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Ovarian Sclerosing Stromal Tumour: A Challenging Diagnosis during Pregnancy

Filipa S^{1-3*}, Daniela M^{1,2}, Fernando C¹, João PM², Ana LA^{1,3,4}, Guilherme T⁴⁻⁶ and Paulo M^{1,3}¹Department of Obstetrics, University Hospital Centre of Coimbra, Coimbra, Portugal²Department of Gynaecology, University Hospital Centre of Coimbra, Coimbra, Portugal³Faculty of Medicine, University of Coimbra, Coimbra, Portugal⁴Coimbra Institute for Clinical and Biomedical Research (iCIBR), Faculty of Medicine, University of Coimbra, Coimbra, Portugal⁵Department of General Surgery, HBP Unit, University Hospital Centre of Coimbra, Coimbra, Portugal⁶Biophysics Institute, IBILL, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

*Corresponding author: Ana Filipa Batista Costa e Sousa, Department of Gynaecology, University Hospital Centre of Coimbra, Coimbra, Portugal, Tel: +351916209080; E-mail: filipabcousa@gmail.com

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Abstract

Ovarian sex cord-stromal tumours differ clinically and morphologically from epithelial tumours. A small number of cases are reported during pregnancy, making diagnosis difficult. We present a case of a 23-year-old healthy nulliparous woman with left-flank abdominal pain for 4 weeks associated with a 20-centimetre painless abdominal mass. Pregnancy had evolved normally until that point. Due to a rise in inflammatory parameters, the differential diagnosis first pointed to an infectious process. The absence of resolution with antibiotic therapy associated with the radiological aspects (consistent with a mesenteric, intestinal or ovarian tumour) required surgical investigation. A caesarean was performed at 34 weeks of gestation; excision of the tumour was carried out, the origin of which was extremely difficult to determine. Histological examination was the key to a definitive diagnosis and clinical follow-up.

Keywords

Ovarian neoplasms; Sex cord-stromal tumour; Pregnancy

Introduction

Ovarian sex cord-stromal tumours (SCST) represent approximately 5% of all ovarian tumours between 15 and 24 years of age [1-3]. SCST appear to derive from stromal cells and/or the sexual cords of ovarian follicles and/or their precursors [2]. First described in 1973, sclerosing stromal tumours (SST) represent 2% to 6% of SCST, with an unknown aetiology [4,5]. We report here a case of an ovarian SST diagnosed at 33 weeks of pregnancy due to symptoms of abdominal compression. Clinical and radiological features were not sufficient to identify the cause, and even surgical

investigation was not able to determine the origin of the tumour with certainty. This case report was approved by our hospital's Ethics Committee and the patient provided written informed consent.

Case Presentation

A 23-year-old healthy nulliparous woman in her 33rd week sought our emergency department with left-flank abdominal pain for 4 weeks. Additionally, she referred to asthenia, constipation, and anorexia but denied fever or weight loss. She also denied nausea, vomiting, gastrointestinal or vaginal bleeding. The pregnancy was uneventful. She had never undergone any surgery; she was not a smoker or alcohol consumer, nor was she overweight (body mass index of 22.8 kg/m²). However, she had never had a gynaecological follow-up before this pregnancy. In her family's medical history there was no relevant pathology. Her first and second trimester routine analyses were all normal, as were obstetric ultrasounds (13th, 21st and 31st weeks). The last one revealed a cephalic presentation with foetal weight estimation and abdominal perimeter in 50th percentile and normal amniotic fluid index. At physical examination we could palpate a painless elongated mass in her left flank with a firm/elastic consistence, almost immobile, of around 20 centimetres. Gynaecological examination was normal with a lengthy and closed cervix. There were raised inflammatory markers and an increase of the lactate dehydrogenase (401 U/L). A thoraco-abdominal-pelvic CT scan was performed (no contrast), and revealed no changes in liver, gallbladder, pancreas, kidneys, spleen or adrenals; absence of thoracic or pelvic adenopathies and pleural suffusion. Nevertheless, it disclosed a solid and heterogeneous mass in the left flank of 15 × 11 × 17 centimetres, associated with ascites. Radiological aspects prompted a differential diagnosis between mesentery, intestinal or ovarian tumours. Tumour marker levels revealed: carcinoembryonic antigen of 0.8 ng/ml; alpha fetoprotein (AFP) of 8.4 ng/ml; cancer antigen 19-9 of 5.5 U/ml; cancer

