

# Sertoli-Leydig cell tumour (SLCT) – the case of a 15 cm diameter ovarian tumour with negative markers and absent hormonal symptoms

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## ABSTRACT

Sex cord-stromal tumours are a group of tumours derived from the stromal component of the ovary and testis that comprise granulosa, thecal, Sertoli, and Leydig cells as well as fibrocytes. Sertoli-Leydig cell tumours (SLCTs) are rare ovarian neoplasms, accounting for less than 1% of all cancers arising from this organ. They differ in size; some might be very small, while some of them are huge (from < 1 cm to 35 cm). Most SLCTs are unilateral and may be functionally diverse. Approximately one-fifth of SLCTs may contain various heterologous elements, e.g. gastric or intestinal-like epithelium or malignant parts. Women with SLCTs may suffer from hormonal disturbances, manifest high alpha-fetoprotein, CA125, and testosterone levels and may suffer from virilisation, oligomenorrhoea, hirsutism, acne, voice changes, clitoris hypertrophy, or alopecia. However, those symptoms do not occur in every case.

Diagnosis of SLCTs is not easy, due to its rarity and varied presentation. Even though SLCTs are rare tumours, they should always be considered as a possibility, even in patients at different ages (typically 20-30 years old) without raised markers and hormonal disturbances.

In this manuscript we report a case of SLCT, 15 cm in diameter, with low marker levels and lacking hormonal disturbances, found in a 36-year-old female.

**KEY WORDS:** Sertoli-Leydig cell tumour, sex-cord stromal tumour, tumour marker, ovary, ovarian neoplasm, ultrasound.

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## INTRODUCTION

Sex cord-stromal tumours are a group of tumours derived from the stromal component of the ovary and testis. Sertoli-Leydig cell tumours (SLCTs) (earlier called arrhenoblastomas or androblastomas) are rare ovarian neoplasms, accounting for up to 1% of all cancers arising from this organ [1-3]. SLCTs most commonly occur in young patients, especially in women under 30 years of age [4]. They differ in size – some of them might be very small (from < 1 cm to 35 cm), while some of them are huge, but most are 12-14 cm [4]. Most SLCTs are unilateral and may be functionally diverse. Approx-

imately one-fifth of SLCTs contain various heterologous elements, e.g. gastric or intestinal-like epithelium [5] or malignant parts [1, 6].

Women with SLCTs may suffer from various hormonal disturbances and manifest high  $\alpha$ -fetoprotein, CA125, and testosterone (T) levels [7]. In some cases androstenedione and other androgen levels may also be increased [4]. Many patients with SLCTs present with abdominal or pelvic pain and may suffer from virilisation, oligomenorrhoea, hirsutism, acne, voice changes, clitoris hypertrophy, or alopecia [7, 8]. However, about half of all SLCTs present no endocrine manifestations [2, 4].

In this manuscript we report an interesting case of a huge SLCT without raised hormones and markers found in a 36-year-old female.

### CASE STUDY

A 36-year-old nulliparous patient with a medical history of acyclic menorrhagia was admitted to the gynaecological department with pain in the lower abdomen. On clinical examination, a well-circumscribed, firm, and mobile abdominal tumour was palpable. Ultrasound and computed tomography (CT) scans revealed an abdominal and pelvic solid-cystic mass about 15 × 13 × 14 cm in size with a regular shape, arising from the right adnexa, presenting acoustic shadows, without papillary lesions, and with low blood flow in colour Doppler imaging (Fig. 1A). The uterus and left adnexa were normal and only a small sign of fluid was found in the pouch of Douglas. No signs of virilisation or hirsutism were detected during the exam as well from medical history. Blood exam results revealed a CA125 marker level of 28.7 U/ml, serum human epididymis protein 4 (HE4) at 22 pmol/l, and no evidence of an active inflammatory process. Carcinoembryonic antigen (CEA) was within normal range. During the diagnostic process the patient reported episodes of severe pain. Due to the inconclusive features (ovarian tumour, adnexal torsion, or a malignant process) the physicians performed a diagnostic laparoscopy, which, due to suspicion of a malignancy, was converted to laparotomy. This revealed a right ovarian tumour with an uneven surface, adhering to the omentum. Thereafter, a salpingo-oophorectomy was performed (Fig. 1B). The surgeons abandoned extending the procedure due to the absence of consent from the patient, who wanted to preserve her fertility. A final histopathological exam revealed a poorly-differentiated SLCT of the right ovary. The results of perito-

neal washing were also positive for malignant cells. The patient was referred to a specialised oncology centre for further therapy.

### DISCUSSION

Sex cord-stromal tumours are a group of tumours that comprise granulosa, thecal, Sertoli, and Leydig cells as well as fibrocytes [1, 2]. SLCTs belong to the group of sex-cord stromal tumours of the ovary frequently seen in the second to fourth decade of life [1, 2, 9].

SLCTs are composed of variable proportions of Sertoli cells, Leydig cells, and in cases of intermediate and poorly differentiated neoplasms, may include primitive gonadal stroma and sometimes heterologous elements. SLCTs are a subject of current genetic research in which somatic DICER1 mutations were identified in approximately 60% of SLCTs [10, 11]. In other studies, Conlon *et al.* reported as much as 80% of DICER1 mutations in those tumours [12], and de Kock *et al.* noted 100% in moderately and poorly differentiated tumours [13]. These results suggest that DICER1 mutation may be a defining feature of undifferentiated SLCT neoplasms [13]. According to Lim *et al.*, the key to understanding SLCT molecular pathogenesis may aid in improving further tumour classification and lead to the discovery of more effective treatment strategies [10].

