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Case Report

Ovarian microcystic stromal tumor: a case report and literature review

Qianqi Liu[1,2], Lei Li[1,2]

[1]*Department of Pathology, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China;* [2]*Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, Sichuan, China*

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Abstract: Microcystic stromal tumor of ovary (MCST) is a rare ovarian sex cord-stromal tumor. This paper presents a case of a 47-year-old female who was admitted to the hospital due to occasional lower abdominal pain and subsequently diagnosed with Microcystic stromal tumor of the left ovary. No recurrence or metastasis was observed after 60 months of treatment. Moreover, all reported clinicopathological features, treatment methods, and prognoses of MCST patients are reviewed herein.

Keywords: Microcystic stromal tumor, ovary tumor, sex cord-stromal tumor

Introduction

Microcystic stromal tumor of ovary (MCST) is a rare ovarian sex cord-stromal tumor. Although ovarian MCST is currently considered benign, little is known about its risk of metastasis and recurrence. In terms of treatment, various surgical options have been explored. The range of choices ranges from extensive surgery to very limited procedures, such as tumor resection/bladder removal. Among patients who undergo very limited surgery, about 40% experience recurrence. While most studies indicate that it is a benign condition, reported cases of recurrence and metastasis suggest that it is not entirely benign in nature, and tumor recurrence may be closely related to inadequate prior treatment. However, due to its rarity and the limited number of related case reports, and since the molecular mechanisms and genetic basis remain unclear, it is not easy to draw relevant conclusions. Therefore, clinicians pay more attention to the choice of surgery to avoid excessive treatment or under-treatment. We encourage more research to explore the unknown characteristics of ovarian MCST and to better target patients with the most effective treatment. In this manuscript, a case of an MCST is reported to raise awareness of this disease.

Case presentation

A 47-year-old woman came to the outpatient clinic in West China Second University Hospital, Sichuan University, due to occasional lower abdominal pain that was not accompanied by fever or menstrual changes. Ultrasound showed a cystic mass measuring 10.9 cm × 11.0 cm × 11.2 cm in size in the left adnexal area, with an irregular shape, a capsule that was full of thin and point-like echoes, and detectable blood flow signals at the cystic wall (**Figure 1**). Cystic occupancy in the left adnexal region was considered (a chocolate cyst of the ovary was suspected). Serological examination showed that the CA-125 level was 45.8 U/mL. After admission to our hospital, "single-port laparoscopic left ovarian cyst removal" was performed under general anesthesia. During the surgery, the left ovary was significantly enlarged, with a maximum diameter of approximately 12 cm. A large cyst was observed inside, the cyst wall was thick and unilocular, and there was brown clear liquid inside. The uterus, bilateral fallopian tubes, and right ovary were normal. Intraoperative freezing was used, and a sex cord-stromal tumor was considered. After communicating with the patient's family, the patient chose to undergo cyst removal only, and the next steps

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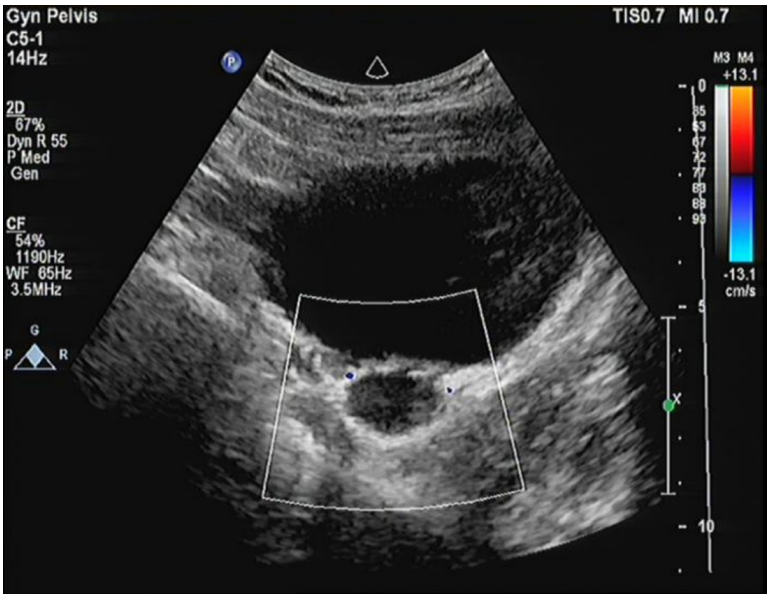

Figure 1. Ultrasound showed a cystic mass in the left adnexal area, with an irregular shape, a capsule that was full of thin and point-like echoes, and detectable blood flow signals at the cystic wall.

