



Case report

Ovarian microcystic stromal tumor: Radiologic-pathologic correlation

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ABSTRACT

Ovarian microcystic stromal tumor (MST) is characterized by microcysts, solid cellular regions with lobulated growth, and collagenous or fibrous stroma forming hyaline plaques. While several reports have evaluated the unique pathologic and immunohistochemical profile of these tumors, there has been limited description of the radiologic findings of ovarian microcystic stromal tumor in the literature. We present a case of a 66 year old female who presented for evaluation of a new cystic pelvic mass found to have ovarian microcystic stromal tumor. To our knowledge, this is one of the first reports to evaluate the radiologic features associated with this tumor. An enhanced understanding of the correlation between imaging appearance and specific histopathologic findings may aid in the early recognition of this rare neoplasm.

1. Introduction

Microcystic stromal tumor (MST) of the ovary was first described in 2009 by Irving and Young and introduced into the World Health Organization (WHO) classification of sex cord-stromal tumors in 2014 (Irving & Young, 2009; Kurman, 2014). This rare subtype of ovarian tumor is characterized by a distinguishing triad of elements: regions of microcysts; solid cellular areas with lobulated growth; and collagenous or fibrous stroma forming hyaline plaques (Oliva, 2014; Irving et al., 2015; Yang & Bhattacharjee, 2014). Additionally, these tumors lack the morphologic features to diagnose alternate sex-cord stromal, epithelial, teratomatous or other germ cell tumors (Yang & Bhattacharjee, 2014). While several reports have evaluated the unique pathologic and immunohistochemical profile of these tumors, there has been limited description of the radiologic findings of ovarian microcystic stromal tumor in the literature. We present a case of a 66 year old female who presented for evaluation of a cystic pelvic mass and was found to have ovarian microcystic stromal tumor. To our knowledge, this is one of the first reports to evaluate the radiologic features associated with this tumor. An enhanced understanding of the correlation between imaging appearance and specific histopathologic findings may aid clinicians in the early recognition of this rare neoplasm.

A 66 year old female, gravida 3, para 3 presented with an incidental finding of a 7 × 6 cm cystic pelvic mass discovered on imaging. Her past medical history included hypertension, asthma, chronic kidney disease stage 3, diabetes mellitus, hyperlipidemia, and obesity. She underwent hysterectomy at age 30 for benign disease and a surgical

breast reduction at 46 years of age. She had been taking estradiol for 16 years following symptomatic menopause at age of 50. Her mother was diagnosed with lung cancer in the past, but the patient had no family history of breast, ovarian, or uterine cancer. Exam was notable for a palpable left adnexal mass. Laboratory testing revealed normal cancer antigen 125 (CA 125) and carcinoembryonic antigen (CEA). F18 Fluorodeoxyglucose (FDG) Positron emission tomography-computed tomography (PET-CT) performed during work-up of a benign pulmonary nodule showed an incidental cystic pelvic mass suspicious for malignancy. The patient underwent pelvic mass resection with bilateral salpingo-oophorectomy. The initial frozen section of the pelvic mass was suggestive of possible carcinoma with typing deferred for permanent sections with due to serous carcinoma remaining on the differential. Therefore, laparoscopic staging procedure was performed including bilateral pelvic and para-aortic lymphadenectomy and infracolic omentectomy with peritoneal biopsies. Although sex cord and stromal tumors rarely present with metastases, the decision for surgical staging was based conservatively on the somewhat inconclusive frozen section results.

2. Radiologic features

PET-CT revealed a 7 × 6 cm complex cystic mass in the left adnexal region (Fig. 1). No fluorodeoxyglucose (FDG) avidity was seen centrally in the cystic portion, although some peripheral focal areas of FDG uptake were seen which correspond to solid components, with a maximum standard uptake value (SUV max) 3.8. Transvaginal ultrasound (US)

