



Microcystic Stromal Tumor of the Ovary

Paulette Mhaweck-Fauceglia¹; Jordy Mehawej^{2*}; Nicole El Helou³; Yan Wang⁴; Tanja Pejovic⁵

¹Department of Anatomic Pathology, Aurora Diagnostics/Sonic Healthcare, Austin, TX, USA.

²Department of Medicine, University of Massachusetts Medical School, Worcester, MA, USA.

³Department of Obstetrics and Gynecology, Washington University, St. Louis, MO, USA.

⁴Department of Surgical Pathology, Monterey Park Medical Center, CA, USA.

⁵Division of Gynecologic Oncology, Oregon Health & Science University, Portland, Oregon, USA.

*Corresponding Author(s): Jordy Mehawej

University of Massachusetts Medical School, 55
Lake Avenue North, Worcester MA 01655, USA.

Email: mehawej@live.com &

Jordy.mehawej@umassmed.edu

Abstract

Microcystic Stromal Tumor (MCST) is an ovarian sex cord stromal tumor that has been recently introduced as a new histologic entity, and thus far is considered benign.

Herein, we discussed a case of a 53-year-old woman who visited her Obstetrics and Gynecologist for a pelvic pain and post-menopausal bleeding. A total laparoscopic hysterectomy with bilateral salpingectomy was performed. The gross examination was most remarkable for multiple intramural fibroids and a right solid ovarian mass measuring 3 x 2 cm. Microscopically, the tumor was arranged in solid and microcystic pattern. The mass was composed of thick fibrous stroma with sheets of medium-to-small round monomorphic cells. The nuclei were round with pale to vacuolated cytoplasm. The cells were positive for CD10, vimentin, β -catenin, and cyclin D1. No mitosis and no necrosis were present.

MCST is a new and rare tumor entity important to be recognized by pathologists as well as clinicians. Even though the clinical behavior of these reported cases appears to be benign, new evidence supports the belief that it should be of 'undetermined malignant potential'. Therefore, due to our limited knowledge, patient follow-up should be recommended.

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Introduction

Microcystic Stromal Tumor (MCST) is a sex cord stromal tumor of the ovary that has been recently described by Irving et Young in 2009 [1]. This histologic entity was described after reviewing 16 cases which presented with discriminative histologic and immunohistochemical features such as: 1. Solid and microcystic patterns with intervening fibrous stroma, 2. Absence of

any of morphologic features enabling the diagnosis of other sex cord stromal tumor category, 3. Absence of epithelial elements and absence of germ cell elements, and 4. Immunohistochemical profile including CD10+/vimentin+/ EMA-. Since its description, almost 45 such cases were reported worldwide.



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We will report a case of MCST in a 53-year-old woman, discussing the morphology, immunohistochemical profile, the differential diagnosis, possible tumorigenesis, and outcome.

Case report

A 53 years old woman visited her Obstetrics and Gynecologist for pelvic pain, and post-menopausal bleeding and fibroids. Her past medical and family histories were negative. On physical examination, the uterus was enlarged, and the patient was diagnosed with uterine fibroids. Both hysterectomy and bilateral salpingo-oophorectomy were performed. The right ovary showed a solid mass measuring 3 x 2 cm. The cut surface was solid, white and homogenous. Microscopically, the entire ovary was occupied by tumor with solid and microcystic patterns. The tumor was composed of thick fibrous stroma with solid sheets of round to ovoid cells with small inconspicuous nucleoli and pale to vacuolated cytoplasm. No atypia, mitosis or necrosis were seen (Figure 1A-1B). Immunohistochemistry (IHC) showed tumor cells to be positive for vimentin, CD10, cyclin D1, β catenin (nuclear pattern), and negative for AE1/3, EMA, SMA, α -inhibin and calretinin (Figure 2A-2D). Special stains for mucicarmine, PAS, and PAS-D were all negative. Based on the morphology and the IHC profile, a diagnosis of MCST was made.

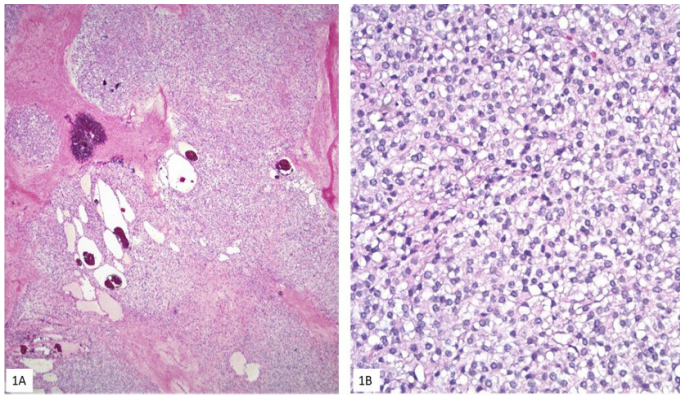


Figure 1: (A) Hematoxylin and Eosin (H&E) section of the mass shows a tumor composed of dense fibrous stroma, solid sheets of tumor cells and microcystic patterns (x10). (B) H&E section at higher magnification show monotonous cells with round to ovoid nuclei, inconspicuous nucleoli, and ample vacuolated cytoplasm (x40).

