the abdominal wall, upper uterine wall, posterior uterine wall, left broad ligament, colonic surface, subhepatic retroperitoneum, retroperitoneal space, retroperitoneal surface, rectal surface, mesorectal mesentery, and anterior peritoneum after comprehensive staging surgery 12 months during the regular supervision. Unfortunately, these lesions were confirmed as metastatic malignant SCTAT by postoperative pathology. Fortunately, the clinical relapse was detected early and timely surgical treatment and appropriate chemotherapy regimens were performed to allow the disease to achieve complete remission.

The mortality of SCTAT is unclear. The prognosis of SCTAT needs to combine with the tumor clinical stage and the nature of neoplasm with benign or malignant. The prognosis of recurrent malignant SCTAT is decided based on the metastatic sites, surgical stage and treatment strategy (21). Qian *et al.* (5) demonstrated a 100% survival rate in 5 year, while their median progression-free survival

time was 97.8 months by a retrospective study, which showed the overall good prognosis. The annual surveillance for 8–10 years with or without ultrasound and tumor makers serology (estradiol and/or progesterin) depending on clinical suspicion was recommended (4,22). In our case, regular supervision has persisted in 2 years. In duration, the physical exam, hormone examination and abdominal/pelvic ultrasonography have been performed every 3–6 months from the last discharge. The disease-free status included no abdominal pain or disorder vaginal bleeding, and no other recurrence signs were proven by monitoring. This patient has been followed up regularly for long-term.

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### Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tcr.2019.12.56>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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