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A Rare Case of Ruptured Malignant Ovarian Brenner Tumor

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Patient: Female, 39-year-old
Final Diagnosis: Ovarian carcinoma
Symptoms: Abdominal pain • abdominal mass • abdominal tenderness
Clinical Procedure: Adjuvant chemotherapy • laparotomy
Specialty: Obstetrics and Gynecology • Oncology

Objective: Rare disease

Background: Ovarian cancer is the leading cause of death in women with gynecological cancers. Ovarian Brenner tumor (BT) is an extremely rare type of epithelial ovarian cancer that accounts for about 1-3% of all ovarian cancers. Herein, we report a rare case of ruptured malignant ovarian Brenner tumor.

Case Report: A 39-year-old P0A0 woman came to the Emergency Department (ED) with abdominal pain and tenderness. Perforated appendicitis was initially suspected and an emergency laparotomy was performed by the General Surgery Department. Then, a 25×20×15 cm grayish cystic mass originating from the right adnexa was found. We consulted intraoperatively with the Gynecology Oncology Department and decided to perform complete surgical staging. Histopathological examination confirmed the diagnosis of malignant Brenner tumor (MBT). The patient was then given adjuvant chemotherapy with a paclitaxel carboplatin regimen. In this case report, we present our case along with a review of the current literature regarding the diagnosis and therapy of malignant Brenner tumor.

Conclusions: Ovarian MBT is an extremely rare ovarian cancer. Diagnosing MBT can be challenging as there are no clinical, laboratory, or imaging features typical for it. Surgery is the mainstay treatment in MBT cases. The role of adjuvant chemotherapy in MBT is still being debated.

Keywords: Brenner Tumor • Carcinoma, Transitional Cell • Ovarian Neoplasms

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/938680

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Background

Ovarian cancer is the fifth most common cause of death among women. It is also the leading cause of death in women with gynecological cancers. Most ovarian cancer cases are diagnosed in advanced stages, which leads to a poor prognosis of the disease [1,2]. Ovarian Brenner tumor (BT) is an extremely rare type of epithelial ovarian cancer and accounts for about 1-3% of all ovarian cancers. Diagnosing MBT is very difficult as there are no clinical, laboratory, or imaging features typical for it [3-5]. Like any other epithelial ovarian tumors, surgery is the mainstay treatment in MBT cases. The role of adjuvant chemotherapy in MBT is still being debated [4,5]. Herein, we report a rare case of a P0A0 woman who was diagnosed with ovarian malignant Branner tumor.

Case Report

A 39-year-old P0A0 woman was diagnosed with unilateral malignant Brenner tumor of the ovary. She first came to Gynecologic Outpatient Clinic at Hasan Sadikin General Hospital with an abdominal mass. She also experienced weight loss and had a 2-year history of bleeding outside of her menstrual cycle. She did not report having any dysmenorrhea or dyspareunia. She had her menarche at the age of 12 and she was married once at the age of 23, but is currently divorced. She was not on oral contraception and she was sexually active. There was no history of vaginal discharge, urinary disturbance, or defecation disturbance. The patient had a history of hypertension, but no history of surgery or family history of malignancy. Gynecological transabdominal ultrasonography (USG) revealed a normal uterus with an adnexal solid mass measuring 11.86×12.50×11.24 cm and normal liver. Ovarian carcinoma was suspected; therefore, a laparotomy was scheduled.

However, around 3 months later, before her surgery schedule was due, she came to the ED with abdominal pain and tenderness of 12 h duration. She was eventually transferred to the General Surgery Department. Her blood pressure was 150/100 mmHg, heart rate was 110 bpm, respiratory rate was 24×/min, and temperature was 38.3°C. On abdominal examination, there was abdominal tenderness and muscle guarding. No ascites was found. The patient was anemic, with high white blood cell and neutrophil counts. Other hematological panels were within normal limits. Ultrasonography was performed but there was no free fluid found. Chest X-ray examination revealed bilateral pleural effusions. Perforated appendicitis was suspected and an emergency laparotomy was performed on by the General Surgery Department.