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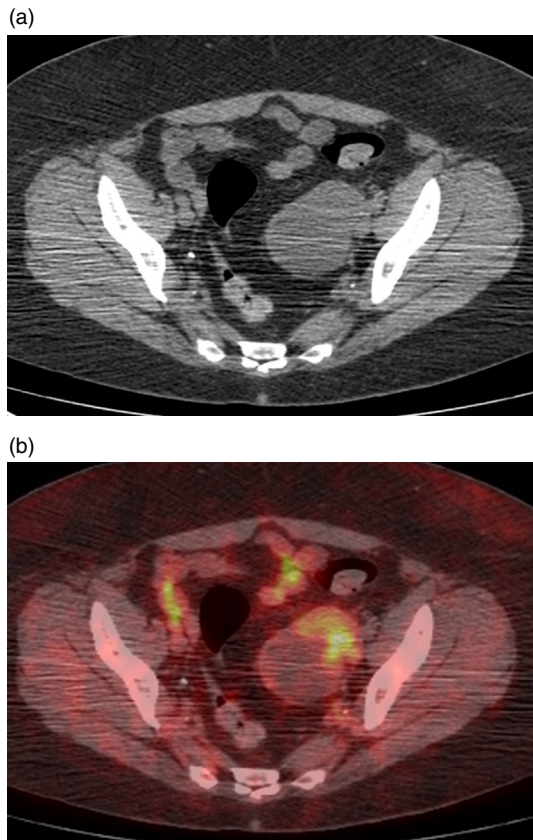


Fig. 1. 66 year old female with an incidental asymptomatic left pelvic mass. A. Axial non-enhanced CT image through the pelvis shows the left predominantly cystic mass with anterior soft tissue components. B. Fused axial FDG PET-CT image shows the nodular nature of the hypermetabolic activity within the solid component of the left adnexal mass.

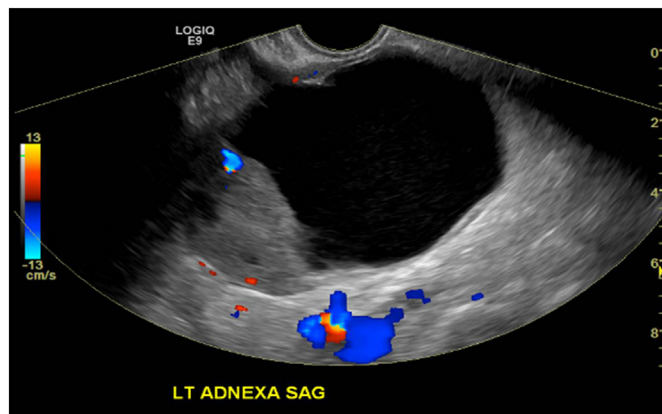


Fig. 2. 66 year old female with an incidental asymptomatic left pelvic mass. Sagittal Doppler Color flow image demonstrates a predominantly cystic mass with a thick mural nodule and mild internal vascularity within the solid component of the mass.

revealed a complex cystic left adnexal mass measuring $7.4 \times 6.0 \times 5.5$ cm (Fig. 2). A dominant homogeneously anechoic cystic component was identified with peripheral solid wall thickening and nodularity. Minimal color flow was noted along the peripheral nodular solid portions of the mass suggesting vascular solid tumor.

