



Case report

Extraovarian sex cord tumor with annular tubules discovered arising from a leiomyoma

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ARTICLE INFO

Keywords:

Extraovarian
Sex cord tumor with annular tubules
Peutz
Jeghers
Leiomyoma

ABSTRACT

Background: Sex cord tumors with annular tubules (SCTAT) are a rare (2%) subtype of ovarian sex cord-stromal tumor. SCTATs are usually cured at time of diagnosis by surgical resection with an oophorectomy. SCTATs have a 100%(disease related) five-year survival. One third of SCTAT tumors are associated with Peutz-Jeghers syndrome. Literature review discovered only two published cases of extra-ovarian SCTAT. Due to the rarity there is no standard treatment for extraovarian SCTATs.

Case: A 39-year-old para-1 female with a symptomatic fibroid uterus, heavy menstrual bleeding, and a history of a uterine myomectomy, underwent an elective total abdominal hysterectomy. Intraoperative findings showed a 7.5 cm retroperitoneal mass adhered between the uterus and the right pelvic sidewall that on frozen section was found to be a degenerating leiomyoma. Final pathology demonstrated a 2 mm focus of incidental SCTAT adjacent to the serosal surface of the leiomyoma. The SCTAT was not associated with ectopic ovarian tissue or endometriosis. The patient's ovaries were normal on direct intraoperative examination, preoperative ultrasound and MRI. Six month postoperative surveillance ultrasound also demonstrated normal premenopausal ovaries.

Conclusion: This is the first extraovarian SCTAT in the published literature arising from a leiomyoma. Our patient had no family history and displayed no syndromic features for Peutz-Jeghers Syndrome. Ultimately, she declined genetic testing. The lack of evidence of ovarian involvement on both imaging and on intraoperative examination made localization to either ovary impossible. The patient is currently being managed with surveillance since the morbidity associated with bilateral oophorectomy in the 4th decade of life exceeds the theoretical risk of SCTAT.

1. Case

We present a case of an incidentally identified extraovarian sex cord tumor with annular tubules arising from a leiomyoma following a routine simple hysterectomy. A 39-year-old Gravida-1-para-1 female with a history of a fibroid uterus presented with progressively worsening pelvic pain and heavy menstrual bleeding. The patient underwent a uterine myomectomy two years prior to bleeding and mass symptoms. After one year, her pelvic mass symptoms gradually returned. Examination revealed a 14 week sized, wide based, globular uterus deviated to the patient's left. Preoperative imaging demonstrated an 11.2 × 4.2 × 5 cm fibroid uterus, normal follicular ovaries (Fig. 1), and a 7 cm right lower pelvic mass, suggestive of a pedunculated fibroid within the broad ligament deviating the uterus (Fig. 2). The patient had up-to-date cervical cancer screening. Her menstrual cycle was regular,

7 days long, but heavy and required pad changes every 3 h on the heaviest days. The patient's mass symptoms were not improved by conservative treatment with a levonorgestrel intrauterine device or a gonadotropin-releasing hormone agonist. The patient had satisfied parity and elected for definitive surgical management via a hysterectomy. She had no personal or family history of cancer.

The patient underwent a total abdominal hysterectomy, bilateral salpingectomy, and cystoscopy. Intraoperatively, a large, boggy, 7.5 cm retroperitoneal mass was identified, adhered to the uterus on the right and extending to the lateral pelvic sidewall. The mass was carefully dissected and removed from the uterus intact. Given the size and atypical location of the mass, it was sent for intraoperative frozen section. Frozen intraoperative consultation returned as an indeterminate, but likely benign smooth muscle tumor with edema and degenerative changes. No evidence of mitotic activity or atypia was identified. The

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<https://doi.org/10.1016/j.gore.2018.06.013>

Received 20 April 2018; Received in revised form 14 June 2018; Accepted 30 June 2018

