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Case Report

Pathology Section

Large Ovarian Microcystic Stromal Tumour: A Report of Rare and Distinctive Pathological Entity

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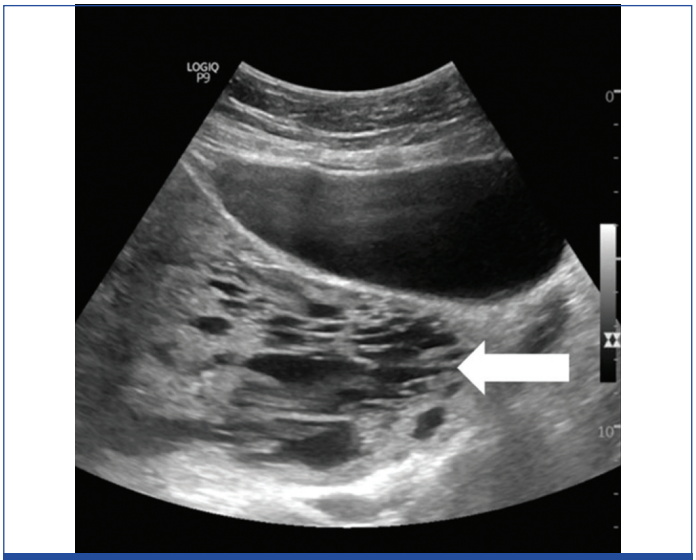
ABSTRACT

Microcystic Stromal Tumours (MCSTs) of the ovary are an exceedingly rare and distinct subtype of ovarian stromal neoplasms, characterised by their unique histopathological features. They were first identified in 2019 as a distinct entity. Hereby, the authors present a case report that focuses on a 48-year-old Indian female patient who presented with complaints of lower abdominal heaviness for the past year. Contrast-enhanced Computed Tomography (CECT) of the abdomen revealed a 29.7×24.4×15.3 cm hypodense lesion extending from the pelvis to the epigastric region, with multiple thick septations, a mural nodule/solid component, and moderate enhancement of the cyst wall. Preoperative blood values for CA 19-9, Carcinoembryonic Antigen (CEA), and CA-125 were 25.3 U/mL, 1.5 ng/mL, and 28.8 U/mL, respectively. Staging laparotomy combined with bilateral salpingo-oophorectomy and total hysterectomy was performed. Microscopic evaluation showed solid areas of spindle-shaped tumour cells intermixed with microcysts, separated by hyalinised fibrous stroma. The tumour cells displayed positive staining for vimentin and CD10 on Immunohistochemical (IHC) examination, but negative staining for calretinin and inhibin. Considering the histopathological features and immunohistochemical marker study, a diagnosis of microcystic stromal tumour was established. To date, approximately 50 cases have been documented worldwide, with only one case reported by an Indian author. This report highlights the importance of considering MCST in the differential diagnosis of ovarian masses and emphasises the role of histopathological and immunohistochemical evaluation in achieving an accurate diagnosis.

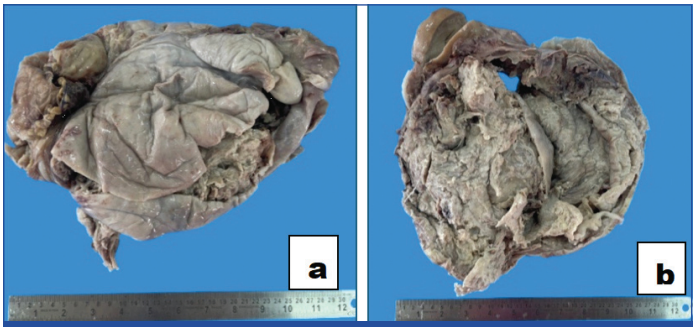
Keywords: Catenin, Microcysts, Ovary, Sex-cord stromal tumour