After the peritoneum was opened, 250 cc of yellowish ascitic fluid was found. On further exploration, they found a 25×20×15 cm grayish cystic mass with solid parts and an irregular surface originating from the right adnexa that adhered to the omentum and peritoneum in the right hypochondrium. There was rupture on the posterior surface, with ±300 cc of blood and blood clotting. We consulted intraoperatively with the Gynecology Oncology Department and decided to perform complete surgical staging. We found the uterus to be enlarged at 16-18 weeks of gestation and on further exploration, we also found peritoneal seeding. The right and left pelvic lymph nodes were also enlarged (2×3 cm and 2×2 cm, respectively). We suspected metastasis to 2 right pelvic lymph nodes, 1 left pelvic lymph node, rectum, pre-vesica, and Douglas pouch (pT2bN1bMx).

Grossly, the mass was a whitish-brown rubbery split cyst measuring 16×13×7 cm with a smooth outer surface. On the cut surfaces, some of the mass was dull and solid, while some was hollow. The solid part was around 15×12×6 cm, while the hollow part had a diameter of 2-5 cm with a wall thickness of 0.1-0.2 cm and it was filled with clear liquid (**Figure 1**).

Histopathological examination revealed the diagnosis of right ovarian malignant Brenner tumors that infiltrated the corpus uteri, invaded the lymph vasculature, and metastasized to 2 right pelvic lymph nodes, 1 left pelvic lymph node, rectum, prevesical space, and Douglas pouch (**Figures 2-4**). The fallopian tube, cervix uterus, left ovary, and omentum were free of malignant cells.

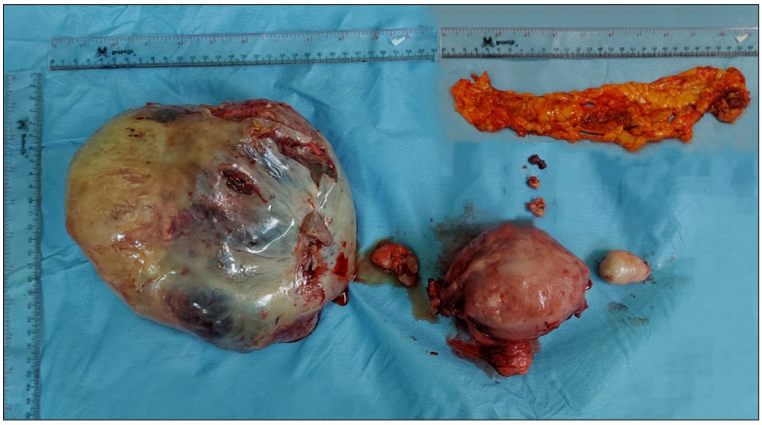

Figure 1. Macroscopic specimen.

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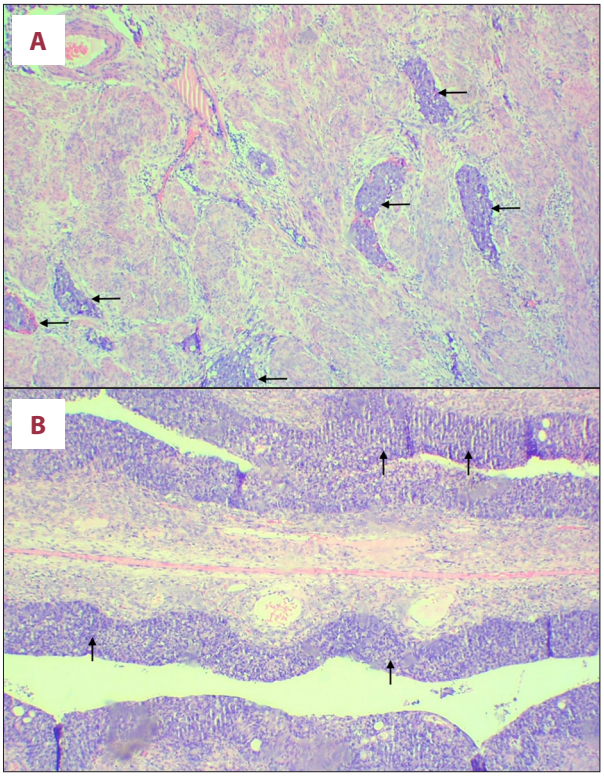

Figure 2. Microscopic findings of right ovarian tumor. (**A**) Condensed hyperplastic round and oval cells forming a glandular structure (arrow). The cells' nuclei were pleomorphic, hyperchromatic, and partially vascular, with clear nuclear daughter cells and mitosis. The tumor mass partially showed squamous differentiation. The surrounding fibro-collagenous connective tissue stroma was filled with lymphocytes, dilated blood vessels, and blood. (**B**) Visible invasion of malignant tumor cells into the lymph vasculature. Extensive areas of necrosis were also seen. Transitional cell differentiation was seen in the cyst wall of the right ovarian tumor mass (arrow).