antigen 125 of 410 U/ml; cancer antigen 15-3 of 7.4 U/ml; and cancer antigen of 72-4 of 1.0 U/ml. After hospital admission, she showed analytical improvement and remained clinically stable and feverless. Surgery was scheduled for the 34th week with the aim of foetal extraction plus investigation of the abdominal mass. It was a multidisciplinary surgical procedure with the collaboration of two obstetricians, one gynaecologist and one general surgeon. The operation started with a medial infra-umbilical incision, followed by an incident-free peritoneal cavity entry. The hysterotomy was performed followed by the delivery of a healthy baby; the dislocation was complete, the blood loss was moderate and the hysterorrhaphy with an invaginating suture was carried out. During the exploration of the abdominal cavity, a bulky tumour formation was seen, located in the left flank and hypochondrium of 17 × 11 centimetres (**Figures 1 and 2**); consistency was soft, and it showed cystic features and abundant vascularization, causing easy bleeding.

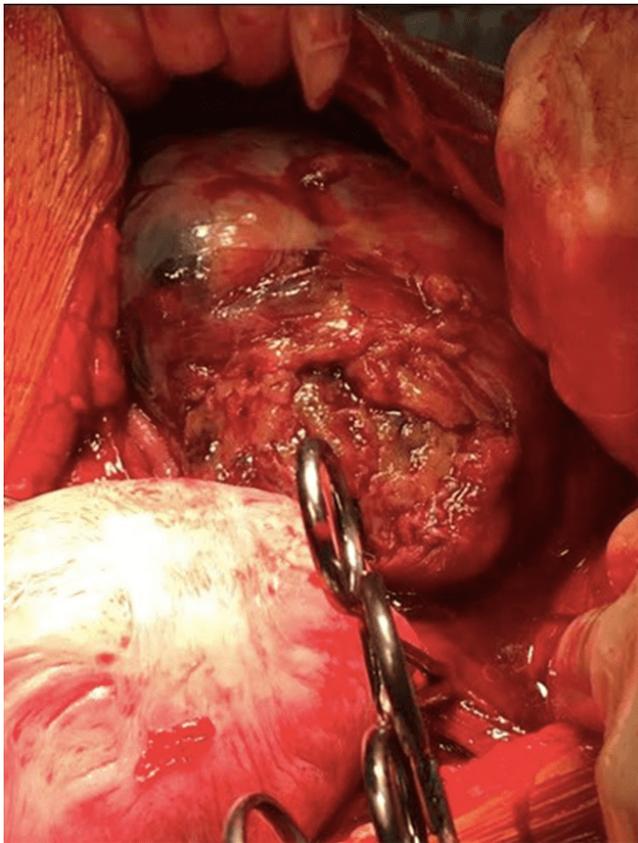


Figure 1: Uterus and tumour.

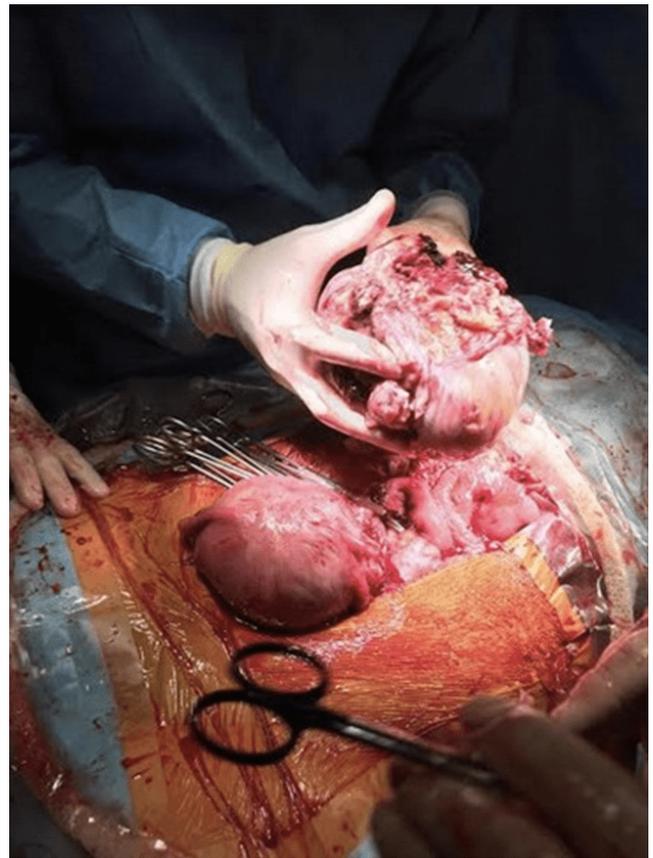


Figure 2: Tumour and uterus.

