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Non-syndromic bilateral ovarian sex cord stromal tumor with annular tubules in a postmenopausal elderly woman as an incidental finding

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ABSTRACT

INTRODUCTION: Sex cord tumors with annular tubules (SCTAT) are very rare neoplasms comprising less than 1% of sex cord ovarian tumors. They usually occur in women of reproductive age and tend to be associated with Peutz Jeghers Syndrome (PJS), be bilateral, multifocal, and small. When diagnosed in older patients they are often described as sporadic, unilateral, predominantly cystic and bigger.

CASE PRESENTATION: A bilateral hysterosalpingo-oophorectomy was performed in a seventy-one year-old-woman with postmenopausal bleeding showing no features of PJS. A bilateral SCTAT was diagnosed, associated with a focus of Leydig cell hyperplasia, an endometrial polyp and endometrioid intraepithelial neoplasia.

DISCUSSION: SCTAT is a very rare histological variant in postmenopausal women. The case we present is special, different to what has been reported in the literature regarding these tumors.

CONCLUSION: It is important to be aware that SCTATs can also be present in older women, they can be bilateral despite not being related to PJS syndrome and must be considered as a differential diagnosis in ovarian tumors.

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1. Introduction

SCTAT are very rare neoplasms comprising less than 1% of sex cord ovarian tumors [1,2]. They are found in two different clinical scenarios: 1) SCTATs associated with Peutz Jeghers Syndrome (PJS) generally occur in younger patients (mean age 27), usually bilateral, small, multifocal, and calcified. 2) SCTATs not associated with the Syndrome occur in older patients (mean age 36), usually larger, predominantly cystic, unilateral and with malignant potential [1]. There are few cases reported in patients over forty, being even stranger finding it in patients in the eighth decade of life. We report this case according to Surgical Case Report (SCARE) guidelines, being the second case of non-syndromic bilateral SCTAT reported in the literature [3].

2. Case presentation

A 71-year-old Mexican woman, housewife, with history of 13 pregnancies (11 deliveries, 2 abortions), last menstrual period reported at 36, hypertension (controlled with 50 mg losartan bid),

no family history of chronic disease or cancer, presented with two-month postmenopausal bleeding. On physical examination, there were no significant findings and she did not show features of Peutz Jeghers Syndrome. On ultrasound, a 1 cm thickening of the endometrial line was observed, in addition to a complex cystic tumor in the right ovary measuring 5.9 cm in diameter with a thin septum of 0.2 cm; the left ovary of 2.1 cm without significant ultrasound alterations. Tumor marker CA-125 (cancer antigen 125) was slightly increased by 66.5 U/mL and Ca 19-9 was within normal limits. It was decided to proceed with surgery with the diagnosis of endometrial hyperplasia. Laparotomy was performed by a gynecologic oncologist: bilateral ovarian tumors were found and bilateral hysterosalpingo-oophorectomy was performed without complications. The surgical specimen was submitted to our laboratory and it was processed routinely.

Grossly, uterus revealed 1.5 cm endometrial thickening and a 3 × 0.7 cm polyp at the fundus level. Right cystic tumor replacing the entire ovary measuring 8 × 5 × 5 cm, presented citrine fluid outflow to the section. The internal surface was septate anfractuous multilobed and yellowish. The left ovary measured 3 × 1 × 0.5 cm with an ocher yellow lobulated surface and a heterogeneous ocher yellow cut surface alternating with light brown areas, without hemorrhagic or necrotic areas. The uterine cervix and fallopian tubes were grossly unremarkable. Microscopically, the tumor was predominantly cystic, with simple and complex circular tubules