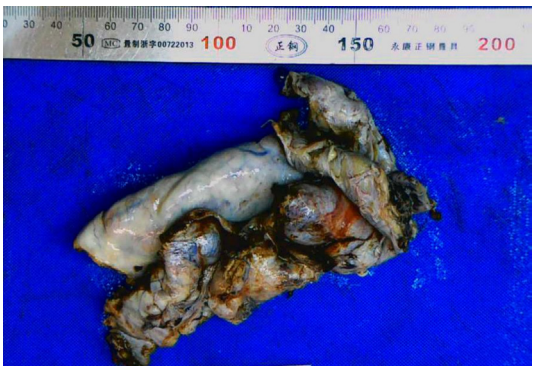

Figure 2. Gross image of a left MCST (the surface capsule was intact, and the cut surface was cystic-solid, with brown substances inside).

were to be determined after the postoperative pathological examination results were obtained.

Pathological findings

Pathological examination of the gross examination revealed that the volume of the left ovary was 10.0 cm × 11.0 cm × 11.2 cm, the surface capsule was intact, and the cut surface was cystic-solid, with brown substances inside (**Figure 2**). Microscopic examination showed that the tumor was sparse and dense and was divided by a large amount of fibrous stroma with hyalinization, which was in the shape of lobes (**Figure 3A**). The dense area consisted of nests of solid cells (**Figure 3B**), and the sparse area was scattered in microcapsule-like structure (**Figure 3C**). Hemorrhage and vascular proliferation and dilatation were observed in some areas of the stroma. The sizes of the microcystic cavities were different (**Figure 3D**). The cystic cavities were empty, and a light blue liquid was occasionally present. There were tumor cells inside the cysts and on the outside of the cystic wall. The cells were mild, round or oval, and the cell sizes were relatively uniform (**Figure 3E**); in the dense areas, the cells had clear cytoplasm or vacuolar small nuclei, inconspicuous nucleoli, fine chromatin, no obvious atypia of the nuclei, and no obvious mitosis (**Figure 3F**).

Immune phenotype

Tumor cells were strongly diffused positive for vimentin, CD10 (**Figure 4A**), CyclinD1 (**Figure 4B**), and β-catenin (**Figure 4C**); SF-1, FOXL-2 (**Figure 4D**), WT-1 and AR (**Figure 4E**) were all positive to varying degrees; calretinin (**Figure 4F**), α-Inhibin, S100, EMA, CK-P, CEA, CA125, CA199, ER (**Figure 4G**), and PR were all negative; and the Ki-67 proliferation index was approximately 3% (**Figure 4H**).

Molecular studies

Genetic detection: In this case, direct polymerase chain reaction (PCR) sequencing was performed, and the gene mutation c.100G>A (p.G34R) in exon 3 of the CTNNB1 gene was detected (**Figure 5**).

Pathological diagnosis: MCST of the left ovary.

Case follow-up

The patient in this study was followed up for 60 months after ovarian cystectomy, and the ultrasound examination showed no signs of recurrence and no other treatment was used.

Discussion

In 2009, Irving et al. became the first to report 16 cases of MCST [1]. In 2014, the World

