Sclerosing stromal tumor (SST) of the ovary: a case report and review of the literature

Vittoria Del Vecchio1,*, Silvia Cardinale1,†, Nicola A. Carlucci1,‡, Giuseppe Trojano1,§
1 Obstetrics and Gynecology Unit, “Madonna delle Grazie” hospital, 75100 Matera, Italy
*Correspondence: vittoria.delvecchiomd@gmail.com (Vittoria Del Vecchio)
†These authors contributed equally.

Sclerosing stromal tumor is a rare benign neoplasm of the ovary. It occurs in women in the second-third decades of life and is generally hormonally inactive. It has nonspecific symptoms like menstrual irregularity, abdominal pain, amenorrhea, infertility and on imaging it is represented by a solid or cystic unilateral ovarian mass. We describe a case of a 17-year-old woman who presented with menstrual irregularity and pelvic pain. She underwent laboratory analysis including serum markers that were within normal ranges and a MRI which showed a solid mass measuring 4 cm of the right ovary. The patient underwent a laparoscopic surgery with the enucleation of the mass and, after the result of the frozen section examination, a conservative approach with preservation of the ovary was possible. Histopathological and immunohistochemical examinations confirmed the diagnosis of sclerosing stromal tumor of the ovary and allowed a differential diagnosis with other benign or malignant ovarian masses. SST of the ovary is a difficult diagnosis to make preoperatively. It commonly occurs in young women in whom ovarian conservation should be considered. Normal serum tumor markers and findings on imaging studies could suggest the diagnosis. However, the definitive diagnosis can only be made by histopathological examination of the removed tumor that can be treated successfully with fertility preserving surgery.

Keywords
Ovarian tumor; Ovarian stromal neoplasm; Sclerosing stromal tumor; Young women

1. Introduction
Sclerosing stromal tumour (SST) is an extremely rare benign neoplasm of the ovary [1, 2]. It accounts for about 6% of tumors that originate from ovarian stroma [3, 4]. The first case was described by Chalvardjian and Scully in 1973. This neoplasm occurs most frequently in the second-third decade of life, it is generally hormonally inactive, but rare hormonal activity (estrogenic or androgenic) has been reported, most often during pregnancy [5, 6].

The most frequent symptoms are pelvic pain and menstrual irregularity associated with a unilateral pelvic mass [7, 8].

Histopathological and immunohistochemical examinations are mandatory for the differential diagnosis with other ovarian masses and to confirm the diagnosis of SST.

We describe the case of a young woman who was diagnosed with SST in our Hospital.

2. Case report
A 17-year-old woman presented with menstrual irregularity and abdominal pain. Patient was virgin, therefore, vaginal examination was avoided. Bimanual abdominal rectal examination revealed abdominal tenderness, an anteverted uterus of normal size and shape. Left ovary was normal, right ovary was painful and characterized by firmness. Pelvic ultrasonography showed a right adnexal round solid mass measuring 4.6 x 4.1 x 4.5 cm with multiple small hemorrhagic necrotic areas and peripheral vascularization (Fig. 1, Fig. 2); the mass normally slid over the other pelvic organs without evidence of pelvic adhesions neither of "crescent sign".

The left ovary, uterus and endometrium were normal. The patient underwent laboratory investigations including HCG, LDH, CA125, CA19.9, CA15.3, CEA and AFP. All were within normal limits. A pelvic MRI was also performed and showed an adnexal round solid mass measuring 4.5 cm with an irregular edge, strong contrast enhancement and central colliquation (Figs. 3, 4). The patient underwent laparoscopic surgery with the removal of the right solid mass and preservation of the ovary: the ovary was mobilized, grasped with forceps and on the antimesenteric surface an incision was made. After identifying the correct plane of cleavage between the mass and the normal ovarian tissue, traction was applied to separate mass from the normal ovarian tissue (Fig. 5). The resected tumor was inserted into a containment bag and removed through the umbilical incision. The intraoperative histological examination of the frozen section revealed an ovarian mesenchymal tumor without evidence of atypical cells. The residual right ovary was reconstructed with monofilament suture. Postoperative hospital length of stay was 2 days.