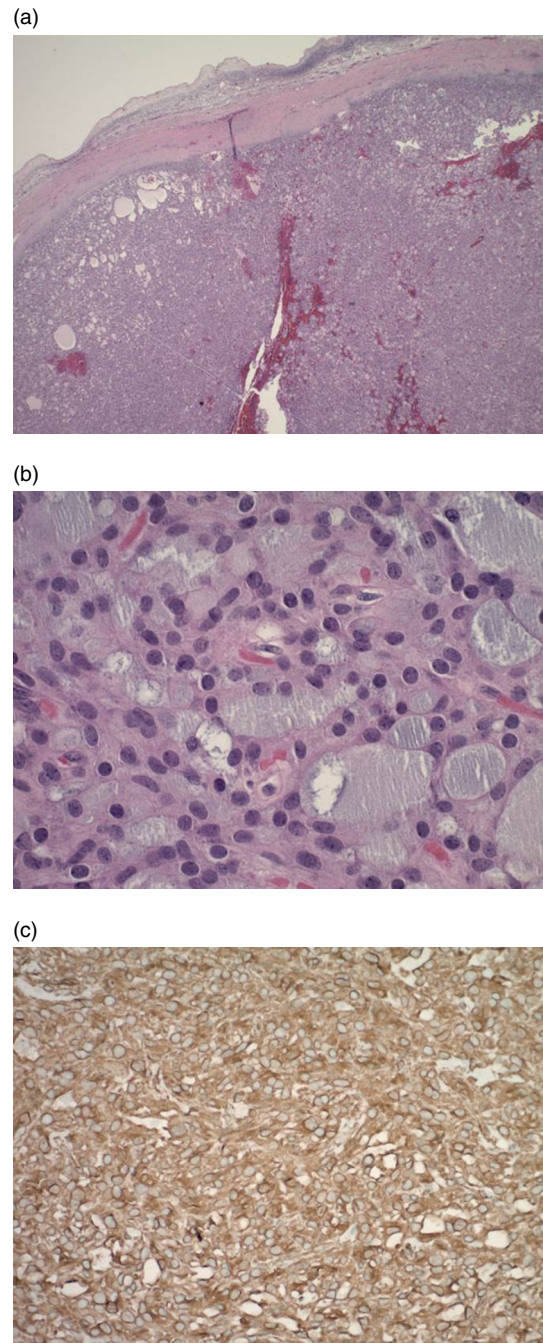


Fig. 3. 66 year old female with an incidental asymptomatic left pelvic mass. (a) Hematoxylin and eosin stained sample at $2\times$ magnification shows cells with abundant eosinophilic granular cytoplasm. (b) Hematoxylin and eosin stained sample at $20\times$ magnification shows largely bland round to oval nuclei, inconspicuous nucleoli and occasional bizarre nuclei with numerous micro-pseudocysts throughout the tumor. (c) Immunohistochemistry test for WT-1 shows the stromal cell nuclei highlighted by WT-1 staining. Immunohistochemistry tests for vimentin, CD10, B-catenin, and cyclin D1 were also positive (not shown).

3. Pathologic features

Gross examination revealed a well demarcated $9.5 \times 7.2 \times 6.5$ cm cyst within the left ovary with a smooth surface and serosanguinous cystic fluid. The cyst wall was approximately 0.1–0.5 cm in thickness and no areas of necrosis or hemorrhage were seen. Microscopic examination revealed a uniform population of cells with abundant

Table 1
WHO classification scheme for ovarian sex cord-stromal tumors (2014) shows Ovarian microcystic stromal tumor as part of the pure stromal tumor classification. Adapted from reference (Kurman, 2014). *NOS- not otherwise specified.

WHO classification		
Pure stromal tumors	Pure sex cord tumors	Mixed sex cord-stromal tumors
Fibroma	Adult granulosa cell tumor	Sertoli-Leydig cell tumors
Cellular fibroma	Juvenile granulosa cell tumor	Well-differentiated
Thecoma	Sertoli cell tumor	Moderately differentiated with heterologous elements
Luteinized thecoma associated with sclerosing peritonitis	Sex cord tumor with annular tubules	Poorly differentiated with heterologous elements
Fibrosarcoma		Retiform with heterologous elements
Sclerosing stromal tumor		Sex cord-stromal tumors, NOS*
Signet-ring stromal tumor		
Microcystic stromal tumor		
Leydig cell tumor		
Steroid cell tumor		
Steroid cell tumor, malignant		

eosinophilic granular cytoplasm with largely bland round to oval nuclei, inconspicuous nucleoli and occasional bizarre nuclei with numerous micropseudocysts throughout the tumor (Fig. 3). Immunohistochemistry showed immunoreactivity for WT-1 and vimentin (Fig. 3). Furthermore, cells were negative for CK20, CK7, CD56, chromogranin, Napsin, GATA-3 and mucicarmine. The ki-67 was mildly elevated. The cells demonstrated negative staining for SF-1, Pan-K, and inhibin, but were positive for CD10, Beta-Catenin and cyclin D1. The histologic features and immunophenotype were consistent with a diagnosis of microcystic stromal tumor. Given the limited number of cases of ovarian MST, there are no well-established surveillance guidelines. In our case, the patient underwent clinic evaluations and contrast enhanced CT chest/abdomen/pelvis exams at 3 month intervals for the first 1.5 years with negative results.

Table 2
Reference table for histology, immunohistochemistry and radiology findings for differential considerations in microcystic stromal tumor of the ovary.

