Case Report

Rare Coexistence of Bilateral Mucinous Cystadenoma and Benign Brenner Tumor

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Abstract

Introduction: Coexistence of ovarian mucinous cystadenoma with benign Brenner tumor is a rare entity. Bilateral coexistence has not been reported before.
Case Presentation: A 58-year-old postmenopausal woman presented with progressive abdominal distension and pain. Imaging revealed a large multilocular cystic mass without obvious solid components in the left ovary whereas right ovary was not clearly visualized due to adhesions. Gross and microscopic examination revealed presence of mucinous cystadenoma and benign Brenner tumor in both the ovaries.
Discussion: This case highlights the importance of thorough gross and microscopic evaluation of ovarian tumors to identify coexisting neoplasms. Knowledge about such coexistence is a must for pathologists as well as surgeons as it may influence treatment decisions.

Keywords: mucinous; cystadenoma; brenner; bilateral; coexistence

Introduction

Ovarian neoplasms often present a diagnostic challenge due to their non-specific symptoms and varied morphology. Epithelial ovarian tumors are a heterogenous group comprising of serous, mucinous, seromucinous, endometrioid, clear cell and brenner tumors. Mucinous tumors comprise 10-15% of the ovarian epithelial tumors whereas Brenner tumors comprise 1-2% of the same.[1] Brenner tumors are usually asymptomatic and are diagnosed incidentally. Coexistence of Brenner tumor with mucinous tumors is uncommon and is reported to vary between 1-16%.[2] We report one such case with coexistent benign Brenner tumor and mucinous cystadenoma in bilateral ovaries. After carrying out search on pubmed using the search term ‘bilateral ovarian mucinous cystadenoma and benign brenner tumor’ we were not able to retrieve even a single such case, although a single case of bilateral malignant Brenner with borderline mucinous cystadenoma exists. To the best of our knowledge, it has not been reported so far.

Case Presentation

A 58-year-old postmenopausal woman presented with a five-month history of progressive abdominal distension and dull aching pain. There was no history of dyspepsia, vomiting, bleeding or discharge per vaginum. On physical examination, a

palpable abdominopelvic mass corresponding to a 14-week uterine size was noted, more prominent on the left side. Tumor markers including CA-125, CEA, CA 19-9 and Beta HCG were within normal limits. All other hematologic and biochemical markers were also within normal limits.

Ultrasonography revealed a well-defined cystic lesion measuring 13.2 × 10.1 × 9.1 cm with thick internal septations arising from the left adnexa. MRI of the pelvis showed a well-circumscribed, thin-walled enhancing cystic lesion in the left pelvis without any calcification, fat, solid components, or papillary projections, suggestive of a cystadenoma. The right ovary was adherent to adjacent structures and not clearly visualized.

The patient underwent exploratory laparotomy with left ovarian cystectomy and right oophorectomy. On gross examination, the left ovary was predominantly cystic, measuring 13 × 12 × 7 cm. The internal surface was multiloculated and filled with thick mucinous material. (Fig 1a) A firm, gritty solid nodule measuring 5 × 2.5 × 2 cm was noted at one end of the cyst wall. It was gritty and hard with a grey yellow cut surface. (Fig 1b, 1c) Adequate sampling from both the cyst wall as well as solid nodule was done. The right sided ovary measured 5.5 × 1 × 0.8 cm. Cut surface was grey yellow and contained three cysts measuring 0.3 cm each. Thorough sampling of both cystic and solid areas was done.

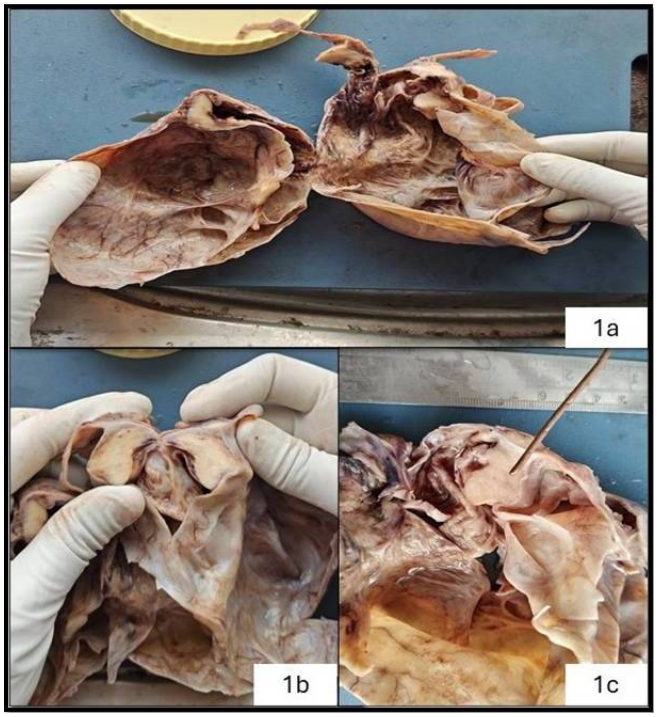

Figure 1: Figure 1a: Multilocular left ovarian cyst. Figure 1b, 1c: Solid nodule with yellow cut surface present within the cyst wall.