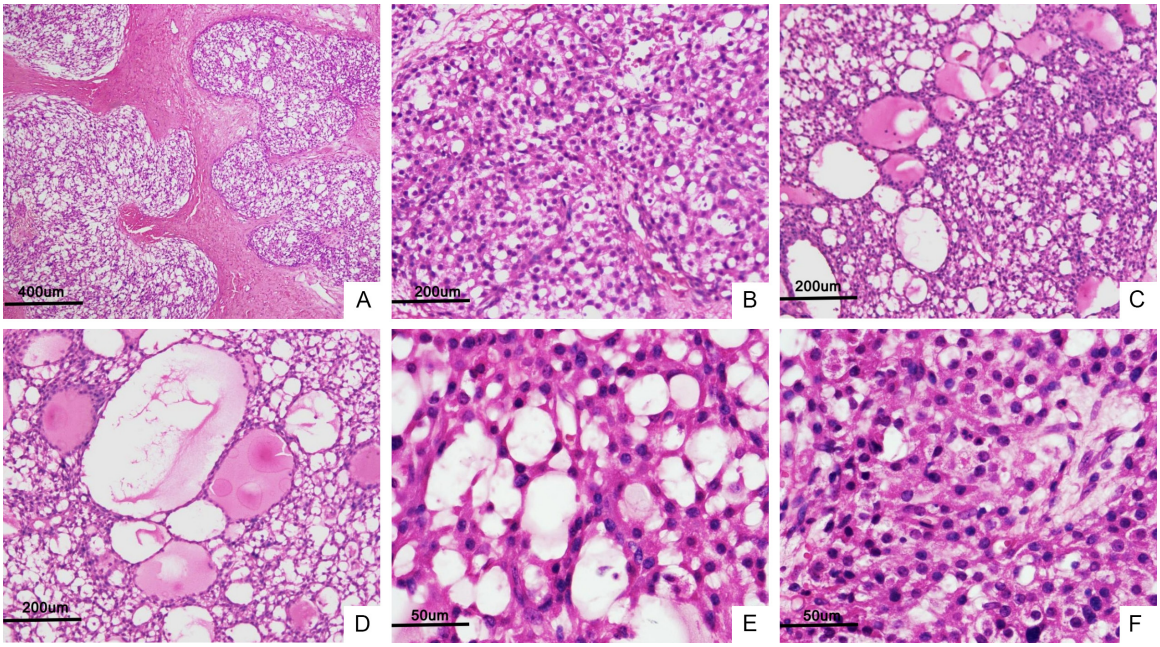

Figure 3. Microscopic appearance of MCST. A: Lobular structure (HE magnification of 40×). B: The dense area (HE magnification of 100×). C: The sparse area (HE magnification of 100×). D: Microcystic cavities of different sizes (HE magnification was 100×). E: The cells of the cystic cavities were mild, round or oval, and the cell sizes were relatively uniform (HE magnification was 400×). F: The cells of the dense area had clear cytoplasm or vacuolar small nuclei, inconspicuous nucleoli, fine chromatin (HE magnification was 400×).

Health Organization (WHO) classified the MCST as a very rare ovarian pure stromal tumor subtype in the category of ovarian stromal tumors, and it is a benign tumor [2]. Approximately 63 cases have been reported in the literature (**Table 1**). MCSTs occur mostly between 23-71 years of age (average age 44-45 years) and most of them manifest as a left solid cystic mass, with the size of the tumors ranging from 1-27 cm (average size 9.5 cm). Most patients were admitted to the hospital due to abdominal pain or a pelvic tumor.

MCST has unique morphological features. It is a cellular phyllodes tumor with fiber in the center. The nests and islands of cellular areas occasionally intersect by collagenous stroma with clear plaques. The cells are usually uniformly round or oval in shape, with small nucleoli and fine-grained pale eosinophilic cytoplasm [3-6]. Multinucleated cells and cells with bizarre pleomorphic degenerative nuclei are rare, and mitosis is also rare in most cases. MCST lacks the morphological features of other sex cord-stromal tumors and does not show any germ cells, teratomas, or epithelial elements. However, the lack of morphological understanding of the MCST may lead to misdiagnosis, especially when the MCST has obviously strange nuclei, which makes intraoperative cryodiagnosis difficult.

MCST has unique immunohistochemistry and molecular profiles, such as strong positivity for β-catenin and cyclin D1 and negativity for inhibin and calretinin combined with CTNNB1 and/or APC mutations [1]. Mutations in Wnt/β-catenin pathway genes (such as CTNNB1 or APC) result in abnormal nuclear immunoreactivity of β-catenin, and the p27Kip1 tumor suppressor gene is also dysregulated. Currently, 3 MCST patients with familial adenomatous polyposis (FAP) have been reported. All of these patients had APC gene mutations. Some researchers believe that MCST may be an extracolonic manifestation of FAP, which is a rare FAP phenotype. However, the specific situation remains to be further verified [7-10]. In this case, direct PCR sequencing of the tumor tissue revealed a mutation in exon 3 of the CTNNB1 gene.

