

Case Report

Bilateral malignant brenner tumour ovary; an extremely rare occurrence

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ABSTRACT

Malignant Brenner tumours (MBTs) are extremely rare ovarian neoplasms, constituting 1–5% of all Brenner tumours. They are typically found in women of the perimenopausal or postmenopausal age group of 50–70 years. MBT often manifest with nonspecific symptoms such as abdominal pain, abnormal uterine bleeding, and weight loss. Definitive diagnosis is possible on histologic examination only, as imaging features and serologic markers are non-specific and give inconsistent results. Being an extremely rare neoplasm, our knowledge about MBT is restricted to case series and case reports. Adding to the rarity, we report a bilateral MBT ovary in a 55-year-old perimenopausal woman presenting with the chief complaint of bilateral lower abdominal pain and discomfort. Ultrasonographic imaging revealed bilateral large adnexal masses of heterogeneous echogenicity, suggesting bilateral malignant ovarian tumour. CA125 was within the reference value. The patient then underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, and after the histopathologic examination diagnosis of bilateral MBT was made. Patient is on regular follow-up and was disease-free for 4 years until recently, when she developed pleural effusion and is under further investigation.

Keywords: Malignant brenner tumour, Ovarian neoplasm, Transitional cell carcinoma, Benign brenner tumour

INTRODUCTION

Brenner tumours are exceedingly rare epithelial tumours of the ovary, accounting for less than 1% of all ovarian tumours.¹ This group of tumours is further classified into benign, borderline, and malignant tumours. The majority of Brenner tumours are benign or borderline, constituting 95% of Brenner tumours. Though pure benign Brenner tumour is rare, it is not so uncommon in association with mucinous tumours. Malignant Brenner Tumours (MBTs) are even rarer, making up less than 5% of all Brenner tumours. Because of its rare incidence, our knowledge about pathology, course of disease, treatment protocol and prognosis of MBTs is limited to a few case series and case reports. To add to the little existing literature, we report an

exceedingly rare case of bilateral MBT of the ovaries in a 55-year-old female.

CASE REPORT

A 55-year-old female presented to the gynaecology outpatient department with chief complaints of bilateral lower abdominal pain and discomfort. On ultrasonography (USG) imaging, bilateral adnexae showed large, heterogeneously hyperechoic masses with solid and cystic areas suggestive of bilateral malignant ovarian tumour. CA-125 was within the reference value. The patient was then operated on for a total abdominal hysterectomy and bilateral salpingo-oophorectomy, and the specimen was

sent to the department of pathology for histopathologic examination.

Gross examination showed bilateral ovarian tumours. The right and left ovaries measured 8×5×9 cm³ and 13×9×9 cm³, respectively. Ovarian surfaces were smooth with slightly bosselated areas focally, and no papillary excrescences were seen. The cut section was solid and cystic with areas of necrosis, hemorrhage, and papillary-like areas seen focally. Bilateral fimbrial ends of the fallopian tubes were edematous and fused with the corresponding ovaries. Endometrial thickness was 1mm, and the endometrial cavity and cervix were grossly unremarkable.

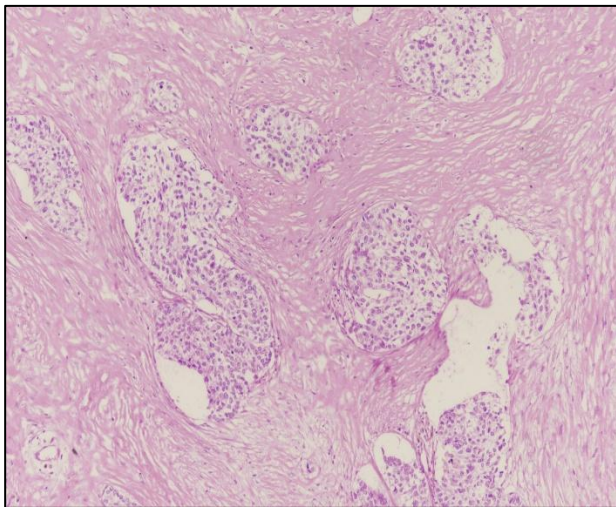


Figure 1: Benign brenner component comprising of variable sized nests of transitional epithelium with smooth borders surrounded by dense fibrous stroma (hematoxylin and eosin stain, original magnification x400).