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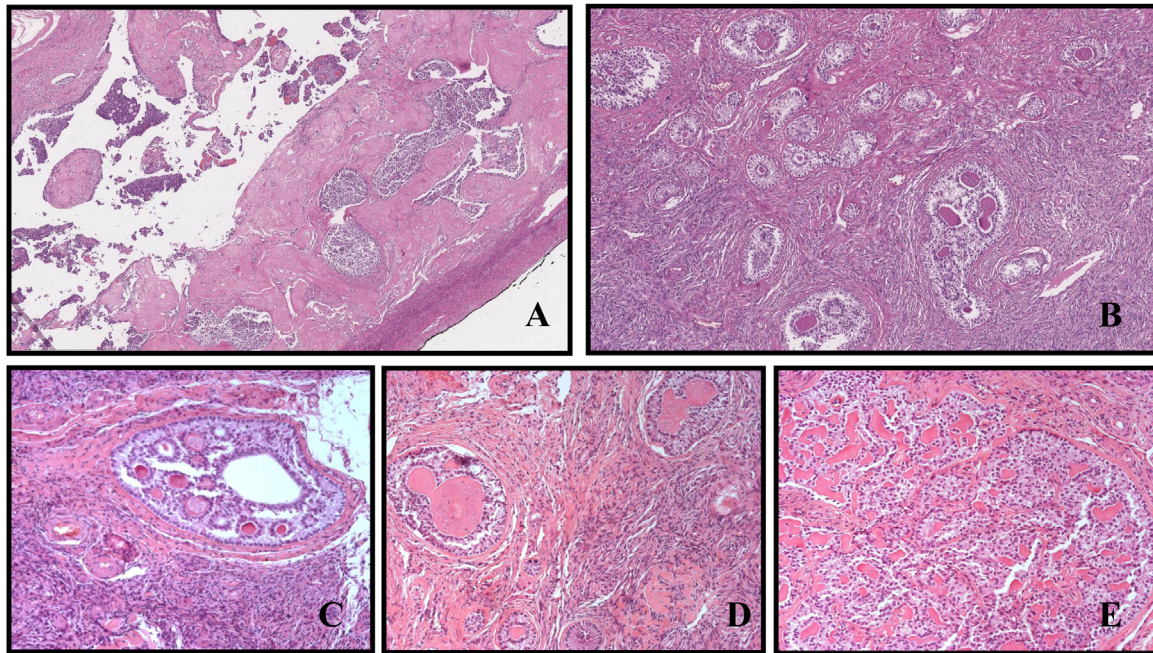


Fig. 1. Right sex cord tumor with annular tubules predominantly cystic (A,B) At higher power, the tumor has many concentric tubules dispersed in the ovarian stroma. (C,D,E) the tubules have prominent basement-type material in the center with antipodal arrangement of the nuclei.

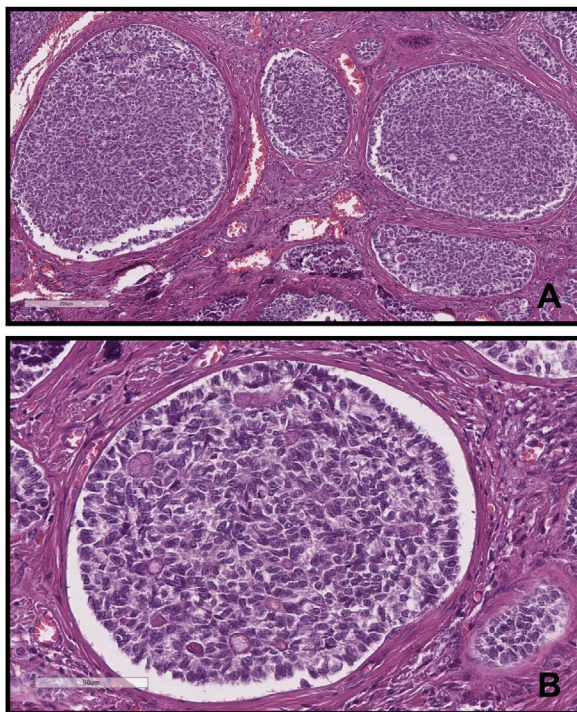


Fig. 2. Left ovarian cortex with confluent annular tubules encircle hyalinized center (A,B) nuclei palisade at periphery of nest and around hyaline material. The tumour cells are columnar and have clear cytoplasm and hyperchromatic nuclei with small nucleoli.

appreciated at low power in the medullary stroma of both ovaries. The tumor cells were columnar showing an antipolar arrangement as well as palisading around basement membrane-like material. The nuclei were uniformly rounded with inconspicuous nucleoli (Figs. 1, 2). Immunohistochemical staining for inhibin and calretinin was strongly positive in the tumor cells, cytoplasm, and nuclei (Fig. 3). Additionally, there was a focus of Leydig cells hyper-