Microscopically, the cystic component of left ovary was lined by mucinous epithelium without atypia, stratification, or architectural complexity. (Fig 2) Sections from the solid nodule of left ovary revealed nests of transitional epithelium embedded in a dense fibrous stroma, without atypia/architectural complexity/mitoses/necrosis/invasion, consistent with a benign Brenner tumor. (Fig 2) The nests of transitional epithelium showed nuclear grooving as well as central cystic degeneration at places. (Fig 2) Sections from the right ovary revealed three cysts, all lined by mucinous epithelium. There was no atypia/stratification/architectural complexity. Surrounding stroma showed nests of transitional epithelium similar to the left ovary, embedded in a dense fibrous stroma. (Fig 2).

Both the components comprised more than 10 percent each, in both the ovaries. On immunohistochemistry, the nests of transitional epithelium were GATA 3 (Clone L50-823, mouse monoclonal antibody, PathnSitu) and p63 (Clone 4A4, mouse monoclonal antibody, PathnSitu) positive while these were negative for PAX8 (Clone EP331, rabbit monoclonal antibody, PathnSitu). (Fig 3)

The final diagnosis was bilateral mucinous cystadenomas with coexistent Brenner tumor.

Discussion

Mucinous cystadenomas are typically multilocular and filled with mucin-rich fluid. The essential diagnostic criteria include tumor with cysts and glands lined by benign mucinous epithelium with no architectural complexity or cytological atypia. Most Brenner tumors are small, solid well circumscribed nodules having a firm yellow cut surface. The essential diagnostic criteria of benign Brenner tumor include nests of bland transitional/urothelial epithelium set within fibromatous stroma. The differentiation from Walthard cell nests is based on presence of the fibrous stroma in Brenner tumor. According to the WHO

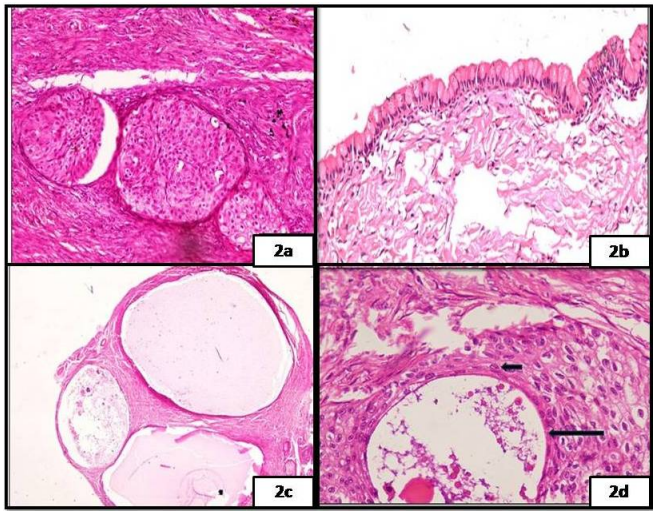

Figure 2: Figure 2a: Brenner tumor composed of nests of transitional epithelium within a fibrous stroma, left ovary, H&E, 200X. Figure 2b: Cyst wall lined by mucinous columnar cells, left ovary, H&E, 200X. Figure 2c: Right ovary showing three cysts along with nests of transitional epithelium towards lower right, H&E, 20X. Figure 2d: Nests of transitional epithelium with short arrow depicting grooving and larger arrow depicting central cystic degeneration, H&E, 400X.

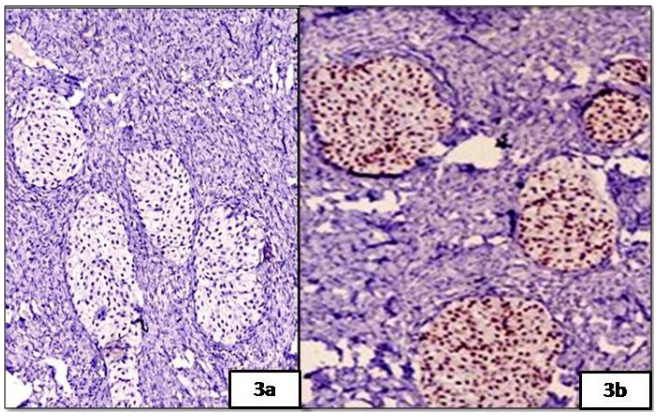

Figure 3: Figure 3a: Nests of transitional epithelium immunonegative for PAX8, IHC, 200X. Figure 3b: Nests of transitional epithelium immunopositive for p63, IHC, 200X.

2020 classification, when both tumor types occupy more than 10% of the neoplasm, it is categorized as a mixed epithelial tumor.[1]

Recent reports indicate that such mixed tumors are often discovered incidentally, as the Brenner component may be small and non-enhancing on imaging.[3] In our case, radiology failed to detect the Brenner element, which was only identified through detailed gross and histopathological sampling. This diagnostic challenge is corroborated by Wilson et al. who emphasized the importance of gross inspection and microscopic examination to identify mixed tumor component which is rarely identified on imaging.[4] As highlighted by this study, adequate sampling of the solid nodule in the cystic lesion led to the identification of Brenner tumor.

