Early View Article: Online published version of an accepted article before publication in the final form.

Journal Name: Journal of Case Reports and Images in Oncology

Type of Article: Case Report

Title: Recurrence of Sex Cord tumor with annular tubules in young patient with Peutz-Jeghers syndrome

Authors: Meher Slimane, Selma Gadria, Manel Hadidane, Houyem Mansouri, Maha Driss, Khaled Rahal

doi: To be assigned

Early view version published: November 1, 2016


Disclaimer: This manuscript has been accepted for publication. This is a pdf file of the Early View Article. The Early View Article is an online published version of an accepted article before publication in the final form. The proof of this manuscript will be sent to the authors for corrections after which this manuscript will undergo content check, copyediting/proofreading and content formatting to conform to journal's requirements. Please note that during the above publication processes errors in content or presentation may be discovered which will be rectified during manuscript processing. These errors may affect the contents of this manuscript and final published version of this manuscript may be extensively different in content and layout than this Early View Article.
TYPE OF ARTICLE: Case Report

TITLE: Recurrence of Sex Cord tumor with annular tubules in young patient with Peutz-Jeghers syndrome

AUTHORS:
Meher Slimane¹,
Selma Gadria¹,
Manel Hadidane¹,
Houyem Mansouri¹,
Maha Driss²,
Khaled Rahal¹

AFFILIATIONS:
¹Oncologic Surgery Departement, Salah Azaiz Institut, Tunis, Tunisia
²Pathology Departement, Salah Azaiz Institut, Tunis, Tunisia

CORRESPONDING AUTHOR DETAILS
Selma Gadria,
Surgical Oncology departement, Salah Azaiz Institute, Postal address: C3 residence Cordoba, Rue Tachkand, 2037, Ennasr1, Ariana, Tunisia.
Email: selma.gadria@gmail.com

Short Running Title: Sex cord tumor and Peutz-Jeghers syndrome

Guarantor of Submission: The corresponding author is the guarantor of submission.
**TITLE**: Recurrence of Sex Cord tumor with annular tubules in young patient with Peutz-Jeghers syndrome

**ABSTRACT**

**Introduction**
Peutz-Jeghers syndrome (PJS) is a hereditary autosomal dominant disease characterized by polyposis in the gastro-intestinal tract and melanin pigmented macules on the skin mucosa. In gynecology, it can be complicated with sex cord tumor with annular tubules (SCTAT). Multifocal, bilateral, small and benign lesions that develop into mucinous and serous ovarian tumors commonly characterize it. SCTATs associated with PJS are usually benign and do not have malignant potentials, thus, unilateral oophorectomy is curative. Recurrence is a common event. Subsequently, radical surgery is recommended in these cases.

**Case report**
We report the case of a 32 years PJS patient, who underwent conservative surgery for SCTAT 5 years ago. She shows up with a recurrent contralateral 75mm adnexal cyst. Because of her will of childbearing, a conservative surgery was planned and the patient underwent a laparoscopic cystectomy. One month after surgery, hormonal rates were measured after ovarian stimulation and didn’t show hormonal activity.

**Conclusion**
SCTAT associated to PJS is a rare and unusual variant of ovarian tumors. Conservative surgery is indicated but recurrence is still a common event. Because of its rarity and high recurrence rates, further studies are needed to confirm the effect of radical surgery and adjuvant therapies.

**Keywords**: Sex cord tumors, ovarian tumors, Peutz-Jeghers syndrome, hereditary disease.
**TITLE:** Recurrence of Sex Cord tumor with annular tubules in young patient with Peutz-Jeghers syndrome

**INTRODUCTION**

Peutz-Jeghers syndrome (PJS) is a hereditary autosomal dominant disease characterized by polyposis of the gastro-intestinal tract and melanin pigmented macules on the skin mucosa. In gynecology, it can be complicated with sex cord tumor with annular tubules (SCTAT). 30% of the SCTAT are associated to PJS. Multifocal, bilateral, small and benign lesions that develop into mucinous and serous ovarian tumors commonly characterize it. SCTATs associated with PJS are usually benign and do not have malignant potentials, thus, unilateral oophorectomy is curative. However, recurrence is a common event. Different from epithelial ovarian cancer, surgery is still the main treatment of choice for recurrent disease. Because of its rarity, there is no standard treatment protocol and the effects of chemotherapy and radiation therapy are still unclear.

**CASE REPORT**

A 32 years old woman case, with a family history of PJS, is reported. The patient presented in 2011 an adnexal mass. Physical exam revealed perioral-pigmented macule (Figure 1). In laparotomy, we discovered a left adnexal mass and an intestinal polyp. No ascites or lymph nodes were reported. The contralateral ovary was normal. The patient underwent a conservative staging including a left oophorectomy. No contralateral adnexal biopsy was performed. Histologic finding confirmed SCTAT associated to PJS intestinal polyp. The ovarian tumor were classified FIGO IA. Subsequently, the patient did not receive adjuvant therapy.

Five years later she presents abdominal pain. CT scan shows a 75 mm right adnexal mass evoking a cystic recurrence (Figure 2). The serum rate of anti-müllerian hormone (AMH) was elevated and measured 325-ng/ml. CA-125 rates were less than 35 UI/ml. In order to investigate PJS, a colonoscopy was performed and showed recto-colic polyposis. Mammogram showed benign cystic lesion of the breast. Papa smear didn’t show any abnormal cells. Radical surgery was
recommended but the patient refused because of her will of childbearing.