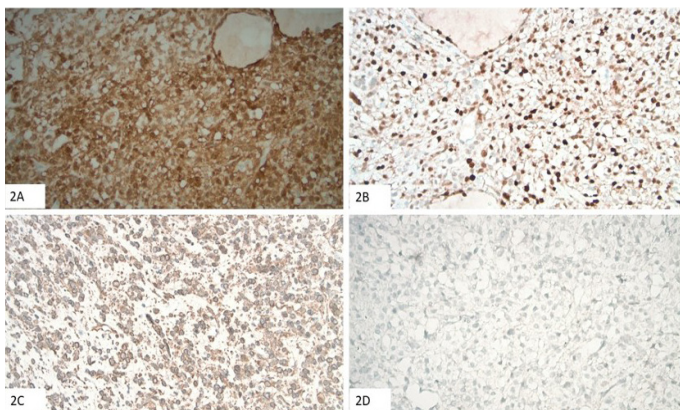


Figure 2: Tumor cells are β catenin positive (A) and calretinin positive (B) and vimentin positive (2C) Calretinin negative (x20).

Discussion

MCST is a new entity of sex cord stromal tumor of the ovary that has been introduced by Irving and Young in 2009 [1]. They described 16 cases with very specific and distinctive morphologic and immunohistochemical profile including; a) microcystic pattern with intervening thick fibrous stroma, b) absence of any morphologic features seen in another sex cord stromal tumor, c) absence of epithelial elements and germ cell elements, d) very specific immunophenotype (vimentin+/ CD10+/ EMA-, α -inhibin- and calretinin -). Our case satisfied all the above criteria, and thus it was diagnosed as MCST.

MCST seems to have no age predilection as they can occur at any age, ranging from 24-69 years of age. Most reported cases described a unilateral mass and only one case was bilateral. The most common presentation is pelvic pain or discomfort. CA125 levels were not done in all patients, but when available, it was frequently in the normal range except in a few cases where it was slightly elevated. Tumor size ranged from 1 cm up to 27 cm. Grossly, they can be cystic, solid, or both cystic and solid. Microscopically, the tumors were composed of 3 components, 1) solid sheets of round to oval cells 2) microcystic regions, and 3) fibrous stroma [2-4].

Since its introduction, a lot of questions regarding MCST remains unanswered. In 2011, Maeda et al reported 2 cases of MCST with positive for β catenin protein (nuclear accumulation) and β catenin gene (*CTNNB1*) mutation in exon 3 [5]. Subsequently additional reports showed that mutation in β catenin gene was related to MCST [6]. β catenin is a protooncogene involved in regulation and coordination of cell-to-cell adhesion, and gene transcription. Its mutation has been found in numerous cancer types including colorectal, ovarian, lung, breast and hepatocellular carcinoma. Furthermore, β catenin and *adenomatous polyposis coli* (*APC*) genes are among the key genes involved in the development of colorectal cancer. In 2014, Yan and Bhattacharjee reported a case of MCST with nuclear accumulation of cyclin D1 protein [7]. Cyclin D1 overexpression has been shown to correlate with early cancer onset and tumor progression. It can also lead to oncogenesis by increasing anchorage-independent growth and angiogenesis via VEGF production. The recent consensus of MCST genesis is that dysregulation of *wt*/ β catenin pathway could be involved in the tumorigenesis of MCST through the activation of β catenin with upregulation of cyclin D1 [8,9]. Recently, Zhang et al published a case of ovarian MCST with recurrence in the iliac fossa. The mutational analysis revealed somatic missense mutation in exon 15 of the APC gene and another in exon 1 of the KRAS gene, suggesting that MCST could represent tumor of undetermined malignant potential rather than a benign tumor [10].

Another point of controversy and focal point of discussion is the classification of this tumor. Even though this tumor is considered to be sex cord tumor, lack of calretinin and α -inhibin expressions, and positivity for other markers, such as CD10 and vimentin, led some to believe that MCST is rather a pluripotent tumor with "uncertain origin" instead of a sex cord stromal tumor [7].

Until these points are resolved with more cases studied and more data accumulated, we believe that these tumors should be classified as tumors of undetermined malignant potential with recommendations of patient follow-up.

Author contribution**Data Curation:** Yan Wang.**Investigation:** Yan Wang, Jordy Mehawej, Nicole El-Helou.**Supervision:** Tanja Pejovic.**Writing- original draft:** Paulette Mhaweck-Fauceglia.**Writing-review and Editing:** Paulette Mhaweck-Fauceglia, Jordy Mehawej, Nicole El-Helou, Tanja Pejovic.**References**

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