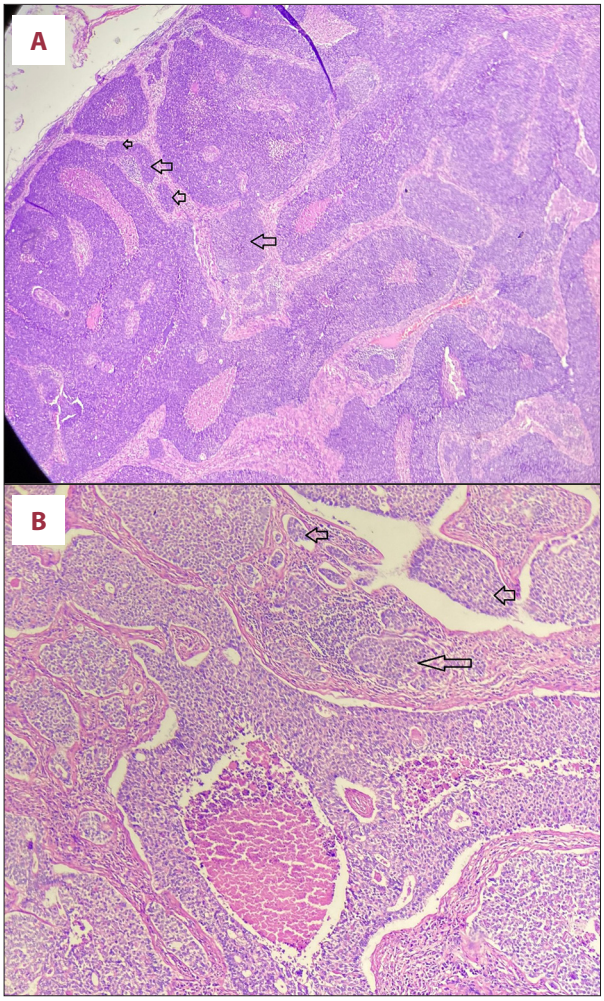

Figure 3. Microscopic appearance of pelvic lymph nodes. Pelvic lymph nodes were partially covered by connective tissue capsule. The subcapsular consisted of lymphoid stroma. Invading malignant tumor cells were seen (arrows). (**A**) Right pelvic lymph node. (**B**) Left pelvic lymph node.

The surgery was successful, in which optimal debulking was done with zero residual tumor (R0). The patient was discharged on postoperative day 3. She then underwent adjuvant chemotherapy with paclitaxel carboplatin 175 mg/m^2 and carboplatin 6 AUC every 21 days for 3 series. The patient was followed up at 1 month after adjuvant chemotherapy completion and appeared to be recurrence-free, with a normal level of CA-125. She will undergo subsequent evaluations at 3 months, 6 months, and 1 year after adjuvant chemotherapy.

Discussion

Tumors originating from the epithelial surface of the ovary are the most common form of ovarian neoplasm. Malignant Brenner tumor (MBT) is a very rare subtype of ovarian epithelial tumor. This subtype was first described by Fritz Brenner in 1907 [1,4]. The exact incidence of malignant Brenner tumor (MBT) is not known. In Surabaya, Indonesia, from 2014 to 2016, MBT accounted for around 0.2% of 403 cases of ovarian epithelial cancer [6]. According to the World Health Organization (WHO), there are 3 main classification of Brenner tumors: benign, borderline, and malignant. Brenner tumors are also called transitional cell tumors because their histologic appearance is similar to that of the urothelium, which resembles an epithelial component [3].

