Case Reports in Women's Health 20 (2018) e00082

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Malignant Brenner tumor: Two case reports

Luke King *, Radhika P. Gogoi, Christopher Hummel, Ashlee Smith

Dept. of Obstetrics & Gynecology, Geisinger Medical Center, Danville, PA, USA

ARTICLE INFO

Article history:
Received 18 September 2018
Received in revised form 29 September 2018
Accepted 8 October 2018
Available online xxxx

Keywords:
Malignant brenner tumor
Transitional cell carcinoma
Ovarian cancer

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.

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 chemo-radiation 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 distension, pelvic discomfort, and unintentional weight loss of

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

* Corresponding author.
E-mail address: ljking1@geisinger.edu (L. King).

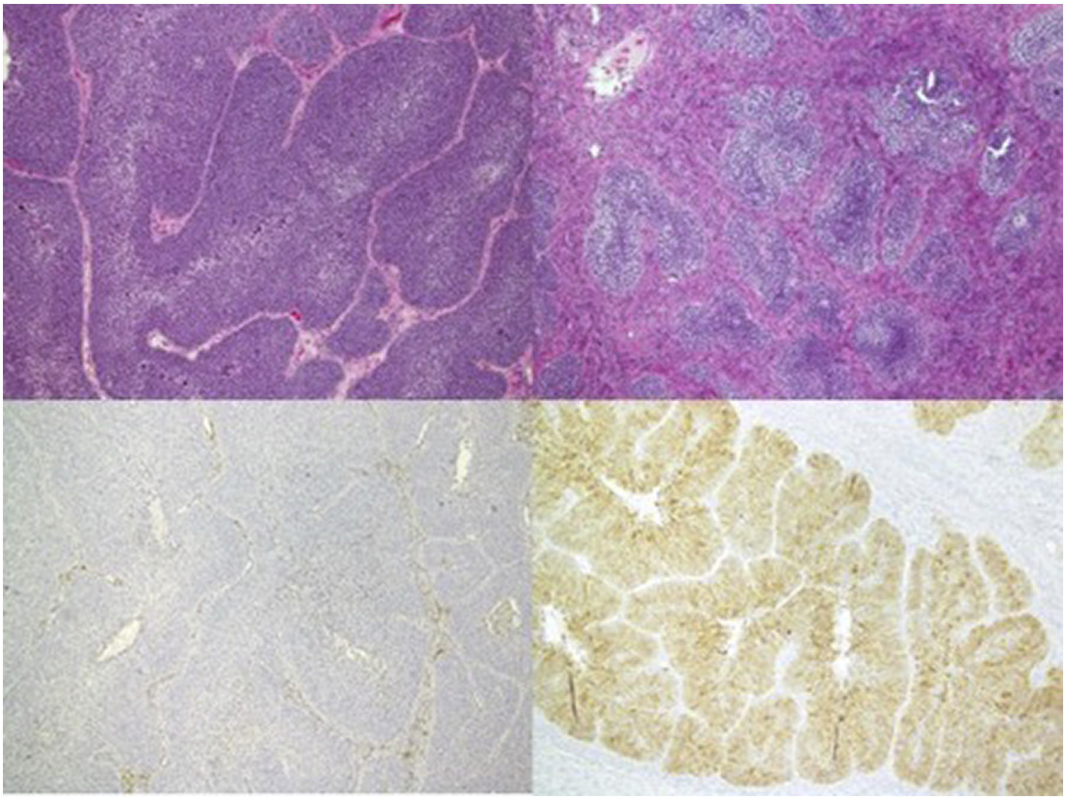

Fig. 1. Malignant Brenner's tumor stained with H&E at 100×. Large confluent nests of Brenner's clusters (top left). Coexisting borderline Brenner's tumor tissue in the same tissue sample (top right). IHC stain for p16 grossly negative (bottom left). IHC stain for CK7 was positive within malignant epithelium.

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 summary.