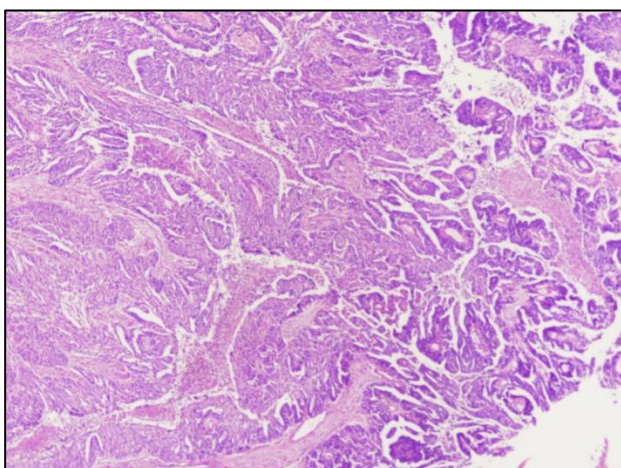


Figure 2: Malignant component comprised of stratified, pleomorphic epithelial cells forming papillae, solid sheets and nests with irregular borders (hematoxylin and eosin stain, original magnification x 200).

Microscopic examination of both ovaries showed a mixture of benign and malignant forms of Brenner tumour. The benign component was composed of stratified transitional epithelium forming nests of variable size with smooth borders surrounded by dense fibrous stroma (Figure 1). The cells were uniform in size, with round to oval nuclei, bland chromatin, an occasional longitudinal groove, and pale to eosinophilic cytoplasm (nuclear grade 1). Malignant component comprised of stratified moderately pleomorphic epithelial cells forming papillae with a central fibrovascular core, solid sheets and nests with irregular borders (Figure 2). At places junction between benign and malignant parts could be easily identified (Figure 3). The cells had a large nucleus with vesicular to dense chromatin, occasionally prominent nucleoli and scant eosinophilic cytoplasm (nuclear grade 2). Invasion into the surrounding stroma with a desmoplastic response was seen. Mitosis was brisk in the malignant component (20/10 high-power field) with frequent abnormal mitotic figures. Areas of necrosis were seen. Ovarian capsular invasion was not seen, though the tumour was reaching up to the capsule. Lymphovascular invasion was not seen. Bilateral fallopian tubes, endometrium and cervix were free of invasion or tumour deposits.

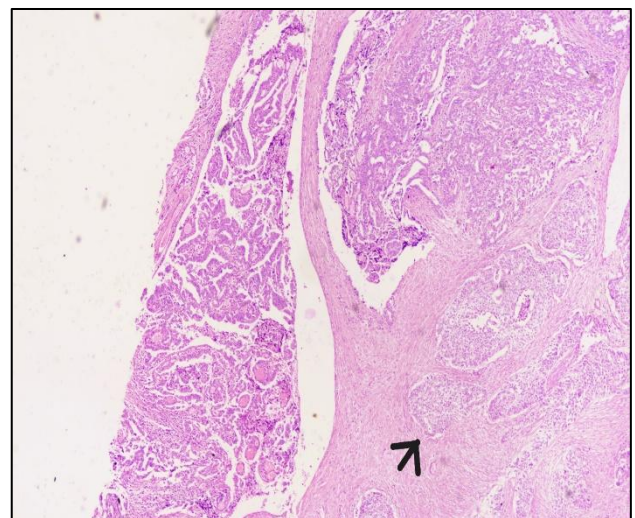


Figure 3: Junction of malignant (left half) and benign brenner component (right half, marked with black arrow) (hematoxylin and eosin stain, original magnification x 200).

Patient was on regular follow-up and after 4 years of disease-free surveillance, she has recently developed pleural effusion and is under further investigation.

DISCUSSION

Median age of patients diagnosed with malignant Brenner tumour is 65 years, in the perimenopausal or postmenopausal timeline. The majority of MBTs are unilateral, with only a few case reports of bilateral MBT. Adding to the rarity, our case was of bilateral MBT.^{1,2}

The chief presenting complaint by the patient is usually vague abdominal pain, abdominal distension, abnormal uterine bleeding, and some patients, a pelvic mass.³ Our patient had bilateral lower abdominal pain and discomfort.