Brenner tumor is known to occur most frequently in the fifth to sixth decades of life, with 71% of patients diagnosed at least aged 40 years. In our case, the patient was 39 years old when she was diagnosed with MBT. A case series by Gezginc et al [7] showed that the age range at diagnosis was between 43-79

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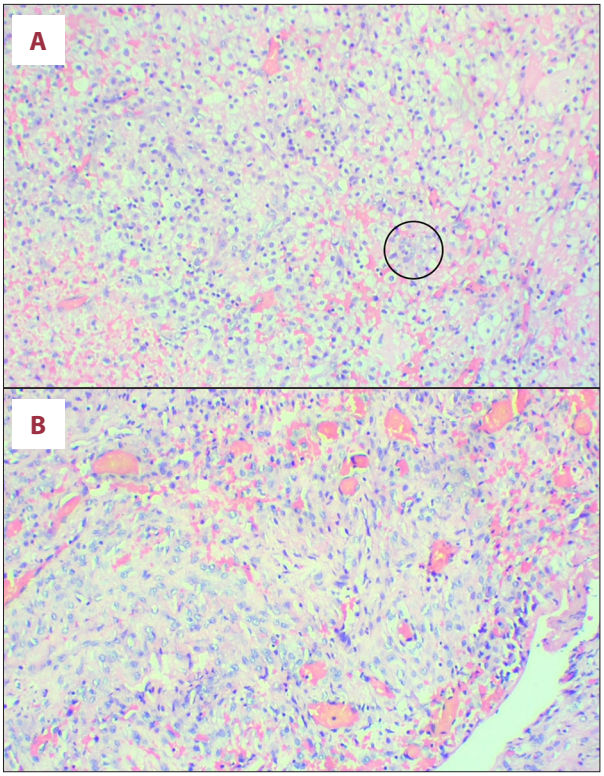

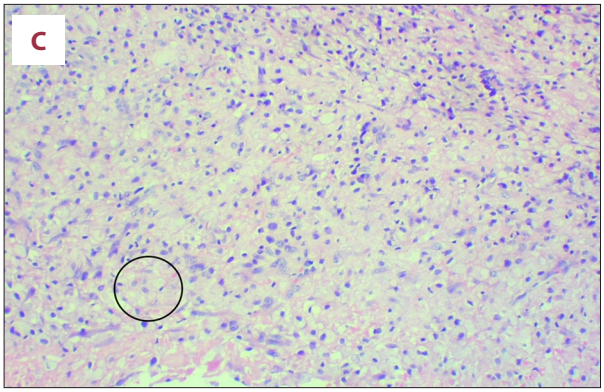

Figure 4. Microscopic findings of seeding tumor. (**A**) Rectal tumor seeding preparation consisted of connective tissue stroma, inflammatory cells (lymphocytes, histiocytes, and plasma cells), bleeding, foamy macrophages (circles), and invasion of malignant tumor cells. (**B**) Prevesical tumor seeding preparations consisted of connective tissue stroma infested by massive inflammatory cells of lymphocytes, histiocytes, plasma cells, and PMN cells, accompanied by dilated blood vessels, bleeding, and malignant tumor cell invasion. (**C**) Douglas cavity tumor seeding preparation consisted of connective tissue stroma, inflammatory cells (lymphocytes, histiocytes, and plasma cells), bleeding, foamy macrophages (circles), and invasion of malignant tumor cells.

years. Lin et al [8] presented a case series with the youngest age at diagnosis being 41 years old, while Han et al [9] presented a case with the youngest age at diagnosis being 37 years old.

Diagnosis of malignant Brenner tumor is difficult to establish because there are no clinical, laboratory, or imaging features typical for it. Further investigations with histopathological examination and immunohistochemistry are therefore essential. Clinical manifestations are often nonspecific and may resemble other ovarian tumors, thus causing a delay in diagnosis. Symptoms usually become more visible in advanced stages (stage III or stage IV) [4-6]. Bouhani et al [4] reported 4 cases of Brenner tumor, which all had nonspecific initial symptoms such as abdominal distention, abdominal pain, pelvic mass, and pelvic pain. King et al [10] reported 2 cases with initial symptoms of postmenopausal bleeding and pelvic mass. Very few patients with malignant Brenner tumors had ascites. In our case, we found yellowish ascitic fluid [5]. Another nonspecific symptom was reported by Baizabal-Carvello et al (2010), whose patient initially came with symptoms of intracranial hypertension originating from dural metastases [11].

