Malignant Brenner tumor: Two case reports

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Abstract

Malignant Brenner tumor (MBT) is a rare ovarian tumor that, given the infrequency of the disease, has not been well documented in the literature. Diagnosing MBT both radiographically and histologically remains a challenge. We report two cases of ovarian MBT, detailing the clinical presentation, radiographic characteristics, and histologic findings with supplementary imaging. Our cases demonstrate the pathologic challenge of histologically diagnosing MBT versus other Brenner tumors and transitional cell carcinoma (TCC) of the ovary.

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- Malignant brenner tumor
- Transitional cell carcinoma
- Ovarian cancer

1. Introduction

Ovarian Brenner tumor (BT) is a rare epithelial ovarian cancer that accounts for less than 2% of ovarian neoplasms [1]. BTs are categorized as benign, borderline, or malignant. Malignant Brenner tumors (MBTs) are a particularly rare subset that account for less than 5% of all BT [1,2].

Clinical presentation of MBT varies but may include abdominal distention, pelvic discomfort, or postmenopausal bleeding [3]. MBT does not possess pathognomonic imaging features, and thus diagnosis of MBT requires surgical excision and pathologic review. Further, diagnosing MBT histologically can be difficult due to overlapping morphologic and histopathologic features with benign BT, proliferative BT, and transitional cell carcinoma (TCC). The cornerstone for treatment is surgical staging and observation. Given the rarity of the disease, there are limited studies investigating the role of adjuvant chemoradiation for MBT. However, the prognosis is generally considered good.

1.1. Case 1

A 58-year-old woman (G4P3013) with a history of hypertension, chronic obstructive pulmonary disease, tobacco use (43 packs a year), and class III obesity was referred for consultation at the gynecologic oncology department for postmenopausal bleeding and a pelvic mass found on transvaginal ultrasound (TVUS). She originally presented to her primary care provider for several months of intermittent vaginal bleeding and passing of clots. Upon consultation with gynecologic oncology, she further reported abdominal fullness with increasing urinary pressure and frequency.

TVUS revealed a normal uterus and a right adnexal mass measuring 13.6 × 8.4 × 11 cm, suspicious for ovarian neoplasm. A computerized tomography (CT) scan revealed a mixed cystic and solid anterior mass 15.1 × 15 × 11.9 cm with thickened septations and peripheral nodularity. Preoperative CA-125 measured 19.8 U/mL (normal range 0-35 U/mL).

The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and lymph node dissection for cancer staging. In surgery, a large cystic mass was noted arising from the left ovary, measuring approximately 20 x15cm. There was no evidence of metastatic disease. Frozen section was interpreted as a carcinoma, with possible MBT. Final pathology confirmed MBT (Fig. 1).

Post-operatively, the patient displayed no evidence of metastatic disease. She was counseled on the benefits of treatment with three cycles of carboplatin and paclitaxel versus observation alone. The patient elected for the latter and after two months (the time of writing) there was no evidence of disease.

1.2. Case 2

A 79-year-old woman (G3P3003) with a history of pulmonary hypertension, pulmonary fibrosis, stage 3 chronic kidney disease, and quintuple bypass was seen in the gynecologic oncology department for evaluation of large pelvic mass found on CT by her primary care provider. An unstaged grade 1 stage IA endometrioid adenocarcinoma had been diagnosed 5 years previously after transvaginal hysterectomy sparing the ovaries. Microscopic examination of the uterus at that time revealed that the tumor was confined to the endometrium. She was then lost to follow-up and without cancer surveillance for 3 years.

Upon consultation for her pelvic mass, the patient complained of abdominal distention, pelvic discomfort, and unintentional weight loss of

Abbreviations: BSO, bilateral salpingo-oophorectomy; BT, Brenner tumor; CT, computed tomography; MBT, malignant Brenner tumor; PET, positron emission tomography; TCC, transitional cell carcinoma; TVUS, transvaginal ultrasound.

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10 pounds. Physical examination revealed nodularity in the vaginal apex and a palpable adnexal mass.

The patient received a positron emission tomography (PET) scan (see Table 1). Preoperatively, her CA-125 measured 563.5 U/mL (normal range 0-35 U/mL). She underwent exploratory laparotomy, bilateral salpingo-oophorectomy (BSO), and removal of a pelvic mass 14 cm in greatest dimension. There was no evidence of metastatic disease. Surgical specimens were sent for pathologic review (see Fig. 2).

Postoperatively, her CA-125 trended down to 13.6 U/mL and remained within normal limits. The patient was discussed at a multidisciplinary tumor board, which recommended observation versus chemotherapy. She was counseled on her options and was amenable to