Definitive pathological examination revealed a sclerosing stromal tumor of the ovary. It was described as a white solid mass measuring 4 cm. Microscopic features included a pseudolobular pattern alternating hypocellular and hypercellular...
areas, the presence of luteinized theca-like cells with vacuolated cytoplasm and fusiform fibroblasts-like cells, fibrosis and oedematous stroma.

There was no significant cytologic atypia and Ki67 was less than 10%. Immunohistochemical analysis revealed positivity for actin, inhibin and calretinin.

Ultrasound follow-up after two months showed a normal right ovary with follicular activity. The patient resumed a normal menstrual cycles and no longer had abdominal pain.

3. Discussion

SST is an extremely rare benign neoplasm of the ovary with distinctive pathological, clinical and radiological features [1, 9]. It accounts for about 6% of tumors that originate from ovarian stroma [3]. It often occurs in the second and third decades of life, it is generally unilateral and, in rare cases, it has been diagnosed during pregnancy [1, 10, 11].

It originates from sex cords and ovarian stroma or mesenchyme. In contrast to malignant epithelial ovarian tumors, it is not associated with a hereditary syndrome [12, 13].

Differential diagnosis from other stromal tumors is mandatory and possible through clinical, pathologic, immunohistochemical [14] and radiologic analysis.

Clinical presentation includes menstrual irregularity, even if the tumor is hormonally inactive, and pelvic pain. This tumor is often hormonally inactive, so that hormonal symptoms are rare. However, some hormonally active cases have been described in the literature and demonstrated estrogenic and/or androgenic effects.

The etiology is not yet well understood. Different hypotheses have been proposed. Ismail et al. [15] proposed that SSTs may develop from pre-existing ovarian fibromas and that an endocrine milieu might be responsible for their morphology. Damnajov et al. [16] proposed that SSTs could
Fig. 4. Pelvic MRI (coronal section): right adnexal round solid mass measuring 4.5 cm with an irregular peripheral rim, strong contrast enhancement and central colliquation.

Fig. 5. Laparoscopic intraoperative view of the adnexal mass.

derive from pluripotent immature stromal cells of the ovarian cortex, basing this on ultrastructural features. It has also been proposed that SSTs derive from a population of muscle-specific actin-positive elements from the theca externa, namely, the perifollicular myoid stromal cells. Moreover, Tiltman and Haffeyee [17] noticed some correlation between SSTs and thecomas because they share some morphologic features and antigenic determinants such as smooth muscle actin and vimentin [5, 7].

Clinical manifestations such as amenorrhea, menstrual irregularity, infertility, virilisation or precocious puberty may be caused by hormonal production of dehydroepiandrostosterone [3, 9, 10]. They can also present with pelvic pain and the presence of a mostly solid or mostly cystic mass measuring from 1 cm to 31 cm in diameter. Endometrial hyperplasia concomitant with SST have also been described, which might indicate hormone production [9]. There also have been reported cases of ascites and elevated CA125 [3, 9, 18]. All of the symptoms associated with SSTs resolve after surgery.

Imaging studies are useful even if they are not sufficient to make a definitive diagnosis. The gross appearance of SSTs ranges from small solid masses to large multicystic masses [5, 19] often with increased peripheral vascularization, as seen in malignant tumors. Magnetic resonance imaging could add some information about typical signal pattern as hypointense nodules, hyperintense stroma, lobulation, strong enhancement after the infusion of contrast agent and the presence of a peripheral rim [9, 20]. In particular, radiological features obtained through an ultrasound examination and MRI could allow to make an important differential diagnosis between SST and mature teratoma (MT): in SSTs, an ultrasound examination generally shows a multilocular cystic tumor with irregularly thickened septa and tumor walls or a solid tumor including or not several small cystic components; in MT, sono-graphic features are generally non-specific and may manifest as an echogenic mass with distal acoustic attenuation, or as a well-defined hypoechoic mass, or as an anechoic lesion with through-transmission. In SSTs, MRI could show in T2 sequences high signal intensities of the cystic components and inhomogeneous for the solid components, ranging from intermediate-high to high; MRI may also show pseudolobulation of the lesion which consists of low-intensity nodules set against high-intensity stroma. In T1 sequences, SSTs are characterized by marked early enhancement of the solid components. On MRI MT could show in T2 sequences an hyperintense mass (due to edema and cystic degeneration), but may be variable and may mimic more common malignant ovarian tumors and the intratumoral lipid may give a chemical shift artefact; in T1 sequences, the degree of contrast enhancement varies with the amount of fibrous tissue within the tumor: if the tumor has a significant fibroma component, the abundant fibrous tissue may produce predominantly low signal intensity on both T1 and T2 weighted sequences [21].