	Histology	Immunohistochemistry	Radiology
Thecoma	Usually not cystic, solid pattern of growth		US: hypoechoic, hypovascular, MR: solid mass, fat elements can be present, iso to low T2 signal common Other: +/- cysts, +/- calcifications
Adult granulosa cell tumor	Cystic and solid components. However cytologically there is pleomorphism, cytologic atypia, and nuclear groves.	+ calretinin, + a-inhibin	US: solid and cystic mass MR: multilocular cystic mass, intracystic hemorrhage, thick septations common, enhancing solid components Other: usually unilateral, average 12 cm + size, low FDG avidity
Sclerosing sertoli cell tumor	Usually no microcysts, cystic and solid components, pleomorphism, cytologic atypia, and nuclear groves,	+ calretinin, + ER	Cystic and heterogeneous solid components, peripheral enhancement
Sertoli leydig cell tumor	Microcysts,	+ calretinin, + a-inhibin	Well defined, enhancing, solid ovarian mass
Yolk sac tumor	Microcysts, but differs from MST by being	+ a-fetoprotein, + cytokeratins, + PLAP	Predominantly solid strongly enhancing mass with irregular cystic, hemorrhagic, or necrotic regions, average size 15 cm
Solid pseudopapillary neoplasm of the ovary	Similar histologic and immune pattern of MST, but pseudopapillary pattern differentiates from MST	+ B catenin mutation similar to MST	Heterogeneous solid/cystic mass, enhancing solid components,
MST of ovary	Microcysts, solid areas, collagenous hyaline plaques, (no necrosis, mitosis, pleomorphism, involvement of the ovary surface, or malignant features);	+ CD10, + B-catenin, + cyclin D1, + WT-1, + vimentin; and -CKs,- a-fetoprotein,- inhibin and -calretinin.	Predominantly cystic mass with solid components. Solid components have shown FDG avidity and mild vascularity.

4. Discussion

The 2014 WHO classification scheme now divides ovarian sex cord-stromal tumors into pure stromal, pure sex cord, or mixed sex-cord stromal tumors (Kurman, 2014). Accounting for approximately 7% of all ovarian tumors, sex cord-stromal tumors are uncommon compared to epithelial ovarian cancers (Horta, 2015). Microcystic stromal tumors fall within the group of pure stromal tumors, which also includes fibromas, thecomas, Leydig and steroid cell tumors (Kurman, 2014). Ovarian MST, like other sex cord-stromal tumors, has generally been found in younger patients with reported ages ranging from the 20s to the 60s (Oliva, 2014; Horta, 2015; Murakami et al., n.d.). These tumors are typically unilateral, often < 5 to 10 cm in size without associated hormone-mediated symptoms and with a favorable clinical course that has not yet been associated with malignancy (Oliva, 2014; Irving et al., 2015; Murakami et al., n.d.).

Given the rarity of ovarian MST, no specific preoperative work up guidelines are available. However, current guidelines from the Society of Gynecologic Oncology for suspected ovarian cancer includes clinical evaluation and CT of the abdomen and pelvis with intravenous and oral contrast (Wright et al., 2016). Chest imaging is also warranted to evaluate extent of disease and resectability. National Comprehensive Cancer Network (NCCN) guidelines recommend pelvic ultrasound and/or CT with magnetic resonance imaging as clinical indicated (Network, 2018). Chest radiograph or CT is also obtained as clinically indicated for extent of disease. Additionally PET/CT may be indicated for indeterminate lesions. Laboratory cancer antigen 125 (CA125) may also be helpful more so in post-menopausal patients (Stany et al., 2010).

Previous reports of ovarian MST suggest a large pelvic mass with a dominant cystic component and peripheral FDG avidity (Lee et al., 2016). On MR, the dominant cystic component has shown to be homogenously high T2 (fluid) signal on T2 weighted images with mild to moderate peripheral enhancement (Murakami et al., n.d.). On ultrasound, ovarian MSTs present with anechoic cystic component with peripheral color Doppler vascularity. Our case shows a corresponding configuration of the mass with a dominant homogenous fluid density cystic component on CT that is anechoic and avascular on ultrasound. Our case also demonstrates the peripheral solid component with a mild degree of vascularity and FDG avidity. The absence of other imaging features helps differentiate ovarian MST from other differential stromal

tumors. For instance, marked low MRI T2 signal with hypoenhancement would be more supportive of a fibroma (Jeong & Outwater, 2000). Thecomas often have internal soft tissue signal and can have greater enhancement. (Horta, 2015; Zhang et al., 2013)