Available online 02 July 2018

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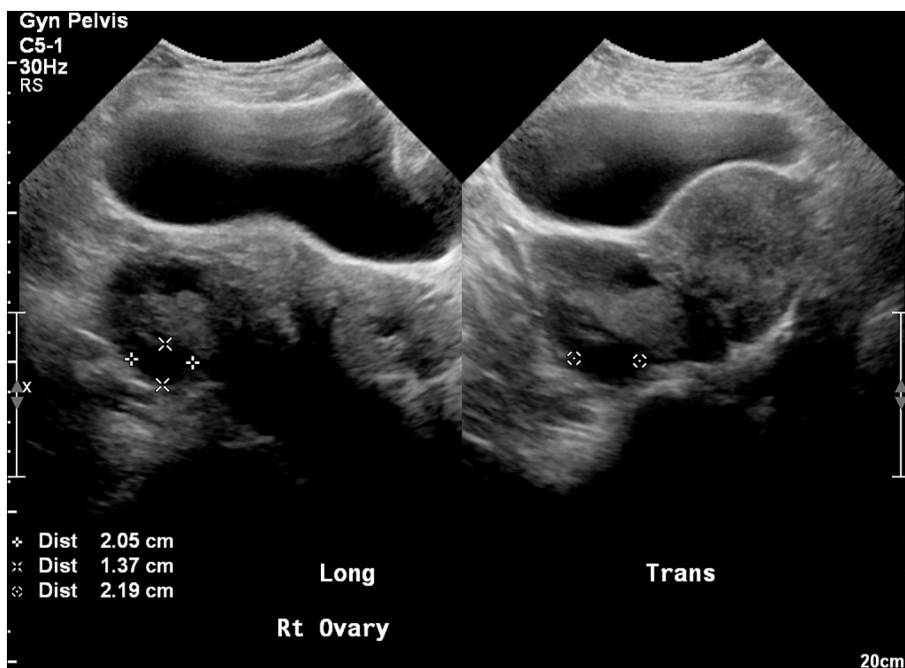


Fig. 1. Preoperative Pelvic Ultrasound Right Ovary.



Fig. 2. Preoperative MRI Pelvis, Right Fibroid.

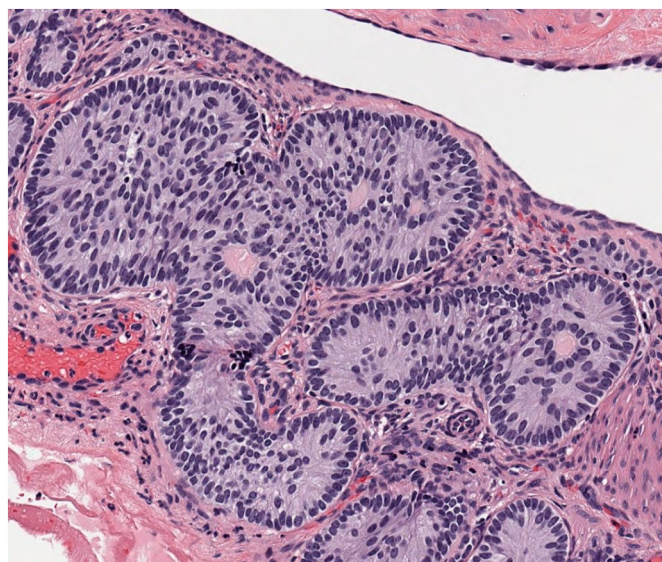


Fig. 3. SCTAT H&E Stain 200x.

ovaries were normal appearing bilaterally, and no other pelvic pathology was noted on abdominal survey.

The final pathology for the sidewall mass returned as a large hydropic leiomyoma with a small focus of incidental sex cord tumor with annular tubules. The tumor measured at least 2 mm and was located adjacent to the serosal surface, on the stalk of the leiomyoma. The tumor displayed simple and complex tubules with palisading of cells around the basement membrane, with dense central hyaline material (Fig. 3). The immunohistochemical staining pattern was characteristic of SCTATs, including diffuse positivity for inhibin (Fig. 4). There was no ovarian or endometrial tissue associated with the tumor. The remainder of the uterine, cervical, and tubal pathology was benign. The specimens

were sent for expert review at a regional referral center. Their pathologists concurred with the rare finding of extraovarian SCTAT arising from a leiomyoma.