**Table 1**

| Case 1                                      | Case 2                                      |
|---------------------------------------------|---------------------------------------------|
| **Preoperative**                            | **Presentation**                            |
| Postmenopausal bleeding, urinary pressure and frequency | Abdominal distension, pelvic discomfort, unintentional weight loss of 10 lb |
| **Ultrasound findings**                     | **PET findings**                            |
| 13.6 × 8.4 × 11 cm mass                     | Complex cystic and solid mass with hypermetabolic activity |
| thick septations, interval vascularity       | Diffuse free fluid in the abdomen and pelvis |
| **CT findings**                             | pelvic ascites                              |
| 15.1 × 15 × 11.9 cm mass                    | Complex cystic and solid mass with hypermetabolic activity |
| mixed cystic and solid components           | Diffuse free fluid in the abdomen and pelvis |
| thickened septations                        | pelvic ascites                              |
| peripheral nodularity                       | Complex cystic and solid mass with hypermetabolic activity |
| **PET findings**                            | Diffuse free fluid in the abdomen and pelvis |
| **CA-125**                                  | pelvic ascites                              |
| 19.8 U/mL                                   | Complex cystic and solid mass with hypermetabolic activity |
| **Surgical Management**                     | Diffuse free fluid in the abdomen and pelvis |
| Total abdominal hysterectomy, BSO, lymphadenectomy, omentectomy | pelvic ascites |
| **Postoperative**                           | **Tumor Size**                              |
| **Tumor Size**                              | 25.0 × 15.0 × 10.5 cm. Weighing 1870 g     |
| 25.0 × 24.0 × 10 cm. Weighing 2700 g        | Focally mottled discoloration with areas of necrosis and white nodularity |
| Tan-pink, smooth, glistening                | Cystic areas filled with hemorrhagic, mucoid material. |
| **Cut section**                             | Solid areas displayed areas of necrosis     |
| Multiple cystic and solid areas             | Benign and malignant Brenner epithelial nests. |
| **Microscopy**                              | Nests of atypical transitional epithelium invading stroma. |
| Irregularly shaped malignant transitional type cells. Cystic areas within the tumor are lined by multilayered epithelium exhibiting hyperchromatic and pleomorphic nuclei and prominent mitotic activity with surrounding desmoplastic fibrotic stroma. | |
| **Immunohistochemistry**                    | Positive CK7                                 |
| Positive CK7, p63, weakly positive Gata3    | Grossly negative areas of p16, p14, WT1, p53, p16, Synaptophysin, CD56 |
| **Management**                              | Surveillance: follow-up every 3 months for 2 years, every 6 months for 3 years, and every 1 year thereafter |
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observation alone. At the time of writing she had been followed for 2 years without evidence of recurrent disease.

2. Case Summary

2.1. Discussion

Transitional cell tumors of the ovary are derived from ovarian surface epithelium and are categorized as either TCCs or BTs. Median age of diagnosis of MBT is 55 years. Similar to most ovarian malignancies, MBT presents with vague symptomatology. There are currently no reliable tumor markers for diagnosis of MBT, although CA-125 has been reported to be elevated in 30–70% of cases [4,5]. Further, there is limited literature supporting the utility of CT or magnetic resonance imaging in diagnosing the various types of transitional cell tumors preoperatively. Thus, definitive diagnosis requires surgical resection of the ovarian tumor and histopathologic evaluation.

One differential diagnosis of MBT is TCC. MBTs are considered low-grade tumors, while TCCs are considered high-grade neoplasms with a more aggressive clinicopathologic behavior. Despite possessing different modes of pathogenesis and tumor grades, both TCCs and BT share histologic features, which can make it challenging to determine a definitive diagnosis. Immunohistochemical markers aid in differentiating between TCC and the various types of BT. MBT cells often overexpress cytokeratin 7 (CK7) and lack p16 expression, while TCC cells overexpress p16. There is some evidence to support positive p63 expression as a possible delineating feature of MBT. Histologically, diagnosis of MBT requires the presence of both benign and malignant epithelial components with cellular atypia, evidence of stromal invasion, and necrosis. In contrast, TCC tissue morphologically resembles urothelial carcinoma and the diagnosis requires the absence of BT cells [1,6,7].

We report two cases of MBT with varying features on pathologic examination (Table 1). The first case presented clear morphologic and histologic features of MBT. The tumor cells were grossly positive for overexpression of CK7 and negative staining for p16. However, tumor tissue also contained numerous nests of atypia that stained positive for p16, favoring a histologic profile of TCC. Staining for p63 was not completed. Pathologic studies ultimately supported a diagnosis of MBT with features of TCC, which was subsequently confirmed by an outside pathology consultation [2,6].

Prognosis for MBT is generally considered good. The 5-year disease-specific survival rate is 94.5% in women with disease confined to the ovary and 51.3% in women with extra-ovarian disease [5]. The recurrence rate has been reported to be as low as 28% with cases of extra-uterine disease to the dura, lung, peritoneum, omentum, skin, and bone [5,8–12]. The mean time to recurrence is 11 months [2]. Given the limited number of reported cases, and thus the inability to study the efficacy of chemotherapy in a large clinical trial, there is currently no standardized chemotherapy regimen for treatment of MBT. The use of platinum-based chemotherapeutic agent plus paclitaxel postoperatively has demonstrated survival benefit in a small, retrospective study [4].

3. Conclusion

We report two cases of ovarian MBT, detailing the clinical presentation, pathologic review, imaging findings, and management. With only a handful of cases reported, we hope to add to the information available by reporting the management options presented to and chosen by our patients, as well as their outcomes. Due to the rarity of these tumors, the best treatment strategy will likely be developed through the reporting of clinical experience.

Contributors

All authors contributed equally to the drafting and revision of this article.
Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Patient consent

Written informed consent was obtained from both patients prior to publication.

Provenance and peer review

This case report was peer reviewed.

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