	Case 1	Case 2
Preoperative		
Presentation	Postmenopausal bleeding, urinary pressure and frequency	Abdominal distension, pelvic discomfort, unintentional weight loss of 10 lb
Ultrasound findings	13.6 × 8.4 × 11 cm mass thick septations, interval vascularity	–
CT findings	15.1 × 15 × 11.9 cm mass mixed cystic and solid components thickened septations peripheral nodularity	12.6 × 7.2 × 14.1 cm mass mixed cystic and solid components stranding of mesenteric fat pelvic ascites
PET findings	–	Complex cystic and solid mass with hypermetabolic activity Diffuse free fluid in the abdomen and pelvis Small left pleural effusions
CA-125	19.8 U/mL	563.5 U/mL
Surgical Management	Total abdominal hysterectomy, BSO, lymphadenectomy, omentectomy	Total abdominal hysterectomy, BSO
Postoperative		
Tumor Size	25.0 × 24.0 × 10 cm. Weighing 2700 g	25.0 × 15.0 × 10.5 cm. Weighing 1870 g
Tumor Surface	Tan-pink, smooth, glistening	Focally mottled discoloration with areas of necrosis and white nodularity
Cut section	Multiple cystic and solid areas	Cystic areas filled with hemorrhagic, mucoid material. Solid areas displayed areas of necrosis
Microscopy	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.	Benign and malignant Brenner epithelial nests. Nests of atypical transitional epithelium invading stroma.
Immunohistochemistry	Positive CK7, p63, weakly positive Gata3 Grossly negative areas of p16, WT1, p53, p16, Synaptophyin, CD56	Positive CK7 grossly negative areas of p16, CK20, Gata-3, p53, WT1, p40
Management	Surveillance: follow-up every 3 months for 2 years, every 6 months for 3 years, and every 1 year thereafter	Surveillance: follow-up every 3 months for 2 years, every 6 months for 3 years, and every 1 year thereafter

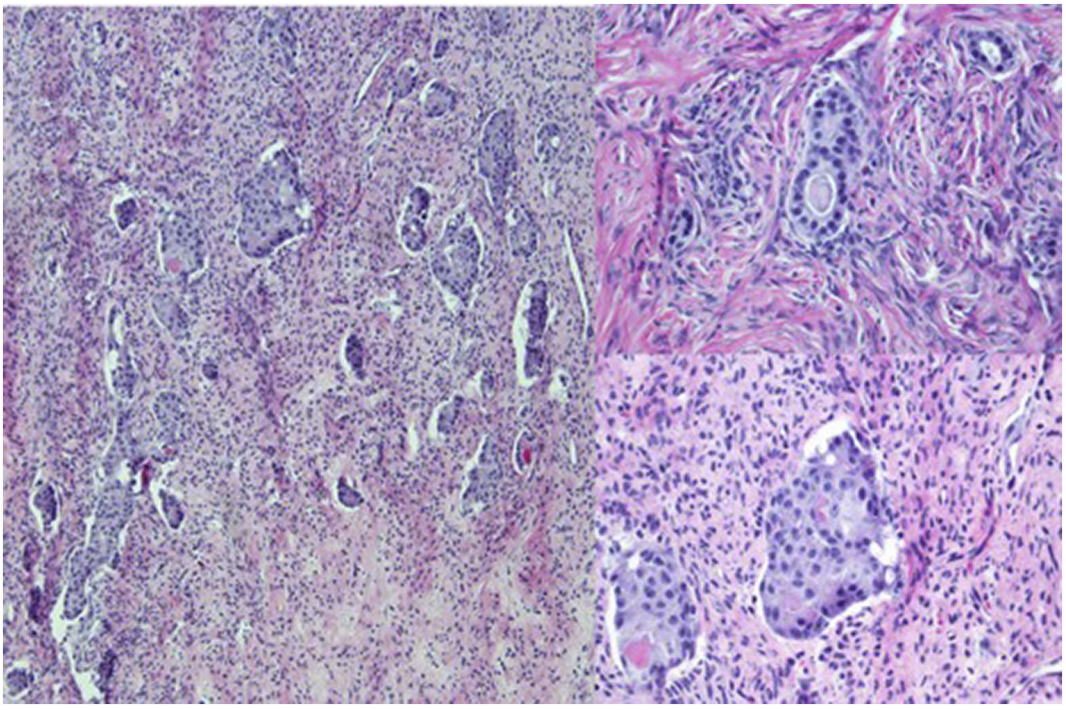

Fig. 2. Malignant Brenner's tumor stained with H&E at 100× (left). Magnification at 400× shows cytologic atypia (top right) and coexisting benign Brenner's cluster with simple monolayered epithelium without any cytologic atypia (bottom right).