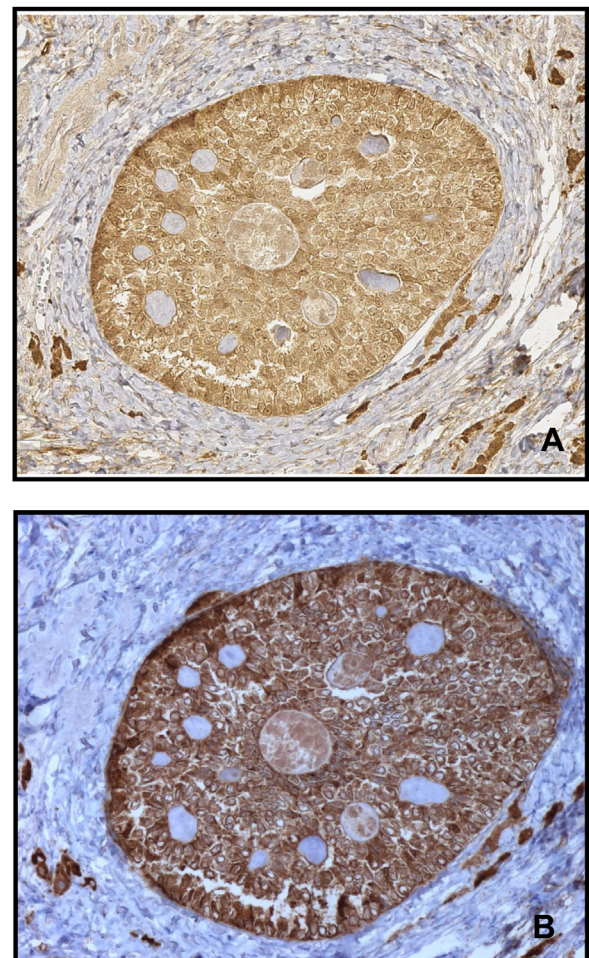


Fig. 3. (A) Inhibin is typically positive in sex cord tumour with annular tubules. (B) The cell tumors show characteristically strong expression of Calretinin.

plasia and the endometrial polyp had endometrial intraepithelial neoplasia. The histologic features of the tumor and its immunohistochemical profile support the diagnosis of sex cord tumor with annular tubules and was classified as FIGO (the International Federation of Gynecology and Obstetrics) Stage IB. No further adjuvant therapy was given, and she remained disease free during her follow up after 1 year.

3. Discussion

SCTAT are very rare neoplasms comprising <1% of sex cord ovarian tumors. They were mentioned for the first time in an article published in 1970 by Robert Scully. The origin is not clear, but Scully considered that these tumors had a distinctive phenotype that was intermediate between granulosa cell and Sertoli cell tumors favoring that the probable origin was granulosa cells with a growth pattern more characteristic of Sertoli cell tumors. Other authors refer that they can originate both from Sertoli cells and granulosa cells or even the pluripotent cells of the sex cords [2,4].

The clinical presentation is related to the secretion of progesterone and estrogens by the tumor depending on the stage of life in which the patient is, that is, precocious puberty in girls, menstrual disorders or amenorrhea in reproductive age and postmenopausal bleeding in older adults. Likewise, the hormonal effect can result in alterations in the endometrium such as decidualization, glandular atrophy, polyps or hyperplasia [4–6]. In this case, such hormonal stimulus resulted in postmenopausal transvaginal bleeding, endometrial hyperplasia and the patient developed intraepithelial neoplasia in an endometrial polyp.

When reviewing the literature, besides ours, we found 16 reported cases of patients with SCTAT who were sampled for preoperative ovarian tumor markers. Ca-125 was increased in 3 patients: the highest (211 U/mL) was reported in a 34-year-old patient with a 12 cm unilateral tumor after her second recurrence; our current case with a bilateral SCTAT greater than 8 cm and Ca-125 level of 66.5 U/mL; and finally, a 14-year-old patient with a unilateral tumor of 27 cm and a result of 42.6 U/ml (being the latter the only one who underwent the serum marker neuron specific enolase reported as 84.29 H G/M). No abnormalities were found in other serum tumor

markers including: AFP (0/12), CA 19-9 (0/10), CEA (0/10), B-HCG (0/5), CA242 (0/2), CA153 (0/2), CA724 (0/1), LDH (0/1) [6–12].

Macroscopically they are described as solid, cystic, or mixed yellow tumors, size ranging from 2 to 30 cm. The main histological finding is the presence of sharply delineated ring-like tubules lined by well-differentiated sertoliform cells with dense hyaline material in the lumen. These tubules are classified as “annular”, the cells have pale cytoplasm and the nuclei are characteristically located antipodally at the periphery of the tubules. Immunohistochemically, the tumor cells are positive for calretinin, inhibin, WT-1, CK, FOXL2, cytokeratin cocktail and CD56, and negative for CK5/6, EMA [13].

It has been described that SCTATs not associated with PJS tend to be more associated with a malignant potential including lymphatic spread to pelvic, para-aortic and supraclavicular nodes, and/or metastasis to peritoneum, liver, kidney, and lung [14]. Malignant behavior has been described in 11–12 cm tumors, with a high mitotic range, that is, 7–10 mitoses in 10 high-power fields, vascular or stromal invasion by individual cells or clusters and/or capsular infiltration [14]. However, none of these characteristics were present in our case: no mitosis, no vascular, lymphatic or capsular invasion were observed, and the patient had a benign course (at least up to 6 months after diagnosis), unlike three of the patients over forty that are described in Table 1, who had a malignant course.