Its origin was extremely difficult to determine as it was adherent to the colon, peritoneum, diaphragm and other abdominal organs. The intra-operative frozen section suggested a mesenchymal neoplasm, so the possibility of malign ovarian tumour or dysgerminoma was excluded. Excision of the tumour was complicated due to the difficulty in its separation from the small bowel, which required bowel suture; partial omentectomy was performed in an area that seemed to be invaded by the tumoural mass and was not excisable. Left adnexectomy was carried out (although with doubt about the inclusion of the left ovary in the tumour). Two units of red blood cells were transfused intraoperatively. After adequate haemostasis, the abdominal wall and skin were closed. Clinical evolution was favourable. She was discharged 9 days after surgery. Placental histological examination was normal for a 34-week pregnancy. Definitive anatomopathological result of the abdominal mass was compatible with a left ovarian SST tumour (**Figures 3 and 4**).



Figure 3: Histology of the tumour, magnification 20x (haematoxylin and eosin staining).

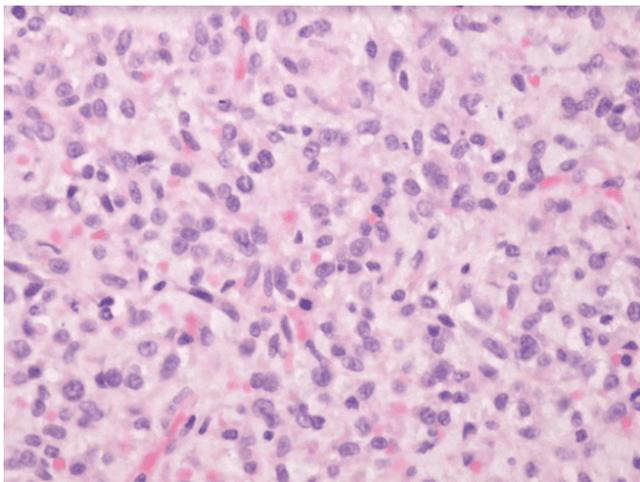


Figure 4: Histology of the tumour, magnification 200x (haematoxylin and eosin staining).

Discussion

Ovarian SCST represent a group of clinically heterogeneous tumours (**Table 1**) which can be diagnosed at all ages, although young adults are the most frequently affected, except for adult granulosa cell tumours which usually appear later in life [6,7]. Typical presentation includes symptoms of compression, such as abdominal distension or pain, swelling, gastrointestinal or urinary disorders [1]. Differing from ovarian epithelial or germ cell tumours (GCT), hormonal production signs (hirsutism, virilization, precocious puberty, delayed menarche or menstrual changes) can often be present in SCST. [1] During pregnancy, they can be incidentally discovered during caesarean delivery. When diagnosed, these tumours are usually large and unilateral, showing frequently haemorrhagic

or necrotic features [1]. They can be solid, firm and lobulated or soft and friable [1].

Table 1: WHO Classification of ovarian SCST [14].

Pure stromal tumours	Fibroma
	Cellular fibroma
	Fibrosarcoma
	Thecoma
	Luteinized thecoma associated with sclerosing peritonitis
	Sclerosing stromal tumour
	Signet-ring stromal tumour
	Microcystic stromal tumour
	Leydig cell tumour
	Steroid cell tumour
	Steroid cell tumour, malignant
Pure sex-cord tumours	Adult granulosa cell tumour
	Juvenile granulosa cell tumour
	Sertoli cell tumour
	Sex cord tumour with annular tubules
Mixed SCST	Well differentiated
	Intermediately differentiated
	Poorly differentiated
	Retiform with heterologous elements
Sex cord tumour, NOS	Gynandroblastoma
	Unclassified
WHO: World Health Organization, NOS: Not Otherwise Specified	

In accordance with these features, our patient presented with pelvic mass symptoms although without signs of hormonal production. SST tend to have a lack of hormonal function, in contrast with other SCST [8,9]. The tumour was large (17 centimetres), agreeing with descriptions in the literature. SST can vary from uniformly solid to a mix of solid and cystic or even mostly cystic [9].