Diagnosing malignant Brenner tumor with imaging studies such as ultrasound, CT scan, or MRI is difficult as MBT does not have any pathognomonic imaging features [6,12]. In our case, ultrasound examination revealed an adnexal solid mass measuring 11.86×12.50×11.24 cm, which can only conclude the presence of an ovarian tumor. Takeuchi et al [13] reported a case of malignant Brenner tumor with CT scan findings that correlated with histopathological examination. They found mild enhancement of a heterogeneous mass on CT scan. MRI findings that are common to Brenner tumors are solid hypointense lesions on T2-weighted images, as well as solid components with higher intensity on T1-weighted images [5,13].

Malignant Brenner tumor does not have any specific tumor marker that can help establish its diagnosis. However, level of tumor markers, specifically CA-125, can be used to assess tumor activity and to better distinguish whether the tumor is malignant or benign [4,5]. A case series by Gezginc et al [7] reported that tumor marker CA-125 was increased in 13 cases of malignant Brenner tumor. However another case series by Bouhani et al [4] found 4 cases of malignant Brenner tumors with normal CA-125 levels. We did not assess CA-125 levels in our patient prior to her surgery because she initially underwent an emergency laparotomy for suspected perforated appendicitis, not an ovarian tumor. Tumor marker CA-125 can be used for post-surgery and post-systemic chemotherapy evaluation.

MBTs were first recognized as transitional cell carcinoma of the ovary (TCCO), but later studies suggest that malignant Brenner tumors are histologically distinct from this subgroup of epithelial ovarian tumors. Brenner tumors can be either benign, borderline, or malignant. Histologically, the diagnosis of MBT can be

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established using the Hull and Campbell criteria, which requires both benign and malignant epithelial components to be present along with cellular atypia, stromal invasion, and necrosis [1,4,5]. Histopathological findings in our case are consistent with other reports. The immunohistochemical profile of MBT shows positivity for CK7, p63, GATA3, uroplakin III, p63, and thrombomodulin [5,14].

Treatment of ovarian cancer in general includes a combination of surgery and chemotherapy. Like other ovarian epithelial tumors, surgical procedure options include hysterectomy, salpingo-oophorectomy, omentectomy, and appendectomy, with or without pelvic and para-aortic lymphadenectomy [1]. In the early stages, a unilateral salpingo-oophorectomy is performed while preserving the contralateral uterus and ovary. However, in advanced stages, debulking surgery, consisting of hysterectomy/bilateral salpingo-oophorectomy (BSO), shows good therapeutic outcomes. It is important to determine whether debulking surgery will benefit the patient by initially performing exploratory laparoscopic surgery [1,5,6].

The role of adjuvant chemotherapy in MBT is still being debated. Even the Surveillance Epidemiology and End Results database does not explain in detail the various drug options and dosages available for treatment of this rare tumor. However, some studies have shown a complete response following adjuvant chemotherapy [4,5]. Our patient received adjuvant chemotherapy with a paclitaxel carboplatin regimen. This adjuvant chemotherapy regimen is the current standard regimen for ovarian epithelial neoplasms. The same regimen was also used in the case report by Alfianto et al [6], where after receiving 5 cycles of paclitaxel carboplatin, the patient showed no residual mass. Other regimens that can be used include monotherapies such as camptobel, gemcitabine, bevacizumab, etoposide, and Adriamycin; and combined therapies such as Taxol-cisplatin, taxol-carboplatin, hycamtin cisplatin, camptobel-carboplatin, gemcitabine-taxol-carboplatin, and docetaxel-cisplatin [10]. The use of combination therapy instead of monotherapy can increase the success rates and produce better outcomes [12,15].

Ovarian MBT generally has a favorable prognosis following surgery, as 80% of cases are diagnosed in stage I. However, advanced-stage MBTs have a poor prognosis. The 5-year survival rate of strictly confined ovarian MBT patients was notably higher than those with extra-ovarian disease (94.5% vs 51.3%, respectively). Adjuvant chemotherapy has been shown to increase survival among women with epithelial ovarian cancer [1,5,6,16]. In addition, anti-FGFR inhibitors, such as pemigatinib and erdafitinib, have potential value in therapy of refractory malignant Brenner tumors [8].

Conclusions

We report a case of ruptured ovarian malignant Brenner tumor and review the clinical manifestations, histopathological findings, imaging findings, and practical management of this rare tumor. The rarity of this tumor poses a challenge in diagnosing and determining the best treatment strategy for each patient.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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