MOH

Journal of Medical Case Reports

Borderline Brenner Tumor of the Ovary: Case Report and Review of the Literature

Hannah Pulido[*1], *Makenzie Ammons*[1], *Rona Bakri*[1], *Brandon Kimbrough*[1], *Zachary Elder*[1], *Janelle Cruz*[1], *Nicole Forte*[1], *and Mohamed Aziz*[2]

Abstract

Ovarian neoplasms are a heterogeneous group of tumors with varying presentation and outcomes. The most common are surface epithelial tumors, including transitional cell tumors and Brenner tumors. Brenner tumors are rare neoplasms of the ovary composed of transitional / urothelial-like epithelium, typically embedded in the fibromatous stroma. Benign, borderline, and malignant variants are recognized based on the presence or absence of stromal invasion and histocytological features of the epithelial cells. The vast majority of Brenner tumors are benign, often incidental findings; however, malignant Brenner tumors do occasionally occur. We present a case of a 75-year-old female diagnosed with a symptomatic borderline Brenner tumor of the right ovary. We discuss diagnostic techniques, differential diagnoses, and treatments of Brenner tumors. We encourage further studies to thoroughly understand the clinical features, diagnostic techniques, and treatment of various Brenner tumors.

Introduction:

Brenner tumor (BT) was first described by Frits Brenner in 1907, originating from the epithelium of the ovary.[1] It represents about 2.5% of all ovarian epithelial tumors.[2] Brenner tumors are characterized as benign, borderline, or malignant based on their histologic features.[1] However, less than 5% of Brenner tumors are malignant.[3] Most Brenner tumors classically present in post-menopausal women in their fifth or sixth decade of life. These tumors are typically unilateral and found incidentally. Patients may complain of symptoms such as a palpable mass, pelvic pain, urinary retention, or vaginal bleeding when accompanied by estrogenic activity.[1,2,4,5] On gross examination, benign tumors are well-circumscribed, fibrous, uniform tumors about 5-6 cm in diameter.[1,4] However, malignant tumors can be as large as 30cm in diameter, with fleshy, polypoid masses encroaching on cystic cavities.[1,4] Histologically, benign

Brenner tumors usually consist of sharply demarcated uniform islands of epithelial cells in a dense fibromatous stroma with coffee bean nuclei in a background of pale cytoplasm and may contain calcifications.[4]

Ovarian neoplasms, in general, have a positive correlation with increasing age in women.[6] It is the only known risk factor; therefore, there have been no known preventative measures.

In this case, we describe a 75-year-old female who presented with vaginal bleeding and abdominal pain. Our patient was diagnosed with the uncommon borderline Brenner tumor following imaging and surgical excision with a histologic examination.

Case Presentation:

A 75-year-old female presented to the clinic with recurrent vaginal bleeding and abdominal pain. Medical history included controlled hypertension and type-II diabetes. Transvaginal ultrasound showed a

large right ovarian mass with an anechoic cystic component. MRI and CT scans revealed a large multi nodular right ovarian mass replacing the entire right ovary with prominent calcification and multiple Leiomyomas of the uterus. The combined CT and MRI findings of a unilateral fibrous ovarian mass containing punctate calcifications associated with a multilocular cystic formation. These findings suggest the diagnosis of a benign ovarian tumor, but excision was recommended for definitive evaluation. The patient's body survey revealed no other masses or lymphadenopathy.