Tumor presence on the ovaries and adnexa was excluded by intraoperative inspection and review of preoperative imaging. Given the patient's young age and remoteness from menopause, our recommendation was for repeat imaging in six months, rather than proceeding with a bilateral oophorectomy to rule out further disease. Due to the association of SCTAT with Peutz-Jeghers syndrome (PJS), the patient was also referred to a genetic counselor. She did not display any syndromic features and ultimately declined genetic testing. On her ultrasound six months later, her adnexa remained normal in appearance and there was no evidence of tumor.

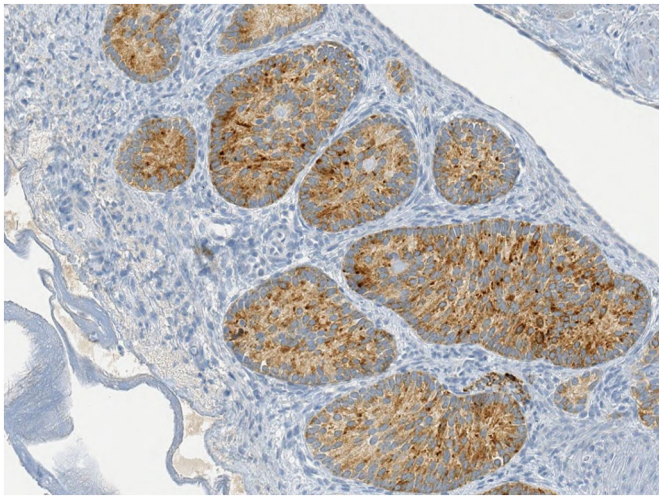


Fig. 4. SCTAT with Inhibin Immunohistochemical Stain 200 ×.

2. Discussion

Sex cord tumors with annular tubules are a rare (approximately 2%) type of ovarian sex cord-stromal tumor. (Brown et al., 2009) In the published literature, SCTATs are described almost exclusively within the ovaries. After extensive review, there have been only two definitive extraovarian SCTAT neoplasms: a fallopian tube primary associated with endometriosis, and a tumor incidentally discovered in an umbilical hernia sac. (Griffith and Carcangiu, 1991; Baron et al., 1998) A small case series described two incidentally noted specimens which closely mimicked SCTAT vs adult type granulosa cell tumor (AGCT) within the fimbriae of the fallopian tube. (McCluggage et al., 2015) In contrast to our case, the described specimens in the fallopian tubes consisted of microscopic submillimeter nests of cells, and one of the cases even noted a nest within the ovarian parenchyma, suggesting actual ovarian origin. (McCluggage et al., 2015)

One third of SCTATs are associated with Peutz-Jeghers syndrome (PJS), an autosomal dominant syndrome characterized by gastrointestinal polyp formation, mucocutaneous pigmentation, and an increased risk of ovarian, cervical, breast and GI cancer. (Jeghers et al., 1949) The characteristics and presentation of SCTATs can vary considerably between those associated with PJS and the non-syndromic varieties. Syndromic SCTAT tumors are typically small, bilateral, calcified, asymptomatic, and predominantly benign. (Young et al., 1384) Non PJS tumors are typically larger at time of diagnosis, unilateral/solitary, non-calcified, and have a 15–20% malignancy rate. (Young et al., 1384)