The differential diagnosis of MCST includes any of the following. (1) Juvenile granulosa cell tumors are likely to occur in young women. Under the microscope, follicle-like structures of different sizes are observed, and the markers

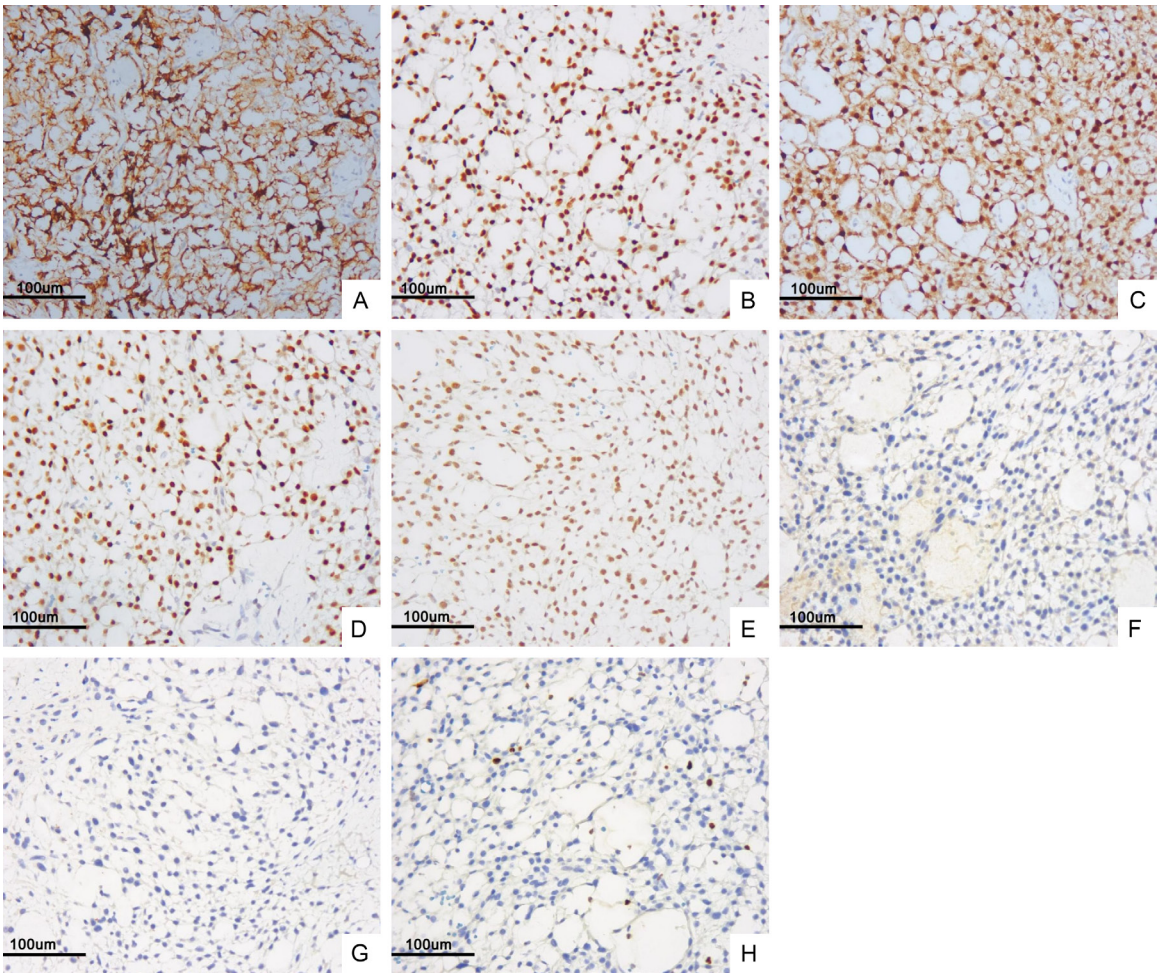

Figure 4. IHC performed using the EnVision method revealed features of MCST. A: Strongly diffused positive for CD-10 (magnification of 200×). B: Strongly diffused positive for CyclinD1 (magnification of 200×). C: Strongly diffused positive for β-catenin (magnification of 200×). D: Positive staining for FOXL-2 (magnification of 200×). E: Positive for AR (magnification of 200×). F: Negative for calretinin (magnification of 200×). G: Negative for ER (magnification of 200×). H: The percentage of Ki67-positive cells was approximately 3% (magnification of 200×).