Affiliations

[1]*American University of the Caribbean Medical School, USA*

[2]*siParadigm Diagnostic Infirmatics, NJ, USA*

A total laparoscopic hysterectomy with bilateral salpingo-oophorectomy (BSO) with frozen section analysis was performed. Frozen section evaluation was compatible with the diagnosis of a Brenner tumor. The right ovary was replaced by a multinodular solid firm mass measuring 11x 9 x 8.5cm. The cut section surface of the tumor showed solid, pick tan yellow changes with prominent calcification. Areas of focal cystic changes were also noted (Figure-1A-B). The tumor showed focal areas of cystic spaces lined by transitional, flattened, cuboidal, and columnar epithelium with apparent changes. Squamous metaplasia and focal mucinous material were seen within some nests. The transitional cells displayed pale eosinophilic and clear cytoplasm, uniform round and ovoid nuclei, some with grooves resembling coffee beans, fine chromatin, and punctate nucleoli. Mild nuclear atypia and focal papillary architecture were also noted. Histopathological examination revealed sharply demarcated uniform islands of epithelial cells lined by multilayered transitional epithelium. No malignant features or stromal invasion were identified (Figure 2-A-B-C). Immunohistochemistry (IHC) studies showed that the tumor cells were positive for CK7, EMA, P16, P63, and GATA-3, while negative for ER, PR, and WT-1. The histomorphology, together with IHC studies, was consistent with the diagnosis of Borderline Brenner tumor associated with a component of benign Brenner tumor, negative for invasive carcinoma.

Multiple uterine submucosal, intramural and subserosal Leiomyomas were identified, with the largest measuring 2.5 cm. Otherwise, there were no other significant pathological findings. No post-operative treatment was administered following surgery. After four years of follow-up, there was no evidence of recurrence or metastasis, after which the patient was lost to follow-up.

Discussion:

Post-menopausal bleeding is an event of immense clinical concern. Women who present with post-menopausal vaginal bleeding menopause should undergo a complete workup to exclude malignant etiology. Vaginal bleeding is the initial sign in more than 90% of post-menopausal women with endometrial malignancy.[7] The patient described in our case presented with recurrent vaginal bleeding along with abdominal pain. It is uncommon for a benign Brenner tumor to have symptoms, as it is usually an incidental finding on ultrasound or a routine physical examination, requiring biopsy with pathological evaluation.[4] With this, our patient required an extensive and definitive workup for exclusion of malignancy, eventually rendering the diagnosis of borderline Brenner tumor.

Differential diagnoses for Brenner tumor include various benign and malignant ovarian tumors such as endometrioid adenofibroma, granulosa cell tumor, carcinoid tumor, high-grade serous carcinoma, squamous cell carcinoma, metastatic squamous cell carcinoma, and metastatic urothelial carcinoma.[1] These tumors contain differing histological characteristics, ultimately differentiating them from Brenner tumors. For example, the endometrioid adenofibroma is mostly granular, lacking multilayered epithelial nests with transitional differentiation. The granulosa cell tumor presents with microfollicular, trabecular or solid growths.[8] The carcinoid tumor has insular or trabecular architecture, lacks prominent fibromatous stroma, and includes the expression of urothelial tract. Initial reports suggested origin directly from ovarian surface epithelium; however, additional reports indicated that these tumors are driven from sites of transitional cell metaplasia within the adnexal area.[9] In general, now there is an agreement that the tumor is derived from surface (coelomic) epithelium, as are the serious and mucinous cystadenomas.[5]

In order to image these tumors, transvaginal and transabdominal ultrasound are the initial modalities. If the imaging is inconclusive or warrants further investigation, CT or MRI imaging is reasonable. However, diagnosing Brenner tumors with imaging studies is difficult because the tumor's appearance is nonspecific.[2] Extensive amorphous calcification in a solid mass or solid component in a multilocular cystic mass is a characteristic finding of the Brenner tumor of the ovary on CT and MRI.[10] Histomorphological,

the tumor consists of sharply demarcated uniform islands of epithelial cells in a dense fibromatous stroma.[4] There is no consistent tumor marker for these tumors. BTS express several IHC markers of urothelial differentiation, including uroplakin 3, thrombomodulin, GATA3, p63, as well as cytokeratin 7.[3] The major pathological variants are the proliferating borderline like our case and the malignant Brenner tumors; a poor prognosis is associated with the latter neoplasm.[5]

Currently, the primary treatment modality for these tumors is surgical excision.[1] Conservative surgery is strongly advised for women with the potential and desire for fertility.[4] This is a rare concern, however, due to the fact that the vast majority of occurrences of these tumors are far past a woman's capability of fertility. Depending on size, affected structure, and risk of seeding, laparoscopic or open laparotomy is decided upon.[11] A decision on the management of BT depends on the age and fertility status of the patient. In young patients, only simple excision with preservation of ovaries is done, while in post-menopausal women, total abdominal hysterectomy with bilateral salpingo-oophorectomy is performed as and is the treatment of choice.[6] Like most benign tumors, complete resection lends to complete resolution. The prognosis of patients with Benign Brenner tumors is usually excellent.[6] Patients with benign Brenner tumors should be informed of their condition and reassured with regular follow-ups. A borderline tumor, sometimes called a low malignant potential (LMP) tumor, is a distinct yet heterogeneous group of tumors defined by their histopathology as atypical epithelial proliferation without stromal invasion. Our case was diagnosed as a borderline Brenner tumor. The patient was followed up for four years with no evidence of recurrence or metastasis and then was lost to follow-up.