Pathogenetically, these tumors may arise from a common Müllerian precursor or through metaplastic transformation, although definitive molecular mechanisms remain unclear. Wang et al., in their study of 10 cases of combined Brenner and mucinous cystadenoma, found a statistically significant clonal relationship between the two tumors using HUMARA (Human androgen receptor assay) to investigate X chromosome inactivation.[5] Tafe et al. used molecular genetic analysis of eight cases of combined Brenner tumours and mucinous neoplasms, and their findings suggested a role of RAS mutations, MYC amplification, and to a lesser extent, PIK3CA mutations in the pathogenesis and progression from a benign Brenner tumour to borderline Brenner tumours and mucinous cystadenoma/mucinous borderline tumour; they hypothesized that Walthard nests cells seed the ovary mainly from the fallopian tubes to form a Brenner tumour and mucinous cystadenoma by transitional metaplasia and mucinous metaplasia, respectively.[6]

Table 1 shows a comprehensive review of the previously reported coexistent mucinous cystadenoma and Brenner tumor. As can be seen, all were unilateral. Bilateral presentation, of coexistent tumors, as in the present case has not been reported before.

Surgical resection remains the cornerstone of treatment. For postmenopausal women, bilateral salpingo-oophorectomy is generally recommended to eliminate the risk of malignant transformation and to ensure complete removal of all tumor

Table 1: Review of clinicopathological characteristics of previously reported cases of coexistent mucinous cystadenoma and Brenner tumor.

Author, Year	Age	Clinical	Duration	Location	Size	Surgery
Sridevi et al. [7], 2015	52	Pelvic discomfort	1 month	Left ovary	8 × 7 × 5 cm	TAH-BSO
Abbas et al. [8], 2015	70	Abdominal pain	2 months	Right ovary	52 × 41 × 36 cm	TAH-BSO
Pradhan et al. [9], 2017	52	Abdominal pain	6 months	Right ovary	25 × 20 × 18 cm	TAH-BSO
Anoedward et al. [10], 2017	59	Abdominal distension	3 months	Right ovary	25 × 15 cm	TAH-BSO
Dougherty et al. [2], 2018	57	Abdominal discomfort	3 months	Left ovary	40 × 22 × 27 cm	TAH-BSO
Nazari et al. [11], 2020	58	Abdominal pain and distension	6 months	Right ovary	20 × 13 cm	TAH-BSO
Maghbool et al. [1], 2021	56	Abdominal discomfort and distension	3 months	Left ovary	30 × 23 × 17 cm	TAH-BSO
Babaria et al. [12], 2022	60	Abdominal pain	2 months	Right ovary	9 × 2.2 cm	Right salpingo-oophorectomy
Frezgi et al. [3], 2023	57	Abdominal pain and distension	8 months	Left ovary	40 × 30 cm	TAH + left salpingo-oophorectomy
Joy et al. [13], 2023	30	Abdominal pain	1 year	Right ovary	9 × 2.2 cm	Right oophorectomy
Samaddar et al. [14], 2023	68	Abdominal pain and distension	9 years	Left ovary	13.1 × 12.5 cm	TAH-BSO
Zahlout et al. [15], 2023	62	Abdominal distension	2 weeks	Right ovary	25 × 20 cm	Laparotomy and cystectomy

components.[3] Prognosis is excellent in benign cases, with no reported recurrence following complete excision.[11]

Conclusion

The bilateral coexistence of mucinous cystadenoma and Brenner tumor represents a rare but clinically significant entity. Bilateral involvement is exceptionally uncommon and has important clinical implications. It raises a broader differential diagnosis including metastatic disease and hence requires detailed clinical, radiological and pathological evaluation. Also, bilateral presentation especially in postmenopausal women requires definitive surgical management i.e. bilateral salpingo-oophorectomy versus unilateral involvement where conservative surgery to preserve fertility in younger patients can be done. Diagnosis often relies on detailed histopathological evaluation due to the subtle nature of the Brenner component. Health professionals should be aware of such mixed epithelial tumors for accurate diagnosis, effective surgical management, and optimal patient outcomes.

Note: The patient consented to the publication of clinical details and images.

Abbreviations: TAH-BSO: Total Abdominal Hysterectomy with Bilateral Salpingo-Oophorectomy; MRI: Magnetic Resonance Imaging; CA-125: Cancer Antigen 125; CEA: Carcinoembryonic Antigen; CA 19-9: Cancer Antigen 19-9; Beta HCG: Beta Human Chorionic Gonadotropin; IHC: Immunohistochemistry; PAX8: Paired Box Gene 8; GATA 3: GATA Binding Protein 3; WHO: World Health Organization; HUMARA: Human Androgen Receptor Assay; RAS: Rat Sarcoma; MYC: Myelocytomatosis; PIK3CA: Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha.

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