The first step in the investigation of a pelvic mass is usually ultrasound, which may be complemented by a CT scan or magnetic resonance [1]. In these cases, ultrasound usually shows a mass with solid and cystic features as well as irregularly thickened septa and heterogeneous echogenicity [6]. Moreover, the possible hypervascularization and solid component are suspicious for malignancy [4]. CT imaging can show a variety of SST aspects, especially if a dynamic contrast-enhanced CT scan is performed [10]. We did not use contrast due to the pregnancy. Differences are based on solid densities for vascularity, cellularity and collagenous distribution, compared to low density for necrotic or cystic degeneration

areas [10]. Owing to the heterogeneous appearance, mesenteric or intestinal tumours were also considered.

Immunohistochemistry, tumour serum markers and sex hormones can help diagnose SCST [1]. There are immunohistochemical markers with high sensitivity and specificity (**Table 2**), which show negativity in epithelial and GCT [3]. Nevertheless, none has absolute sensitivity or specificity and they are limited in distinguishing different subtypes of SCST [3]. In particular, the combination of four markers (**Table 2**) is described as typical of SST, and justifies a stromal origin of these tumours [7]. In our case, there was weak diffuse α -inhibin and calretinin staining (**Figures 5 and 6**) and diffuse vimentin staining (**Figure 7**), which is in accordance with the literature. There were also some scattered inflammatory cells with leukocyte common antigen positive staining, focal positivity for Melan-A and focal weak smooth muscle actin staining.

Table 2: Immunohistochemistry of SST [3,7].

High sensitivity and specificity for SCST
α -inhibin
Calretinin
SF-1
FOXL2
Joint positivity typical of SST
Inhibin
Calretinin
Smooth muscle actin
Vimentin
SF-1: Steroidogenic factor-1, FOXL2: Foxhead box protein L2

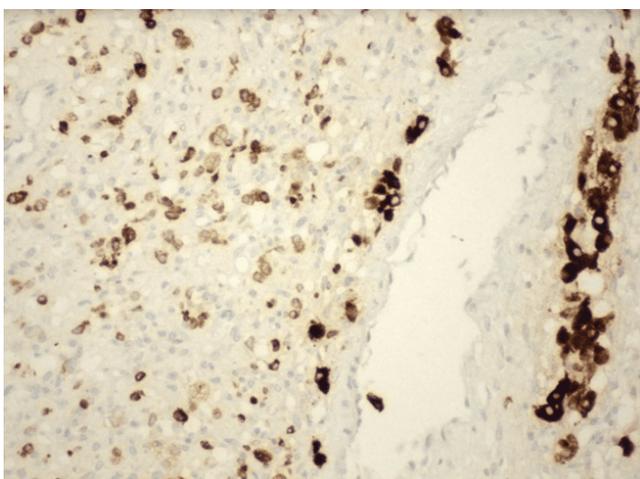


Figure 5: Histology of the tumour, magnification 200x (weak diffuse α -inhibin staining).

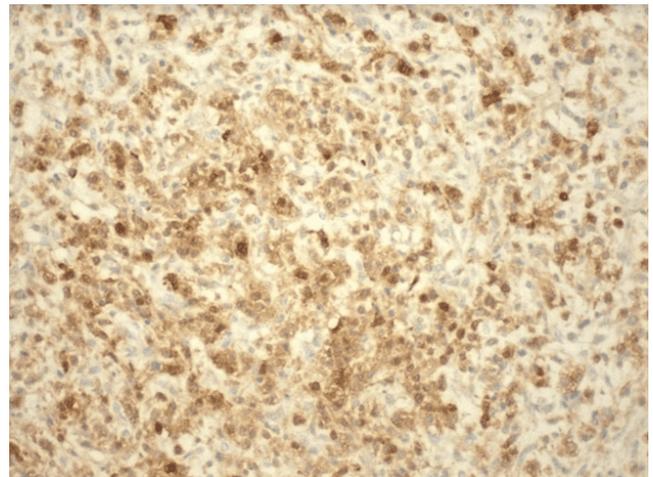


Figure 6: Histology of the tumour, magnification 200x (weak diffuse calretinin staining).