Staging for sex cord stromal tumors is performed surgically as for other ovarian primary carcinomas. Due to the rarity of SCTATs there are no standardized treatment protocols. SCTATs are usually diagnosed early stage, and primary treatment seen in case series involves surgical excision of the tumor. (Qian et al., 2015) In postmenopausal patients a simple hysterectomy and bilateral salpingo-oophorectomy is preferentially performed. As SCTATs are predominantly diagnosed in reproductive age patients, a unilateral salpingo-oophorectomy with follow-up imaging, cervical cancer screening, and endometrial biopsy is often performed to avoid iatrogenic menopause. (Qian et al., 2015) Older literature has described wedge resections of contralateral ovaries with suspicious lesions; however this practice has largely fallen out of favor with other ovarian neoplasms. (Qian et al., 2015) Currently there is no data that supports this practice in patients with SCTATs. (Qian et al., 2015) Further staging procedures such as lymph node or omental sampling are reserved for tumors with features concerning for malignancy, and are usually omitted given the indolent nature and excellent prognosis of most SCTATs. (Brown et al., 2009) There is a described

association between PJS, SCTATs, and adenoma malignum of the cervix, and thus cervical cancer screening, imaging, or removal is recommended to exclude this condition. (Young et al., 1384; Qian et al., 2015) In the absence of PJS, standard cervical cancer screening guidelines are recommended. Treatment of SCTAT recurrence typically consists of tumor resection, with consideration for adjuvant chemotherapy for advanced disease. (Qian et al., 2015) Prognosis for SCTATs is excellent with disease specific survival approaching 100%. (Meserve and Nucci, 2016)

As this is a rare presentation of an already rare disease, we relied on existing literature for our diagnostic and management approach. The patient's pathology specimens consisted of the patient's uterus, cervix, bilateral fallopian tubes, and the retroperitoneal leiomyoma which contained the SCTAT. Thorough pathological examination of this specimen as well as preoperative imaging and intraoperative exam reasonably assured us of a unifocal SCTAT associated with the fibroid. No evidence of ovarian involvement or metastasis was noted. Pathologic examination of the cervix excluded concurrent adenoma malignum of the cervix. The patient was seen for genetic counselling, but ultimately declined formal testing. Our patient has no family history of Peutz-Jeghers syndrome, nor does she display other characteristic clinical manifestations: mucocutaneous pigmentation or hamartomatous polyps. While a late presentation of the disease is possible, most present between the ages of 10 and 30, making PJS unlikely in our patient. (Jeghers et al., 1949)

The non-malignant pathologic features, unifocal nature, and small pathologic size of our specimen, in combination with her young age led us to pursue ovarian conservation for our patient. Given the rarity of the disease, the long-term risk of recurrence and disease specific mortality for SCTATs are unclear, but likely quite low. In their short term case series of SCTAT, Qian et al. demonstrated a 100% 5 year survival rate. (Qian et al., 2015) While their median progression-free survival was 97.8 months, these cases all represented larger and more aggressive SCTATs. (Qian et al., 2015) Given the small, confined nature of our neoplasm, combined with the low malignant potential of SCTATs in general, we anticipate a favorable prognosis and recurrence risk. In contrast, the increased cardiovascular mortality and decrease in sexual function are well documented in an elective bilateral oophorectomy at her age. (Matthews, 2016) In consultation with the patient, the decision was made for ovarian conservation with initial 6 month pelvic ultrasound surveillance to evaluate the unaffected ovaries. (National Comprehensive Cancer Network, 2018) Previous literature describes a mean duration to initial recurrence of 45.5 months (range 7–108 months) in SCTATs. (Qian et al., 2015) We thus recommend annual surveillance for 8–10 years with or without ultrasound depending on clinical suspicion. (National Comprehensive Cancer Network, 2018) There is insufficient evidence to support monitoring specific tumor markers. (National Comprehensive Cancer Network, 2018) SCTATs occur in young premenopausal patients. Further literature is needed to document favorable outcomes with ovarian and fertility preservation, so that we can optimize the survivorship in this patient population.

Funding

This project has not received any funding.

Informed Consent

Written and Verbal consent was attained from the patient for this manuscript.

Conflicts of interest

None.

Acknowledgments

Dr. Jeffery Saenger, Department of Pathology, San Antonio Military Medical Center for his work on the pathology samples. Department of Pathology at MD Anderson Cancer Center, Houston for their review of the pathology specimens.

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