Patients that are diagnosed with borderline or malignant Brenner tumors should undergo surgical excision. However, research and guidelines for neoadjuvant or adjuvant chemotherapy are greatly under-researched. Therefore, patients with borderline or malignant features should be counseled extensively on the risk and benefits of chemotherapy. Fortunately, less than 5% of Brenner tumors have been found to be malignant.[12] Anytime a physician uses the word 'tumor,' it is reasonable for the layperson to feel alarmed. Although this diagnosis is, in fact, a tumor, there is a great deal of value in reassuring patients that they are not suffering from malignancy. Reminding patients that they did not cause this finding and that there is no familial relationship is important as well.

Currently, there are no published reports of a concrete etiologic cause for the Brenner tumor. This case report serves as an addition to published reports of borderline Brenner tumors and their presentation and prognoses, along with important differential diagnoses to consider before, during, and after treatment. Our study may contribute to the awareness of the Brenner tumor and thus minimize patients' fear of an ovarian cancer diagnosis neuroendocrine markers. Lastly, squamous cell carcinoma has high levels of keratinization and high-grade cytological features.[1]

The pathogenesis of BT has not been clearly detailed. Although BTs demonstrate transitional-type differentiation as is seen in bladder and ureters, most reports favor that these tumors do not originate in the while also reducing the number of unnecessary laparotomies and extensive surgical procedures, especially in young patients. We hope that this report raises awareness of borderline Brenner tumors and that continued investigation drives further development of efficacious diagnosis and safe treatments for improving patient outcomes.

Figures:

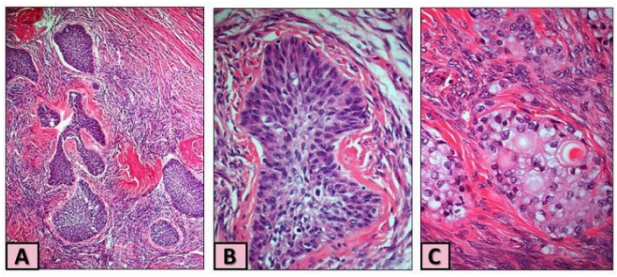

Figure-1: Histopathological features of the tumor

1A: Low power view showing sharply demarcated uniform and focally papillary islands of epithelial cells in a dense fibro collagenous stroma (H&E stain X 20)
1B: Medium power view showing uniform round ovoid nuclei, some with grooves resembling coffee beans, with fine chromatin, punctate nucleoli in a background of pale cytoplasm, and scattered calcification (H&E stain X40)
1C: High power view showing squamous metaplasia and focal mucinous material within some nests (H&E stain X60)

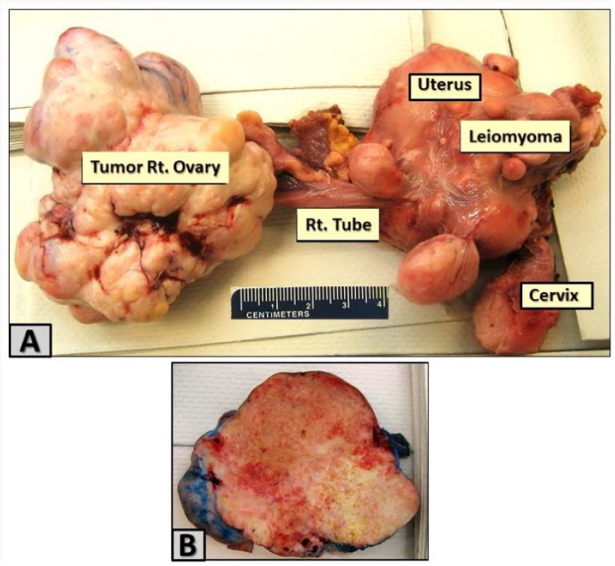

Figure-2: Hysterectomy with bilateral salpingo-oophorectomy
2A: Surgical excision including cervix, uterus, fallopian tubes, and both ovaries with right ovary tumor
2B: The cut section surface of the tumor shows solid, pick, tan, and yellow changes with prominent calcification and areas of focal cystic changes.