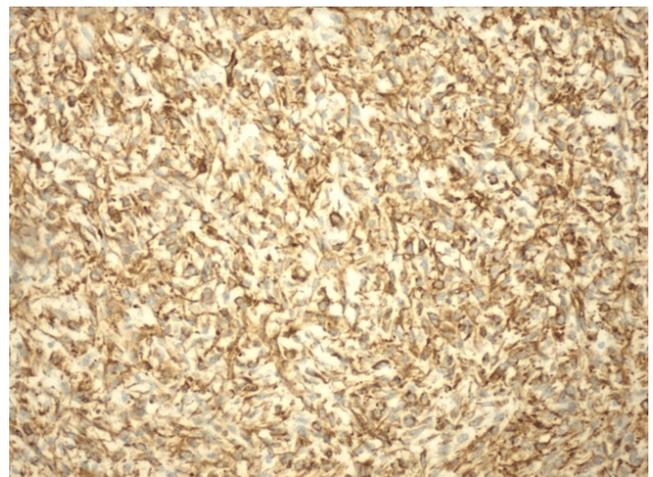


Figure 7: Histology of the tumour, magnification 200x (diffuse vimentin staining).

Some cases have described a rise in CA 125 [7], as occurred with our patient. Testosterone, estradiol and AFP can be useful [1]. Only the latter was investigated. The possible hypervascularization might be correlated with overexpression of angiogenic factors, which in the future may be used as a marker of SST [4]. Even though an ovarian tumour was suspected, SST diagnosis was far from being the first option, due to its rarity and clinical and radiological similarity to borderline or malignant epithelial tumours and other SCST [6].

Routine treatment is fertility-sparing surgery if the uterus and contralateral ovary and tube are spared, as in our patient [1]. Time and type of surgical intervention are similar for pregnant or non-pregnant women, with no standardized recommendations [1]. A sample of omentum was removed due to its invasion by the tumour, but as there were no radiological or intraoperative signs of lymph node invasion, lymph node resection was not performed. Histology also revealed the left ovary transformed into a cystic formation and

an omentum snip with haemorrhagic infiltration, marked fibroblastic proliferation, as well as a decidualized aspect.

Histological diagnosis remains a challenge, especially during pregnancy [5,10]. At a microscopic level, SST are characterized by a jumbled admixture of fibroblasts and weakly luteinized cells [5,7,10]. The typical histologic features can help distinguish them from thecomas, fibromas, and other benign SCST [5,7,10,11]. An alternating pattern of hyper and hypocellularity, the presence of luteinized cells and the characteristic vasculature can also be helpful [6]. There are three mandatory features: vascular ectasias with a haemangiopericycystic aspect within the nodules, admixed luteinized and nonluteinized cells and pseudolobular architecture composed of cellular and vascularized areas in a fibrous/collagenous or oedematous stroma [6,8,9,11]. Accordingly, this tumour had peripheral cellular nodules, alternating with a hypocellular oedematous or fibrous stroma. Round or polygonal cells with vacuole-like or eosinophilic cytoplasm with fine granules were present and suggestive of lutein cells. Vascular structures with a haemangiopericycystic pattern were found. Centrally, there were extensive areas of haemorrhagic necrosis, favouring a pseudocystic aspect.

During pregnancy, there might be a higher number of luteinized cells with abundant eosinophilic cytoplasm that distort typical histological characteristics [8-11].

According to the literature, the mitotic index is diverse but generally low (< 5/10 high-power fields – HPF) [3]. Our histological examination revealed disperse figures of mitotic activity of 4/10 HPF and proliferation index of 30% with Ki-67. There are some reports of cases with higher mitotic activity (7 to 14/10 HPF) [12-14]. These led authors to suggest the term mitotically active sclerosing tumour for those with > 4/10 HPF [12]. As one case recurred, further reported cases of these SST with higher mitotic activity are needed to determine the exact prognosis, as these cases might need a longer-term follow-up [14].

In this case, a combined hormonal oral contraceptive with 2 mg dienogest + 0.03 mg ethinylestradiol was prescribed. The patient will have annual follow-up appointments with ultrasound evaluation in our department for the next 5 years.

Conclusion

In conclusion, SST has been almost invariably classified as a benign entity. and thus have a good prognosis. Aetiology and pathogenesis of SST remain a topic of investigation. Some authors believe they originate from immature stromal cells, others from muscle-specific actin-positive elements of the external theca. Pregnancy brings a challenge to the diagnosis, especially in terms of suspicion before histology. Therapeutic

approaches are the same as in non- pregnant women. To date, SST is considered a benign pathology, with few cases described in pregnancy and the scientific community should be aware of their different forms of presentation and their follow-up.

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