Important prognostic factors for SLCTs are patient's age, degree of differentiation, and clinical staging [14]. These tumours are considered to be of unknown malignant potential. Young and Scully defined this potential as none in a well-differentiated tumour, about 11% in the intermediate types, 59% in poorly differentiated tumours, and about 19% in tumours with heterologous elements [2]. One-third of female patients present with a progressive masculinisation, anovulation, oligomenorrhoea, or amenorrhoea [7].

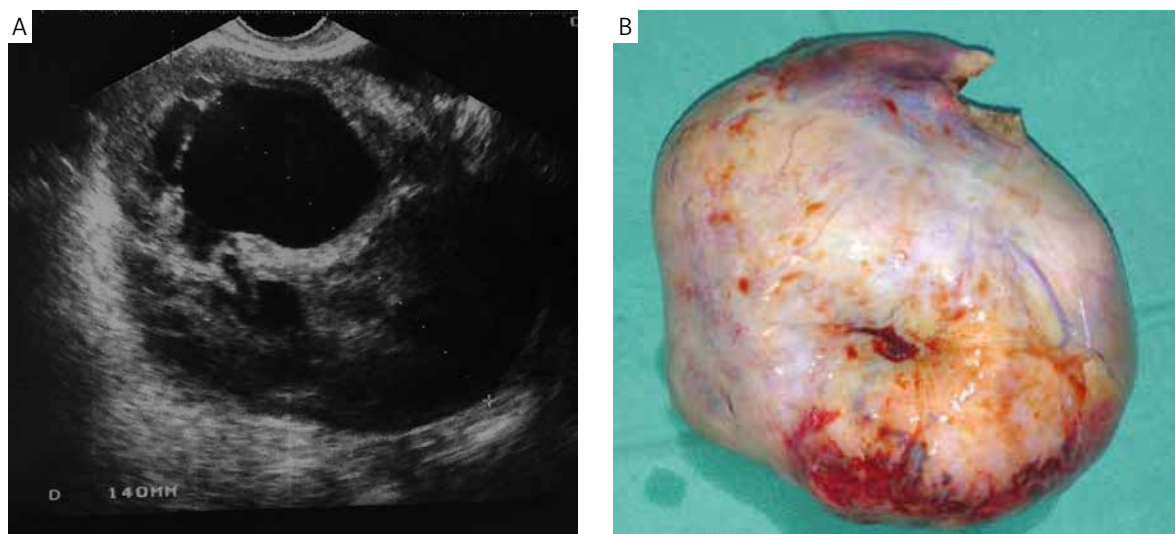


FIG. 1. Sertoli-Leydig cell tumour (SLCT). **A**) SLCT in ultrasound – measurement. **B**) SLCT after surgery

Surgery is the standard treatment for SLCT. In patients with stage IA tumours, unilateral salpingo-oophorectomy is the treatment of choice. In older women or patients at an advanced stage, removal of the uterus, ovaries, the omentum, and (to the extent possible) metastatic deposits are considered to be standard procedures [15, 16]. The value of postoperative adjuvant therapy, including various types of combination chemotherapy, as well as radiation therapy, has not been proven [15]. Mortality depends on the stage and differentiation; patients who present at a higher stage have a poorer prognosis [4].

Diagnosing SLCTs is often difficult, as in the present case, due to their rarity and varied presentation. Demidov *et al.* reported that ultrasound morphology of these tumours may be quite revealing and a diagnosis might be made on the basis of endocrine symptoms, patient's age, and ultrasound findings [4]. In CT or magnetic resonance imaging (MRI), SLCTs present as solid or mixed solid-cystic masses, with heterologous elements in some cases. Enhancement in this tumour is constant after administering contrast [7].

Currently, International Ovarian Tumour Analysis (IOTA) Simple Rules, due to the very good results, are the basis of an ovarian tumour clinical management system [17, 18]. However, despite its great potential in tumour diagnosis, this system was inconclusive in this case [18]. An inconclusive CT also delayed the final diagnosis. On the other hand, it should be emphasised that the main problem in diagnosing this patient was the absence of hormonal disturbances and related symptoms. Similarly to 50% of patients, she did not present any hormonal changes [7].

## CONCLUSIONS

This SLCT example shows once again that routine tests for ovarian neoplasm markers are not useful for rare cancers, and that diagnostic decisions should therefore be made based on clinical symptoms, ultrasound imaging, CT, or MRI, and then verified during diagnostic laparoscopy or laparotomy. Even though SLCTs are rare tumours, they should always be considered, even in patients without raised levels of markers and hormones, as was shown in the present case.

This case might support the need for surgery in persistent ovarian masses even in non-symptomatic patients. The scope of the initial treatment should be discussed with the patient and depend on her consent. A full range of optimal treatments should be performed after the final histopathologic examination in specialised oncological centres.

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## DISCLOSURE

The authors report no conflict of interest.

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## AUTHOR'S CONTRIBUTIONS

MC, AB, ASF, CW and GF prepared the research concept and design, collected data, wrote the article, revised the article and finally approved it.