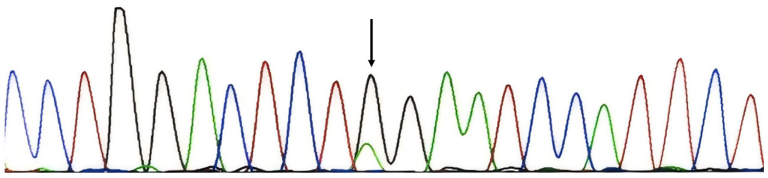

Figure 5. Direct polymerase chain reaction (PCR) sequencing demonstrates the gene mutation c.100G>A (p.G34R) in exon 3 of the CTNNB1 gene.

are positive expression of inhibin and calretinin by immunohistochemistry. (2) Most sclerosing stromal tumors occur before the age of 30 and can be accompanied by symptoms of hormone secretion. The cut surface is mainly solid, with edema and cystic degeneration, and the characteristic crack-like thin-walled vessels are visible under the microscope, but there is no microcystic manifestation. (3) A yolk sac tumor occurs mostly in women under the age of 40. Under the microscope, reticular, microcystic structures, SD bodies, cell atypia, deep staining and irregular nuclei, obvious nucleoli, and more mitosis can be observed. The serum AFP levels are increased in most patients, and the tumors are positive for AFP, SALL4, and glypican-3. (4) Steroid cell tumors can occur at any age and are often accompanied by hormonal changes. The gross manifestation is a tumor with a clear boundary; the cut surface is mostly solid, yellow or orange; the tumor cells are diffusely distributed under the

Table 1. The reported cases of MCST

Case	Reference	Age	Tumor location	Tumor size (cm)	Clinical presentation	Surgery status	Imaging finding	Follow-up (month)	Molecular finding		Type	Nucleotide	Amino acid
									Gene	Location			
1	Irving et al., 2009 [1]	62	L ovary	27	Pelvic mass	TH-BSO, LND, OM	Solid-cystic	NK	NK				
2		45	L ovary	10	Abdo pain	TH-BSO	Solid-cystic	NK	NK				
3		51	L ovary	12	Pelvic mass	TH-BSO, OM	Solid-cystic	NK	NK				
4		29	L ovary	10	Pelvic mass	LO	Multilocular cystic	NK	NK				
5		58	R ovary	6.2	Pelvic mass	TH-BSO, LND	Unilocular cystic	NK	NK				
6		26	NK	8.5	Abdo pain	BSO	Solid-cystic	NK	NK				
7		29	R ovary	6	Pelvic mass	RO	Solid-cystic	NK	NK				
8		45	L ovary	4	Pelvic mass	TH-LSO	Solid	NK	NK				
9		63	R ovary	4.6	Pelvic mass	RO	Solid-cystic	NK	NK				
10		56	NK	4.2	Pelvic mass	BSO	Solid-cystic	NK	NK				
11		45	R ovary	4.5	Pelvic mass	TH-LSO	Solid-cystic	NK	NK				
12		55	L ovary	24	Pelvic mass	TH-LSO	Solid-cystic	NK	NK				
13		44	L ovary	7	Pelvic mass	TH-LSO	Solid-cystic	NK	NK				
14		36	L ovary	3	Pelvic mass	LSO	Solid-cystic	NK	NK				
15		37	R ovary	2	DUB	TH-LSO	Solid	NK	NK				
16		39	R ovary	6.4	Pelvic mass	LSO	Solid	NK	NK				
17	Maeda et al., 2011 [11]	33	R ovary	11.5	Pelvic mass	RSO-OM	Solid-cystic	14	CTNNB1	Exon 3	Heterozygous missense mutation	c.98C>G	p.S33C
18		41	R ovary	9.5	Abdo pain	BSO	Cystic	4	CTNNB1	Exon 3	Heterozygous missense mutation	c.98C>G	p.S33C
19	Yang et al., 2014 [12]	45	L ovary	16	Abdo pain	Tumor resection	Solid-cystic	NK	NK				
20	Niu et al., 2014 [13]	42	L ovary	4.5	NS	TH-BSO	Solid	NK	NK				
21-24	Irving et al., 2015 [14]	29-63, mean 43	NK	Mean 7.3	NK	NK	NK	NK	CTNNB1	Exon 3	Heterozygous missense mutation	c.95A>T	p.D32V
25	Kang et al., 2015 [15]	41	L ovary	7.8	Abdo pain	LSO	Solid	NK	CTNNB1	Exon 3	Heterozygous missense mutation	c.97T>C	p.S33P
26	Lee et al., 2015 [8]	40	L ovary	15	Pelvic mass	LSO, R ovary partial resection, colon resection	Solid-cystic	9	APC*	Exon 11	Heterozygous deletion mutation	c.1540_1540delG	p.A514fs*9
									CTNNB1/ FOXL2		Wide type		
27	Bi et al., 2015 [3]	69	L ovary	15	Pelvic mass	LSOa	Solid-cystic	60	CTNNB1	Exon 3	Heterozygous missense mutation	c.122 C>T	p.T41I
28		29	L ovary	5.5	Pelvic mass	LSO, R ovary sampling	Solid-cystic	18	CTNNB1		wide-tipe		

