Ovarian seromucinous tumor: A case series of WHO newly introduced entity

**Dwivedi E, Dhameja N, Lader M, Kar AG**
Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

**ABSTRACT**

Introduction: Ovarian epithelial tumors account for the majority of female ovarian neoplasms but seromucinous tumors are rare and not adequately described in the literature. The recent World Health Organization (WHO) 2014 classification of tumors of female reproductive organs introduced this new category of ovarian neoplasm as “seromucinous tumors.”

Materials and Method: Sectioning of tissue followed by staining and immunohistochemistry.

Results: Four of our cases which were diagnosed as cystic lesion clinically and radiologically, on histopathological examination two of them reported as seromucinous cystadenoma and rest two as seromucinous borderline tumors (SMBT). One of the case of SMBT also showed microinvasion along with focal areas of intraepithelial carcinoma high grade and clear cell component.

Conclusion: Proper histopathological diagnosis is very important for better treatment and to reduce the use of aggressive therapies.

Key words: Clear cell component; intraepithelial carcinoma; microinvasion; ovarian epithelial tumor; ovarian neoplasm; seromucinous borderline tumors.

**Introduction**

Worldwide, ovarian cancer is the sixth most common cancer and the seventh leading cause of cancer deaths among women. The recent World Health Organization (WHO) 2014 classification of Tumors of female reproductive organs introduced a new category of ovarian neoplasm designated as “seromucinous tumors” as they exhibit both serous and mucinous features. These groups like other epithelial tumors include adenomas, borderline tumors, and invasive carcinomas. Seromucinous cystadenoma are benign cystic neoplasm with two or more Müllerian cell types, all accounting for at least 10% of the epithelial ovarian tumors (WHO 2014). Seromucinous borderline tumors are characterized by papillary architecture reminiscent of serous tumors but composed of mucinous epithelium similar to that of the endocervix. These tumors are associated with endometriosis. A few studies have reported tumors coexisting with SMBTs, such as endometrioid adenocarcinoma and squamous cell carcinoma.

**Case Presentation**

Case 1

A 26-year-old female patient G3P2+0 admitted for LSCS with a complaint of lower abdominal pain and backache in the
department of obstetrics. Intraoperatively, a left ovarian cyst was noted. Partial cystectomy was done and excised tissue was sent for histopathology examination. Grossly, it was an already cut open cyst measuring 5 × 2.5 cm with a wall thickness of 0.1–0.2 cm. Outer surface as well as inner surface of cyst was smooth and congested. Microscopically, sections from cyst wall was lined by variable admixture of serous and mucinous cells with a fibromatous stroma. Based on the above findings, diagnosis of Seromucinous cystadenoma was made [Figure 1].

Case 2
A 40-year-old female patient P2+1 L2 came with a complaint of lower abdominal pain for 10-15 days in gynecology outpatient department. A contrast-enhanced computerized tomography of pelvis revealed a well-defined hypodense thick-walled cystic lesion with intermediate signal content left to the uterus, measuring about 146 × 126 mm displacing uterus toward right side likely to be ovarian cyst? endometriotic cyst? hemorrhagic cyst? Transvaginal ultrasonography Doppler is suggestive of ovarian cystadenoma. The patient underwent transabdominal hysterectomy with left adnexal cystectomy and sent for histopathological examination. Grossly, uterus showed focal areas of adenomyosis with nabothian cysts in cervix. The cystic tissue piece measured 10 × 7 cm with wall thickness of 0.4 cm. Outer surface was congested and hemorrhagic, while inner surface had much polypoidal growth with areas of hemorrhage. Microscopically, cyst showed epithelial proliferation with intracystic papillae [Figure 2a] and glands with focal areas of mucinous epithelium. Papillae and glands are lined by highly atypical cells with abundant eosinophilic to clear cytoplasm [Figure 2b] and prominent nucleoli. Dense neutrophilic infiltrate was seen within the papillary creases as well as in the epithelium. Foci of necrosis, few mural nodules [Figure 2d], and few mitotic figures and psammoma bodies were also identified. At places, there was infiltration of the cyst wall less than 5 mm [Figure 2c]. Sheets of pigment laden macrophages and histiocytes were also seen. Immunohistochemistry was positive for CK7, ER [Figure 3a and b] and negative for WT-1 [Figure 3c], p53 [Figure 3d]. Based on above findings, diagnosis of microinvasive seromucinous borderline tumor (SMBT) with focal areas of intraepithelial carcinoma high grade and clear cell component was made.