MBT remains a diagnostic challenge preoperatively because it usually does not have diagnostic imaging features, nor is there elevation of any tumour-specific serum marker. The increase in CA125 is inconsistent between studies. While Gezginç et al reported a rise in CA-125 in 13 cases of MBTs, conversely another case series by Bouhani et al found 4 cases of MBTs with normal CA-125 levels.^{4,5} The present case had CA125 within the reference value.

Radiologic investigation may help in assessing the tumour size, nature and extent of the tumour as well as with surgical planning. Definitive diagnosis of MBT is made on histopathology only, which requires thorough and meticulous gross and microscopic examination.

Histologically, the essential criteria for diagnosing MBT require the presence of a malignant tumour with urothelial differentiation invading into the stroma, in a benign or borderline Brenner tumour background. The benign Brenner tumour is characterised by sharply demarcated epithelial nests of uniform transitional epithelium-like cells with prominent cell borders and eosinophilic cytoplasm surrounded by dense fibrous stroma. These cells have oval nuclei with small nucleoli and a longitudinal groove. Borderline Brenner tumours are usually cystic with intracystic papillae lined by transitional epithelium, or there may be compactly packed solid areas/nests of transitional epithelium. The major difference between MBT and its benign and borderline counterparts is the presence of invasion in the former, characterised by infiltrative growth with prominent cytologic atypia at the papilla base or border of solid nests.⁶

The essential criteria, having a benign or borderline Brenner tumour background, also help differentiate it from its very close differential of other high-grade surface epithelial tumours, especially high-grade serous carcinoma (HGSC) with transitional cell carcinoma (TCC)-like features, where a benign and borderline Brenner component must be absent. Both the tumours resemble histologically but differ in histogenesis. While HGSC with TCC-like features originates from pluripotent cells of ovarian surface epithelium, MBT develops from benign or borderline Brenner tumours. It is important to differentiate HGSC with TCC-like features from MBT, as the former is more aggressive and has a worse prognosis.⁷ This requires a diligent search for a benign or borderline component.

Immunohistochemical markers may help differentiate between TCC and MBT, where a benign or borderline Brenner component is difficult to find. Cuatrecasas et al suggested that MBT cells are often strongly positive for

Cyclin D1, Ras, and EGFR and lack p16 expression, while the reverse is true for TCC.⁸

Due to limited data on MBT, there is no clear consensus on the treatment approach, but the mainstay of therapy remains optimal surgical resection. Many authors have evaluated the role of chemotherapy, although to the best of our knowledge, no large clinical study has assessed its efficacy in MBT. In a cohort study, Ellaithy concluded that adjuvant chemotherapy combined with surgery offered no additional survival benefits.⁹ Conversely, another study by Han et al suggested that intensive systemic chemotherapy can be effective against recurrent malignant Brenner tumour of the ovary.¹⁰

The current preferred regimen is carboplatin-paclitaxel, which aligns with treatment approaches for other epithelial ovarian cancers.

Lymph node dissection (LND) remains a debated topic in these patients. Recent cohort studies indicate that LND yields limited benefits in MBT.^{2,11} The decision to perform LND should consider radiologic and clinical findings, clinical staging, and the patient's comorbidity status. In our case, no radiologic signs of tumour spread were observed, and the patient had no additional comorbidities; therefore, LND was not performed.

MBT generally has a favourable prognosis. In one of the largest studies, the 5-year disease-specific survival rate was 94.5% in women with disease confined to the ovary and 51.3% in women with extra-ovarian disease.²

CONCLUSION

MBTs are rare neoplasms, and our knowledge is limited to a few case reports and case series. Bilateral MBT is even rarer, with only a handful of cases documented in the literature. Imaging features and serologic markers are nonspecific, and definitive diagnosis relies solely on histopathologic examination. Given the extreme rarity of this neoplasm and the limited literature, there is a pressing need for large, comprehensive studies covering all aspects of pathology and treatment. Moreover, every case of MBT should be documented and carefully followed up.

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