29		40	L ovary	8	Pelvic mass	LO	Solid-cystic	7	CTNNB1	Exon 3	Heterozygous missense mutation	c.110C>G	p.S37C
30		65	L ovary	11	Pelvic mass	TH-BSO	Multilocular cystic	NK	CTNNB1	Exon 3	Heterozygous missense mutation	c.101G>A	p.G34E
31		57	L ovary	10	Pelvic mass	TH-BSO	Cystic	59	CTNNB1	Exon 3	Heterozygous missense mutation	c.97T>C	p.S33P
32		41	L ovary	7	Pelvic mass	TH-BSO, OM	Cystic	2	CTNNB1		wide-tipe		
33	Podduturi et al., 2015 [16]	50	R ovary	14	Abdo pain	TH-BSO, LND, OM	Solid-cystic	NK	CTNNB1	Exon 3	Heterozygous missense mutation	c.101G>A	p.G34E
34	Chen et al., 2015 [4]	47	L ovary	6	Pelvic mass	LSO	Solid-cystic	18	NK				
35	Gunes et al., 2015 [17]	52	NK	NK	NK	TH-BSO, OM	NK	3	CTNNB1	Exon 3	Heterozygous missense mutation	c.110C>A	p.S37Y
36	Lee et al., 2016 [18]	24	L ovary	18	Abdo pain	LSO	Cystic	8	CTNNB1	Exon 3	Heterozygous missense mutation	c.98C>G	p.S33C
37		31	L ovary	24	Pelvic mass	LSO-LND	Solid-cystic	3	CTNNB1	Exon 3	Heterozygous missense mutation	c.98C>G	p.S33C
38	Liu et al., 2016 [7]	23	R ovary	16	NK	TH-BSO	Solid-cystic	NK	APC*	Intron 6	Heterozygous missense mutation	c.730-1G>T	in abnormal splicing of Exon 7
									CTNNB1		wide-tipe		
39	Murakami et al., 2017 [19]	26	L ovary	6	Cervical disease	LSO	Solid-cystic	36	CTNNB1		wide-tipe		
40	NK et al., 2017 [20]	33	R ovary	8.6	Pelvic mass	RSO	Solid-cystic	57	CTNNB1	Exon 3	Heterozygousdelation mutation	c.88_99del12	p.Y30_S33del
41		31	L ovary	24	Abdo pain	LSO, LND sampling	Solid-cystic	20	CTNNB1	Exon 3	Heterozygous missense mutation	c.122 C>T	p.T41I
42-44	Meurgey et al., 2017 [5]	37-47, mean 43	2 L ovaries, 1 R ovary	7.5-11, mean 9.25	Abdo pain	2LSO, 1 RSO	Solid-cystic	NK	FOXL2/ DICER1		wild-types		
45	Qureshi et al., 2017 [21]	50	L ovary	NK	NK	LO	NK	NK	NK				
46	Jeong et al., 2018 [22]	66	L ovary	7	NK	BSO, bilateral pelvic and para-aortic LND, infra-colic OM	Solid-cystic	18	NK				
47	Zhang et al., 2018 [9]	33	R ovary	7	Abdo pain	RO	Solid-cystic	108	APC*	Exon 15	Heterozygous missense mutation	c.1590C>T	p.G530E
									CTNNB1		Wide-type		
48	Hasanzadeh et al., 2019 [23]	60	NK	5	Abdo pain	TH-BSO	MaligNKnt features	15	NK				
49	McCluggage et al., 2019 [24]	61	NK	NK	NS	BSO	Solid-cystic	NK	CTNNB1	Exon 3	Heterozygous deletion mutation	c.100G>A	p.G34R
50		56	R ovary	1	Pelvic mass	TH-BSO	Solid	NK	CTNNB1	Exon 3	Heterozygous deletion mutation	c.98C>G	p.S33C