CASE REPORT

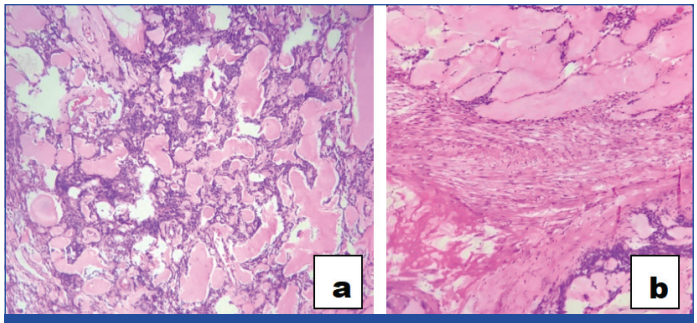
A 48-year-old Indian female, P3L3A2, with no co-morbidities, presented with progressive lower abdominal heaviness for one year and irregular menstrual cycles for six months. She reported no weight loss, appetite changes, or hormone-related symptoms. Physical examination revealed significant abdominal distension with a large cystic mass extending to the epigastrium; the liver and spleen were not palpable. Vaginal examination showed a cervix displaced against the pubic symphysis and obliterated fornices due to the mass. Ultrasound imaging revealed a large, isoechoic, predominantly cystic lesion with multiple septations and a mildly vascular solid component in the right adnexal region [Table/Fig-1], abutting the posterior uterine wall and extending to the epigastric region. The ovaries were not separately visualised. A CECT of the abdomen showed a hypodense cystic structure measuring 29.7×24.4×15.3 cm, with multiple thick septations, a mural nodule, and moderate enhancement of the cyst wall. Based on the clinical and CECT findings, a provisional diagnosis of a malignant ovarian tumour was made. Serum levels of CA 19-9 (25.3 U/mL), CA-125 (28.8 U/mL), and CEA (1.5 ng/mL) were all within normal ranges prior to surgery. Following staging laparotomy, a bilateral salpingo-oophorectomy, bilateral dissection of pelvic lymph nodes, an infracolic omentectomy, and a total hysterectomy were performed and submitted for pathological analysis. Gross examination revealed a right ovarian mass measuring 30×25×16 cm, which was encapsulated, glistening, and upon cutting open, drained 350 mL of yellowish fluid. The cut surface was predominantly solid, featuring multiple myxoid to spongy areas, with a few cystic areas [Table/Fig-2a,b]. Histopathological examination by Haematoxylin and Eosin (H&E) reveals that the tumour cells were organised in compact solid sheets and cords intermixed with microcysts filled with eosinophilic secretions, interspersed with hyalinised dense fibrous stroma [Table/Fig-3a,b]. These spindle-shaped tumour cells featured moderate eosinophilic cytoplasm and rounded to oval vesicular nuclei with inconspicuous nucleoli [Table/Fig-4]. Additionally, numerous basaloid



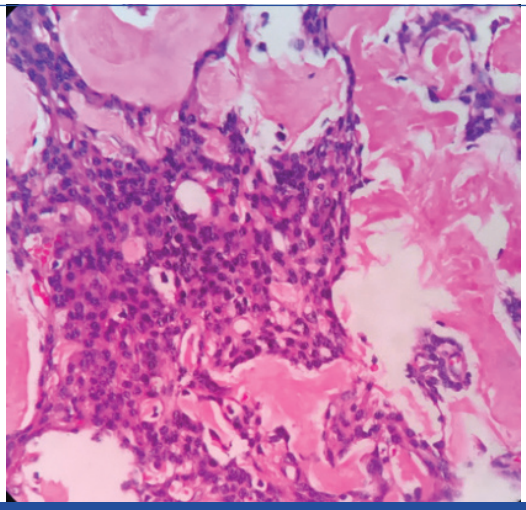
[Table/Fig-1]: Ultrasound abdomen and pelvis showing large isoechoic, predominantly cystic lesion with multiple septations and a mildly vascular solid component (thick arrow).



[Table/Fig-2]: a) The external surface of the lesion was capsulated and glistening; b) The cut surface was predominantly solid, featuring multiple myxoid to spongy areas, with few cystic areas.

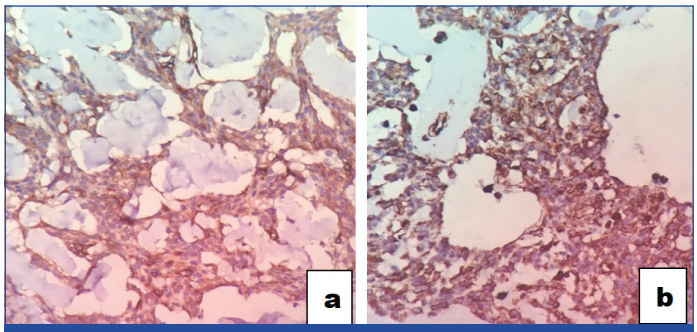


[Table/Fig-3]: a) Tumour arranged in solid sheets and cords intermixed with microcysts filled with eosinophilic secretions (H&E, 100x); b) Tumour cells with intervening fibrous stroma (H&E, 100x).



[Table/Fig-4]: Tumour cells are spindle-shaped with moderate eosinophilic cytoplasm, round to oval nuclei with inconspicuous nucleoli (H&E, 400x).

cells with dark, dense chromatin and a few signet ring-shaped cells with bland nuclei were observed. Immunohistochemical (IHC) analysis showed focal membranous positivity for CD10 and strong diffuse positivity for vimentin [Table/Fig-5], while inhibin and calretinin were negative. Given the tumour's characteristic features of solid cellular regions with spindle-shaped cells, microcysts, and hyalinised fibrous stroma, a diagnosis of ovarian MCST was confirmed. The left ovary, omentum, and bilateral pelvic lymph nodes were histologically normal. Four months postoperatively, both CECT findings and serum tumour markers were unremarkable.