As reported in the literature, SCTAT not associated with PJS tend to be unilateral tumors, bigger than 3 cm and predominantly cystic, which matches with the characteristics reported in the right ovarian tumor in the case that we present (an 8 cm septate cystic right ovarian tumor). However, what makes this case relevant is the bilaterality, since our patient also presented SCTAT in the left ovary (this last one with characteristics that are seen in SCTAT associated with PJS: a 3-cm solid tumor). This is the second case reported in the literature of a bilateral SCTAT in a patient who lacks clinical features of PJS. The first case is described in Table 1, published in 2007 in a 14-year-old patient [15].

We searched for all the cases of SCTAT in patients over 40 and summarized the most important characteristics in Table 1. With the observed data, we can conclude that when these tumors occur in this age group, it is more frequent that they are sporadic. If SCTAT is associated with PJS it is usually an incidental finding except in

Table 1
Clinicopathologic features of SCTAT cases in patients over 40 and the first case of a bilateral SCTAT in a patient who lacks clinical features of PJS.

AUTHOR	AGE	LATERALITY	PJS	DIMENSION	SYMPTOMS	ENDOMETRIUM	Adenoma Malignum	Malignant potential
Shah (2007) [15]	14	Bilateral	NO	N/A	Abdominal distension and pain	N/A	N/A	NO
Mangili (2004) [16]	41	Unilateral	YES	Multifocal microscopic	incidental (borderline mucinous cystadenoma)	Simple hyperplasia	YES	NO
Takeshima (1992) [17]	41	Unilateral	NO	L: 8 cm	Amenorrhea and abdominal distension	Proliferative endometrium	NO	NO
Clements (2009) [18]	43	Bilateral	YES	Multifocal microscopic	incidental (metastatic breast cancer)	N/A	YES	NO
Crissman (1980) [19]	43	Unilateral	NO	L: 1225 kg	menstrual irregularities and infertility	N/A	NO	YES
Bembde (2014) [20]	45	Unilateral	NO	L: 8 cm	One-year postmenopausal bleeding	Simple hyperplasia	NO	NO
Lele (1999) [14]	47	Bilateral	YES	L: 8.5 cm D: 3.5 cm	5-month transvaginal bleeding	proliferative endometrium and endometrial polyp	YES	YES
Oluwole (2004) [5]	48	Unilateral	YES	L: 4 cm	incidental (metastatic breast cancer)	N/A	NO	NO
Gloor (1979) [21]	48	Unilateral	NO	N/A	N/A	Simple hyperplasia	NO	NO
Kuhara (1991) [17]	52	Unilateral	NO	L: microscopic	Transvaginal bleeding	N/A	N/A	N/A
Barker (2009) [22]	54	Bilateral	YES	R: 4 cm L: 2 cm	abdominal distention, urinary incontinence	Proliferative endometrium	NO	YES
Omata (1985 [17])	64	Unilateral	NO	L: 7 cm	Transvaginal bleeding	Simple hyperplasia	N/A	N/A
Gloor (1979) [21]	64	Unilateral	NO	L: 15 cm	Postmenopausal bleeding	N/A	NO	NO
Gloor (1979) [21]	71	Unilateral	NO	R: 13 cm	Postmenopausal bleeding	Proliferative endometrium	NO	YES

patients in whom the SCTAT has a malignant behavior. On the other hand, the clinical presentation in patients over 40 with SCTAT not related to PJS begins with transvaginal bleeding secondary to hormone production by the tumor.

The differential diagnoses that we must consider are the sertoli cell tumor, granulosa cell tumor and gonadoblastoma. Sertoli cell tumor lacks the complex architecture and the hyaline centers. It is less positive for FOXL2 and could be positive for S100, smooth muscle actin (SMA). Granulosa cell tumor has characteristic architectural patterns such as Call-Exner bodies and could be positive for SMA and desmin, in addition to being negative for CK7. Finally, gonadoblastoma is almost always bilateral, but these patients typically have abnormal development of the gonads and may be associated with a germ cell component [13].

To date, there is no standardized treatment protocol for this type of tumor due to its oddity. However, the initial treatment of choice is surgery considering the age of the patient to determine how conservative the procedure should be performed. Regarding prognosis, a 5-year survival of 92% has been reported [1,6].

4. Conclusion

The importance of this case lies in the fact that it is the second reported case of a patient with bilateral SCTAT not associated with PJS and the age of presentation is very rare. Therefore, it is important to consider it as a possible diagnosis when the histopathological characteristics meet the SCTAT criteria.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

None

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Ethical approval

This article does not involve patients.

Consent

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Author contribution

All author contributed equally in the conception and design, acquisition of data, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content.

Registration of research studies

Not applicable.

Guarantor

There is no Guarantor.

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