Submitted: June 2nd, 2022 | **Accepted:** July 6th, 2022 | **Published:** July 21th, 2022

***Corresponding author:** Hannah Pulido*, Department of Pathology, American University of the Caribbean School of Medicine, Email: hannahleahpulido@gmail.com

Citation: Pulido H, Ammons M, Bakri R, Kimbrough B, Elder Z, Cruz J, Forte N, and Aziz M, (2022) Borderline Brenner Tumor of the Ovary: Case Report and Review of the Literature. MOH Journal of Medical Case Reports, 1(1), 1-5.

Acknowledgements:

Special thanks to Meha Munir, Christina Rolquin, and Victoria DeTrolio, MD candidates at the American University of the Caribbean, for their assistance in preparing manuscript images and reviewing the final manuscript.

References:

1. Balasa RW, Adcock LL, Prem KA, Dehner LP. The Brenner tumor: a clinicopathologic review. Obstetrics and gynecology. 1977 Jul 1;50(1):120-8.
2. Brenner T. Das oophoroma folliculare. Frankfurt Z Pathol. 1907;1:150.
3. Dougherty D, Onyemkpa C, Engel M, Oyasiji T. A case report of an incidental Brenner tumor found after resection of a large ovarian mucinous neoplasm. International journal of surgery case reports. 2018 Jan 1;49:40-3.
4. Gaur JH, Hassan MJ, Elahi AA, Khetrapal S, Khan S, Jetley S. Synchronous benign Brenner's tumor of ovary with leiomyoma and endometrial adenocarcinoma in a postmenopausal female. Journal of Cancer Research and Therapeutics. 2019 Oct 1;15(6):1418.
5. Pathology Outlines. Brenner tumor. https://www.pathologyoutlines.com/topic/ovarytumorb9brenner.html. Accessed March 19th, 2022.
6. Moon WJ, Koh BH, Kim SK, Kim YS, Rhim HC, Cho OK, Hahm CK, Byun JY, Cho KS, Kim SH. Brenner tumor of the ovary: CT and MR findings. Journal of computer assisted tomography. 2000 Jan 1;24(1):72-6.
7. Ruggiero S, Ripetti V, Bianchi A, La Vaccara V, Alloni R, Coppola R. A singular observation of a giant benign Brenner tumor of the ovary. Archives of gynecology and obstetrics. 2011 Aug;284(2):513-6.
8. A Asher N, Chan M, Leonard S, Rountree C, Aziz M (2020) Metastatic Ovarian Granulosa Cell Tumor to the Clavicle Bone Twenty Years After Primary Diagnosis: A Case Report and Literature Review. JSM Clin Cytol Pathol 2020 Aug 2(3): 4.
9. Ali RH, Seidman JD, Luk M, Kalloger S, Gilks CB. Transitional cell carcinoma of the ovary is related to high-grade serous carcinoma and is distinct from malignant brenner tumor. International journal of gynecological pathology. 2012 Nov 1;31(6):499-506.
10. Lang SM, Mills AM, Cantrell LA. Malignant Brenner tumor of the ovary: Review and case report. Gynecologic oncology reports. 2017 Nov 1;22:26-31.
11. Weinberger V, Minář L, Felsinger M, Ovesná P, Bednaříková M, Číhalová M, Jandáková E, Hausnerová J, Chaloupková B, Zikán M. Brenner tumor of the

ovary—ultrasound features and clinical management of a rare ovarian tumor mimicking ovarian cancer. Ginekologia Polska. 2018;89(7):357-63.

12. Zhang Y, Staley SA, Tucker K, Clark LH. Malignant Brenner tumor of the ovary: Case series and review of treatment strategies. Gynecologic Oncology Reports. 2019 May 1;28:29-32.