Definitive differential diagnosis from SSTs and other benign or malignant ovarian tumors could be made based on particular microscopic and immunohistochemical findings.

The surgical approach could be laparotomy or minimally invasive (straight laparoscopy or robotic-assisted) [22]: it depends on patient’s conditions, characteristics of the tumor, surgeon’s expertise and hospital’s surgical instrumentation availability.

Histologic examination of SSTs generally shows a pseudolobular pattern with the alternation of hypocellular and hypercellular areas. These areas comprise of spindle cells among oedematous and collagenous stroma. The hypocellular areas are often characterized by the presence of hemangiopericytomatous-like pattern of dilated vascular structures, the hypercellular ones by the presence of luteinized theca-like cells with vacuolated cytoplasm and fusiform fibroblasts-like cells [9, 19]. According to the literature, the mitotic index is diverse but generally low (< 5/10 high-power fields–HPF). There are some reports of cases with higher mitotic activity (7 to 14/10 HPF). These led some
authors to suggest the term mitotically active sclerosing tumour for those with $>4/10$ HPF. The exact prognosis of the mitotically active SST needs to be determined, as these cases might need a longer-term follow-up [23].

These tumors are characterized by constant change in vascular, sclerotic and oedematous stromal pattern because of the local elaboration of some factors like vascular permeability factor and vascular endothelial growth factor [5, 10, 24].

Immunohistochemically, SSTs are often positive for vimentin, inhibin, calretinin, smooth muscle actin and CD 199; they are negative for S100 protein and epithelial markers, favoring the stromal origin of SSTs [5, 9, 19]. In our case, immunohistochemical analysis revealed positivity for actin, inhibin and calretinin.

Laboratory investigations including serum markers, pathologic examination and radiologic evaluation with ultrasound and MRI are necessary for the differential diagnosis with other ovarian masses such as the other sex-cord stromal tumors including fibroma, thecoma, and lipid cell tumor. The differential diagnosis includes also juvenile granulosa cell tumor with sclerosis, Krukenberg tumor and hemangiopericytoma. The preoperative diagnosis includes the much more common epithelial ovarian cancer and non-neoplastic conditions such as massive oedema of the ovary, ovarian torsion or ruptured hemorrhagic cyst [3, 5, 9].

The definitive diagnosis is made only by pathological evaluation; the intraoperative analysis of a frozen section could suggest a SST through the identification of the pseudolobular pattern, the heterogeneity of the cellular areas and a densely hyalinized or markedly oedematous stroma [5] and could allow for a conservative surgical approach [3, 25].

4. Conclusions

Due to its rarity, and features that overlap with other ovarian masses (benign and malignant) it is difficult, if not impossible, to make a preoperative diagnosis but it should be considered in young women with a unilateral solid or cystic ovarian mass after appropriate laboratory and radiological investigations. The definitive diagnosis can only be made after the identification of specific histopathological features [7] and it can be treated successfully with fertility preserving surgery [19].

Author contributions

VDV, SC, NAC, GT designed the research study, performed the research, analyzed the data and wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The subject gave her informed consent for inclusion before she participated in the study; the study was conducted in accordance with the Declaration of Helsinki.

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Conflict of interest

The authors declare no conflict of interest.

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