Laparoscopic exploration found a right adnexal cystic mass (figure 3), with no evidence of ascites or peritoneal carcinosis. We underwent a cystectomy; leaving an ovarian tissue. The histologic findings showed circumscribed columnar epithelial nests composed of ring shaped tubules, which are encircled by hyalinized basement membrane-like material and concluded for a recurrent SCTAT. No mitotic count was reported (Figure 4 and 5). One month after surgery, hormonal rates were measured after ovarian stimulation and didn’t show hormonal activity. Fertility preservation attempt was a failure and the patient is proposed for a complementary surgery.

Recurrence of SCTAT in young patient with PJS is a common event. Conservative surgery is always a challenge. We attend to find the best alternative to treat them.

DISCUSSION

SCTATs are rare tumors. They represent only 2.3% of sex cord tumors. 30% of SCTATs are associated to PJS [1]. Only few series reported SCTAT associated to PJS cases. In 1970, Scully reported 6 cases of SCTAT associated to PJS. Young and al reported in 1982, 27 additional cases. Most of the publications are case reports. The diagnosis of SCTAT is usually based on pathological examination of the tumor and typical presentations are most of the time consistent with hormone secreting tumor [2, 3]. Researchers have demonstrated that SCTAT secretes not only estradiol, but also progesterone, resulting as for our patient in menstrual disturbances. Young and al confirmed that SCTATs associated to PJS was multifocal, bilateral and small [1]. In contrast, SCTAT non associated to PJS are usually unilateral, large and have malignant behavior [4]. SCTAT includes ovarian Sertoli cell tumors, ovarian mucous or serous epithelial tumors and ovarian mature teratoma [5].

A preoperative diagnosis is difficult. It was reported in Qian study for two pediatric patients who underwent ovarian biopsy for suspected physiological ovarian cyst [6]. Ovarian biopsy is still dangerous and risky of disrupting the capsule and changing prognosis by tumoral spread.

Because of its rarity, there is no standard treatment protocol for SCTAT patient. Surgery remains the initial management. Because of its occurrence in young or
adolescent patient, fertility sparing surgery is important. Unilateral salpingo-
oophorectomy is curative for intact capsule tumors confined to one ovary with no
involvement to the uterus and the contralateral ovary [6]. Despite that, SCTAT
associated to PJS are bilateral tumors, and not commonly synchronous. Wedge
section or biopsy of the contralateral ovary is not a routine procedure, but it should
be considered, especially for PJS patients. There are no studies that compared
unilateral to bilateral oophorectomy [1, 6].

Adjuvant treatment for SCTAT is still a controversial point. The effects of
chemotherapy and radiotherapy are still not clear. Further studies are still needed to
confirm the effect on prognosis and survival [6].

Recurrent SCTAT should be suspected by clinical symptoms related to hormone
secreting. A rise of the AMH is a major sign. Recurrent tumors can be located in the
contralateral ovary or in the retro peritoneum. They can be detected by imaging such
as ultrasonography, CT-scan or PET-scan. It is a fundamental evaluation of tumor
size, number and location [6, 7].

Surgery for recurrent disease in SCTAT is a total hysterectomy, associated to
salpingo-oophorectomy, and lymph node dissection. Our patient had a 75 mm
adnexal cyst. A fertility sparing surgery consisted on a cystectomy, leaving a normal
residual ovarian tissue. Just like epithelial ovarian cancer, recurrent disease can be
located in the pelvic or para-aortic lymph nodes. A pelvic and para-aortic
lymphadenectomy should be considered [8]. Qian et al reported four cases of lymph
node dissection achieving complete response in three of them [6]. There is
unfortunately a lack of long term follow up. More studies should be considering
lymph node dissection [4].

Prognosis for SCTAT is relatively favorable although recurrence rate is very high.
Literature reports a 1-year and 5-year PFS of 92% and 67% respectively. The
median PFS time was 97.8 months. The 5-year OS was 100% [1, 6, 9].

CONCLUSION

SCTAT associated to PJS is a rare disease. Oophorectomy is a curative surgery for
unilateral tumors. Contralateral ovarian biopsy is a good alternative especially for
PJS because of the frequency of bilateral tumors. Although prognosis of SCTAT is
favorable, recurrence rate is high. Long-term follow up is essential. Serum rates of estradiol and progesterone in addition to AMH could be used as tumor markers during follow-up. Further studies are needed to confirm the best surgery and the effect of adjuvant therapies.

LIST OF ABBREVIATIONS:
SCTAT: Sex cords tumors with annular tubules
PJS: Peutz-Jeghers syndrome
AMH: anti-müllerian hormone

CONFLICT OF INTEREST
No conflict of interest are reported

AUTHOR’S CONTRIBUTIONS
Meher Slimane, Selma Gadria, Manel Hdidane and Houyem Mansouri made substantial contributions to conception and design of the manuscript. Maha Driss have been involved in drafting the manuscript and revising it critically for important intellectual content. Khaled Rahal have given final approval of the version to be published.

ACKNOWLEDGEMENTS
We would like to thank the head of the department and all staff members of department of Surgery and Pathology for their support and encouragement to prepare this report. The authors declare that there is no conflict of interest.

REFERENCES
3. Roberet. Scully M. Sex cord tumor with annular tubules a distinctive ovarian


**FIGURE LEGENDS**

- **Figure 1:** Perioral pigmented skin macula
- **Figure 2:** CT-scan showing 75mm right adnexal mass
- **Figure 3:** adnexal cystic mass
Figure 4: Sex cord stromal tumor with annular tubules of the ovary (H&E x10)

Figure 5: Sex cord stromal tumor with annular tubules of the ovary (H&E x20)

FIGURES

Figure 1: Perioral pigmented skin macula
Figure 2: CT-scan showing 75mm right adnexal mass.
Figure 3: adnexal cystic mass

Figure 4: Sex cord stromal tumor with annular tubules of the ovary (H&E x10)
Figure 5: Sex cord stromal tumor with annular tubules of the ovary (H&E x20)