51		45	Both ovaries	7	Pelvic mass	TH-BSO	Solid	NK	NK				
52		71	R ovary	4	Pelvic mass	BSO	Solid-cystic	NK	CTNNB1	Exon 3	Heterozygous deletion mutation	c.97T>G	p.S33A
53	Liu et al., 2019 [25]	46	R ovary	4.5	NK	RSO	Cystic	54	NK				
54		56	R ovary	8	Pelvic mass	TH-BSO	Solid-cystic	46	NK				
55	Deng et al., 2020 [26]	25	L ovary	NK	Pelvic mass	LROT	Solid-cystic	4	NK				
56	He et al., 2020 [6]	33	R ovary	3.2	Pelvic mass	LROT	Solid-cystic	19	NK				
57	Carlos et al., 2021 [27]	41	L ovary	9	Abdo pain	TH-BSO	Solid	NK	APC	NK	NK	c.1256 deletion-insertion c.2547_2550 deletion	p.T419I p.D849E
58	Maria et al., 2021 [28]	46	L ovary	16	Abdo pain	LSO-OM, left pelvic LND, appendectomy	Solid-cystic	24	CTNNB1	NK	Heterozygous deletion mutation	NK	NK
									APC		Wide-type		
59	Bushra et al., 2024 [29]	44	L ovary	14	Pelvic pain	LSO, R ovarian and OM biopsy	Solid-cystic	4	NK				
60	Bao et al., 2024 [2]	39	R ovary	10	Pelvic mass	TH-BSO	Solid-cystic	24	CTNNB1	Exon 3	Heterozygous deletion mutation	c.110C>T	p.S37F
61	Li-Xia Lu et al., 2024 [30]	31	R ovary	1.9	NS	NK	NK	NK					
62		52	L ovary	10.6	Abdo pain	NK	NK	NK					
63	Deepak et al., 2023 [31]	38	R ovary	5.2	NS	RO	Solid-cystic	48	CTNNB1	Exon 3	Heterozygous deletion mutation	NK	p.S37A
64	Current case	47	L ovary	10	Abdo pain	Tumor resection	Solid-cystic	60	CTNNB1	Exon 3	Heterozygous deletion mutation	c.100G>A	p.G34R

Abbreviations: L ovary, left ovary; R ovary, right ovary; LSO, Left salpingo-oophorectomy; RSO, right salpingo-oophorectomy; NK, Not known; OM, Omentectom. *, Detected in patients with familial adenomatous polyposis.

microscope; and the stroma is not obvious. They contain eosinophilic cytoplasm, the nucleus is centered, the nucleoli are prominent, and the immunohistochemistry markers are positive for CD10, inhibin, and calretinin. Other tumors that need differentiation, such as follicular theca cell tumors, signet ring stromal tumors, and goiters, require careful observation of their morphological characteristics and immunohistochemistry for differentiation.

In terms of treatment, extensive or very local surgical methods, such as total hysterectomy, double adnexal resection, lymph node dissection or lumpectomy alone, can be chosen. Among MCST patients who received very limited surgery, approximately two-fifths (40%) experienced recurrence. Although most studies have shown that MCSTs are benign lesions, the correlation between the risks of metastasis and recurrence and FAP is still not completely clear, and tumor recurrence may be closely related to insufficient previous treatment. The patient in this study was followed up for 60 months after ovarian cystectomy, and the ultrasound examination showed no signs of recurrence.

Conclusion

In summary, MCSTs are rare, and it is not easy to achieve accurate pathological diagnosis. Pathologists should pay attention to its characteristic microcystic and lobular structures, and clinicians should pay attention to surgical options to avoid overtreatment or undertreatment.

Disclosure of conflict of interest

None.

Address correspondence to: Lei Li, Department of Pathology, West China Second University Hospital, Sichuan University, No. 20, Section 3, South Renmin Road, Chengdu 610041, Sichuan, China. Tel: +86-28-85501359; Fax: +86-28-85503875; E-mail: lipath@163.com

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