[Table/Fig-5]: a) Tumour cells exhibiting focal membranous positivity for CD10 (IHC, 400x); b) Tumour cells exhibiting diffuse strong positivity for vimentin (IHC, 400x).

DISCUSSION

Ovarian microcystic stromal tumours are an uncommon and relatively new form of ovarian neoplasm. To date, about 50 cases have been reported in the English literature [1], with only one case documented by an Indian author [2]. Under the 2020 World Health Organisation (WHO) classification of tumours of the ovary, it is categorised as a sex-cord stromal tumour [3]. These tumours were first identified in 2019 as a distinct entity by Irving JA and Young RH [4]. These tumours are unique in their histopathological presentation, which includes three essential components: solid cellular regions, microcysts, and fibrous stroma. In addition to these essential features, other crucial characteristics include the absence of epithelial cells and germ cell components, as well as morphological features that facilitate diagnosis within the category of sex-cord stromal tumours [4]. McCluggage WG et al., described four MCST cases with variant morphologies, expanding the tumour's morphological spectrum [5]. These variations exhibited tiny cystic foci with bland epithelioid cells separated by fibrous septa in three cases, which displayed corded, tubular, and nested configurations. Bizarre nuclei were found only in a small number of cases [4,6].

The majority of MCST cases have been found to have a heterozygous point mutation in exon 3 of the β-catenin gene (CTNNB1), suggesting that the Wnt/β-catenin pathway may play a critical role in their pathogenesis [6-10]. Additionally, certain cases of ovarian MCST have been identified in individuals with Familial Adenomatous Polyposis (FAP), a genetic condition characterised by an APC gene mutation on chromosome 5q21. This suggests that MCST could be an extracolonic expression of FAP [11-13]. According to McCluggage WG et al., APC mutations do not coincide with CTNNB1 mutations and are found in a small percentage of MCSTs. In all cases, including those without β-catenin mutations, nuclear β-catenin staining can be attributed to aberrant cytoplasmic and nuclear accumulation of β-catenin caused by APC or CTNNB1 mutations [10].

Although MCSTs originate from the ovarian stroma, they exhibit a unique immunophenotype. Conventional sex-cord stromal immunohistochemical markers, including calretinin, epithelial membrane antigen, and inhibin, which are found in Sertoli-Leydig cell tumours and Juvenile Granulosa Cell Tumours (JGCTs), are not present in these tumours [4]. These tumours are important differentials for MCSTs. Instead, MCSTs consistently show positive staining for CD10, vimentin, Wilms' tumour protein (WT-1), Forkhead box Ligand 2 (FoxL2), Steroidogenic Factor 1 (SF1), Cyclin D1, and nuclear β-catenin [1,7]. Vimentin positivity indicates a mesenchymal origin. These features align with those observed in present case.

Steroid cell tumours and those with small, homogeneous nuclei and abundant cytoplasm are morphologically similar to MCSTs. While these tumours may display vacuolated cytoplasm, they stain positive for inhibin and calretinin, unlike MCSTs. Although JGCTs lack nuclear β-catenin, Cyclin D1, and CD10 staining, they can still be considered, particularly if they exhibit significant cytological atypia. However, they do express inhibin and calretinin. Solid Pseudopapillary Neoplasms (SPNs) also present with β-catenin mutations and share similar immunophenotypic characteristics with MCSTs, being positive for CD10, nuclear β-catenin, and Cyclin D1, while negative for calretinin and inhibin. These tumours can be differentiated by their distinct morphological features [1].

The MCSTs have been found in post-pubertal females of various ages, usually presenting unilaterally and confined to the ovary [4]. Most cases follow a benign course after surgery, although rare instances involve local spread at initial diagnosis or recurrence. Man X et al., reported a patient with a CTNNB1 mutation who had omental involvement at the time of diagnosis [14]. A patient with a germline Adenomatous Polyposis Coli (APC) mutation and Familial Adenomatous Polyposis (FAP) syndrome was reported to have a recurrence in the peritoneum after a period of nine years [11]. Donthi D et al., documented a CTNNB1-mutated MCST that recurred after four years in the omentum, peritoneum, and residual ovary [15]. The initial case with omental involvement occurred in a patient with no prior surgeries, indicating that MCST can locally spread without surgical intervention. Both recurrent cases had undergone ovarian cystectomy instead of oophorectomy, suggesting that cystectomy might be insufficient for treating MCSTs, and oophorectomy may be more appropriate. To date, MCSTs have not been reported to metastasise distantly [1].

CONCLUSION(S)

Ovarian MCSTs are rare tumours with unique histopathological features. Although they may appear malignant clinically and radiologically, they often have a benign course. Accurate diagnosis relies on a thorough pathological examination. Increased awareness and documentation of MCST cases are crucial for understanding their behaviour, ensuring correct diagnosis, and improving management strategies.

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