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 histochemical features of MBT. In contrast, the second case possessed a diverse gamut of both MBT and TCC features, demonstrating the difficulty in delineating between MBT versus TCC. Tissue from the pelvic mass contained both benign and malignant cells throughout, with clear evidence of stromal invasion, supporting a diagnosis of MBT. 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 histochemical 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 extrauterine 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.

Funding

This work received no specific grant from any funding agency in public, commercial, or non-for-profit sectors.

Patient consent

Written informed consent was obtained from both patients prior to publication

Provenance and peer review

This case report was peer reviewed

References

[1] K.R. Lee, F.A. Tavassoli, J. Prat, et al., Tumors of the ovary and peritoneum. In: World Health Organization Classification of Tumours. Pathology and Genetics of Tumors of the breast and Female Genital Organs, IARC Press, Lyon, 2003 113–145.
[2] S.M. Lang, A.M. Mills, L.A. Cantrell, Malignant Brenner tumor of the ovary: review and case report, Gynec Oncol Reports. 22 (2017) 26–31.
[3] K. Gezginc, R. Kartatayli, F. Yazici, et al., Malignant Brenner tumor of the ovary: analysis of 13 cases, Int. J. Clin. Oncol. 17 (4) (2012) 324–329, https://doi.org/10.1007/s10147-011-0290-7.
[4] J.H. Han, D.Y. Kim, S.W. Lee, et al., Intensive systemic chemotherapy is effective against recurrent malignant Brenner tumor of the ovary: an analysis of 10 cases within a single center, Taiwan . Obstet Gynecol. 54 (2) (2015) 178–182, https://doi.org/10.2016/j.tjog.2014.03.008.
[5] D. Nasioudis, G. Sisti, K. Holcomb, T. Kanninen, S.S. Witkins, Malignant Brenner tumors of the ovary: a population-based analysis, Gynecol. Oncol. 142 (2016) 44–49, https://doi.org/10.1016/j.ygyno.2016.04.538.
[6] M. Cuatrecasas, L. Catasus, J. Palacios, J. Prat, Transitional cell tumors of the ovary: a comparative clinicopathologic, immunohistochemical, and molecular genetic analysis of Brenner Tumors and transitional cell carcinomas, Am. J. Surg. Pathol. 33 (4) (2009) 556–567, https://doi.org/10.1097/PAS0b013e318188b84c.
[7] R.J. Ingin, S.K. Andola, A.A. Zubair, Transitional cell carcinoma of the ovary: case series and review of literature, J. Clin. Diag. Res. 8 (8) (2014) 7–8, https://doi.org/10.7860/JCDR/2014/9104.4733.
[8] A. Ahr, G. Arnold, U.J. Goring, Cytology of ascetic fluid in a patient with metastasizing malignant Brenner tumor of the ovary: a case report, Acta Cytol. 41 (4) (1997) 1299–1304, https://doi.org/10.1159/000325184.
[9] L. Akman, A. Akdemir, M.C. Terek, O. Zekiogiu, Ovarian malignant Brenner tumor in patients over 65 years of age, Kaohsiung J. Med. Sci. 30 (3) (2014) 159–160, https://doi.org/10.1016/j.kjms.2013.01.020.
[10] J.F. Baizabal-Carvallo, H.M. Barragan-Campos, M. Alonso-Juarez, et al., Dural metastases as presentation of a Brenner tumor, J. Clin. Neurosci. 17 (4) (2010) 524–526, https://doi.org/10.1016/j.jocn.2009.01.038.
[11] H. Beck, D. Raahave, P. Bolesen, A malignant Brenner tumour of the ovary with subcutaneous metastases, Acta Pathol Microbiol Scand. 85 (6) (1977) 859–863.
[12] K.T. Chen, Bilateral malignant Brenner tumor of the ovary, J. Surg. Oncol. 26 (3) (1984) 194–197.