Case 3 and 4
A 46-year female patient P3 L3 came with a complaint of menorrhagia and abnormal uterine bleeding in gynecology department. CECT of pelvis showed well defined, mixed solid cystic lesion of size 55 × 43 × 40 mm in anterioposterior (AP), transverse and craniocaudal axis, respectively, in right adnexa. The lesion showed few internal septae and enhancing solid mural component within the lesion. Similar mixed solid cystic lesion of size 44 × 40 × 28 mm in AP, transverse and craniocaudal axis, respectively, in left adnexa was suggestive of complex bilateral ovarian cysts. Transabdominal hysterectomy with bilateral salpingoopherectomy was done and sent for histopathology examination. Uterus-cervix was grossly normal with a small intramural fibroid measuring 1 × 0.5 cm. Right cystic ovary measured 7.5 × 4 × 2 cm with smooth, shiny and focal areas of congestion at outer surface. On cutting, ovary showed multiloculation with mucinous fluid in it. One of the cystic spaces showed papillary growth measuring 3 × 2 × 2 cm and rest few cystic spaces filled with solid yellowish areas measuring 1.5 × 1 × 1 cm and friable papillary growth measuring 1.5 × 1 × 0.3 cm [Figure 4b]. Left ovary measured 4 × 3 × 1 cm with three cystic spaces measuring 2 × 1 cm, 1 × 1 cm and 1 × 1 cm along with hemorrhagic and grayish-white areas. Two cystic spaces were filled with brownish jelly-like material and 3rd one with serous fluid. Microscopically, right ovary sections were lined by ciliated columnar epithelium with interspersed mucous
areas along with epithelial proliferation and intraluminal broad papillae formation at places [Figure 4c]. These papillae showed neutrophilic infiltrate within them [Figure 4a]. No invasion was seen within cyst wall. Areas of hemorrhage with collection of pigment laden histiocytes was also seen. Sections from left ovary showed follicular cyst, hemorrhagic cyst, and cyst which was lined by ciliated columnar epithelium with interspersed mucous areas. Mucoid material was also present. Based on above findings diagnosis of SMBT of right ovary and seromucinous cystadenoma of left ovary was made.

Discussion

In 1976, Fox and Langley first introduced the word seromucinous tumor which was composed of endocervical type mucinous epithelium and serous type of cells. Later in 1988, Rutgers and Scully described similar appearing borderline tumor into two subclasses. In 2002, Shappell et al.\[6\] reused the term “seromucinous tumor” as they found these neoplasms were composed of a mixture of different cell types with clinically significant differences between these two classes, hence combined into single group.\[4,9\] The recent WHO classification of tumors of the female reproductive organs introduced this new class of ovarian neoplasms.\[4\] Morphologically, these tumors are composed of serous and endocervical type mucinous epithelium along with endometroid, indifferent, and squamous types of epithelium.\[3,4\] Seromucinous cystadenoma composed of endocervical type mucinous, serous but endometroid cells and undifferentiated cells without cellular atypia. Our first case and third case (left ovary) were of same morphology. SMBTs usually arise in young women (34–44 years old) and present as unilocular or paucilocular cysts averaging 8–10 cm in diameter often with intracystic papillae.\[6,10\] Our both cases (2,3) were of age 40 years and 46 years, respectively, with cystic ovary of size 10 cm and 7.5 cm showing intracystic papillae with complex papillary architecture. SMBTs may show microinvasion, intraepithelial carcinoma, and micropapillary features.\[6,7,10,11\] Our case no 2 shows microinvasion as well as intraepithelial carcinoma of high grade. Clear cell changes are very rare finding associated with SMBT.\[12\] Dube et al.\[7\] reported a case of SMBT with endometrioid/clear cell adenofibroma. D’Angelo et al.\[8\] reported a case of squamous cell carcinoma that arose from a SMBT in the same ovary. In case (2), we identified clear cell component and SMBT within the same ovary. Unlike the other endometriosis-associated borderline tumors, SMBT is the most common type of tumor far exceeding benign seromucinous tumors and seromucinous carcinomas.\[13\] Both of our reported cases of SMBTs were associated with endometriosis. The immunohistochemical profile of atypical SMBTs reported by Vang et al.\[14\] reveals frequent expression of ER (100%), PR (67%), CA125 (92%), infrequent expression of WT1 (8%), and lack of expression of CK20 and CDX2, an immunostaining pattern consistent with a “müllerian” immunophenotype. A recently reported study by Taylor and McCluggage described the almost identical immunoprofile in a series of seromucinous carcinomas. Specifically, they found consistent positive expression for CK7, hormone receptors, CA125, PAX8, and CA19.9 but only a minor proportion of the tumors was positive for WT1. None of the tumors were positive for CK20 and CDX2.\[13\] We have used Immunohistochemistry (IHC) ER, CK7, WT-1, p53 and it was positive for ER, CK7 and negative for WT-1 and p53.

Conclusion

Seromucinous cystadenoma and SMBT association with endometriosis and immunohistochemistry profile expression shows a close relationship to endometrioid and clear cell neoplasms. These tumors are associated with a good outcome. Therefore, proper histopathological diagnosis is very important for better treatment and to reduce the use of aggressive therapies.
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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