In addition, other mixed solid and cystic ovarian neoplasms must be considered on the radiological differential diagnosis, given that the radiological findings for ovarian MST could also be seen with other lesions including those of low malignant potential. Endometriomas often present on MRI with high T1 weighted signal and lower T2 weighted shading signal that results from hemoconcentrated cystic components, which could help differentiation from other cystic ovarian neoplasms. Benign serous or mucinous cystadenomas tend to be unilocular but can have papillary or solid components that enhance and demonstrate vascularity on Doppler ultrasound imaging. Increasing solid components within an ovarian mass can be suggestive of a malignant lesion such as serous cystadenocarcinoma or mucinous cystadenocarcinoma of the ovary. Cystadenocarcinomas tend to be multilocular with increasing degrees of solid component vascularity. Thick irregular septa also suggest malignancy.

The radiologic appearance of ovarian MSTs also reflects their characteristic histopathologic features. As presented in our report, ovarian MST appears as a complex unilateral mass with predominant cystic components as well as solid nodular portions with minimal color flow on ultrasound. These imaging findings reflect the characteristic microcysts and lobulated, solid cellular areas with intervening hyalinized fibrous stroma, respectively. CT shows a heterogeneous mass with hypo- and hyperattenuating areas, while FDG uptake on PET corresponds to solid cellular components. Although MR images were not obtained in our patient, Murakami et al. reported MRI findings in a 26 year old with ovarian MST, revealing a predominantly cystic lesion with high-signal intensity on T2-weighted imaging and isosignal intensity on T1-weighted imaging (Murakami et al., n.d.). These imaging findings reliably reflect underlying histopathologic characteristics and may aid in early recognition of these benign neoplasms.

Nevertheless, diagnosis of ovarian MST requires careful pathologic and immunohistochemical examination. Consistent with our case report, microscopic examination typically reveals cells with small vacuoles, pale to eosinophilic cytoplasm, low mitotic activity, and largely bland cytology with foci of bizarre nuclei (Irving & Young, 2009; Oliva, 2014). There are no morphologic features to diagnose alternate sex-cord stromal, epithelial, teratomatous or other germ cell tumors (Yang & Bhattacharjee, 2014). Immunohistochemical studies reveal cells which are positive for the following: CD10, cyclin-D1, FOXL2, nuclear β -catenin, SF-1, vimentin, and Wilms Tumor (WT)-1 (Irving & Young, 2009; Oliva, 2014; Irving et al., 2015). MST cells have been found negative for the following: CD56, calretinin, chromogranin A, desmin, epithelial membrane antigen (EMA), inhibin, smooth muscle actin, synaptophysin, and vascular markers (CD 31, CD34, D2-40) (Irving & Young, 2009; Oliva, 2014). Finally, MST cells may be focally positive for cytokeratin (Irving & Young, 2009). These studies, along with clinical and radiologic variations help to differentiate ovarian MST from alternate aforementioned diagnoses.

Although sex-cord stromal tumors have not been shown to be hereditary and the potential for malignancy of MST is unknown, there has been growing research elucidating the genetic mechanisms leading to its tumorigenesis. Investigations by Irving et al. (2015) and Maeda et al. (2011) found evidence of point mutations in exon 3 of β -catenin (CTNNB1). Along with aberrant nuclear B-catenin expression, accumulating data shows dysregulation of the Wnt/B-catenin pathway may be involved in the formation of MST but further research is needed.

Due to the new WHO classification and a limited number of

reported cases, the clinical course of ovarian MST has not been established yet, but has a seemingly favorable outcome. Our case has not recurrence of tumor since surgery for > 6 months.

5. Conclusion

Microcystic stromal tumor of the ovary is a rare subtype of sex cord-stromal tumor that necessitates further exploration. MST of the ovary presents radiologically as a complex mixed cystic and solid mass with a dominant cystic configuration. Peripheral mural soft tissue shows vascularity on Doppler imaging with post contrast enhancement and solid component FDG avidity. To our knowledge, this is one of the first reports to evaluate the radiologic features associated with this tumor in conjunction with histopathology. An enhanced understanding of the clinical history, radiologic appearance, and histopathology can aid radiologists in the early recognition of this rare neoplasm (Tables 1 and 2).

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Conflicts of interest

There are no conflicts of interest.

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