

Computed tomography imaging features of benign ovarian Brenner tumors

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Abstract. The present study aimed to describe the computed tomography (CT) imaging features of ovarian Brenner tumor for diagnostic accuracy and disease understanding. The CT imaging features of 9 cases of ovarian Brenner tumor confirmed by surgery and pathology were retrospectively analyzed and compared. Of the 9 cases of ovarian Brenner tumor, 3 were right located and 6 were left located with clear borders; 7 with round or oval shapes, while 2 were with irregular and lobulated morphology; 5 solid lesions presented with multiple scattered calcification shadows inside with moderate enhancement, while 3 cystic lesions were presented with mixed solid and cystic composition, and significant enhancement was identified in the solid component, but not in the cystic component. Furthermore, papillary projections inside and mild nodular enhancement were observed in one case of cystic lesion. The pathological analysis demonstrated that an epithelium nest composed the tumors with urothelial like cells and fibrous matrix. Of the 9 cases, 5 epithelial nests exhibited adeno-like cystic lumen without cell mitosis phase. All cases were diagnosed with benign ovarian Brenner tumor. Specific CT imaging features of ovarian Brenner tumor can be identified and pathological examinations are required for diagnosis confirmation.

Introduction

Brenner tumors are uncommon surface epithelial-stromal tumors of the ovary, frequently presented in women between their fifth and seventh decades of life. The majority of Brenner tumors are benign, and these tumors predominantly present as solid on imaging and pathological examination, although in <30% of cases, serous and mucinous-associated cystadenomas may account for the cystic appearance when the Brenner tumor

itself is very small or visually inseparable from the coexisting cystic neoplasm (1). There is little information regarding their appearance on computed tomography (CT) examination (1,2). Although ovarian tumors have similar clinical and radiological features, predominant or specific imaging features may be present in certain types of ovarian tumors. Characterization of an ovarian mass is of the utmost importance by CT in the preoperative evaluation of an ovarian neoplasm (3). It enables the surgeon to anticipate carcinoma of the ovary prior to surgery so that adequate procedures are planned. Therefore, familiarity with the clinical and imaging features of various ovarian tumors is important in determining the likelihood of a tumor being benign or malignant. The aim of the present study was to describe the clinical and CT characteristics of Brenner tumors.

Materials and methods

Patients. Patients with a histological diagnosis of a Brenner tumor of the ovary who had undergone preoperative CT examination prior to surgical removal of the mass between June 2003 and December 2012 from the clinical databases of the Department of Obstetrics and Gynecology, Huzhou Central Hospital (Huzhou, China) were retrospectively analyzed. The study protocol was approved by the Institutional Review Board of Ethics Committee of Huzhou Central Hospital and written informed consent was obtained from all the patients.

CT examinations. CT examinations were performed with Toshiba Aquilionor (Toshiba Medical Systems, Otawara, Japan) or Philips Brilliance 16-slice CT scanners (Philips Medical Systems, Amsterdam, The Netherlands). All patients were placed in the supine position and given an appropriate amount of water to drink to fill the bladder prior to the scan. The CT scan covered the entire primary lesion from the ilium attachment and ischial tuberosity attachment, and the scan range was adjusted according to the lesion size in certain cases. Contrast-enhanced CT images were obtained following the injection of 80-100 ml of a nonionic iodinated contrast material at a concentration of 370 mg/ml [iopamidol (Iopamiron 370; Bayer AG, Leverkusen, Germany)] or 300 mg/ml [iohexol (Omnipaque 300; Daiichi-Sankyo Health Care, Tokyo, Japan)] at a rate of 2.5-3.0 ml/sec. The parameters of the CT scan were 120-150 kV, 120 mAs, slice thickness of 1.0-2.0 mm. Arterial and venous phase images were obtained during 25-30 sec and 65-80 sec delay, respectively.

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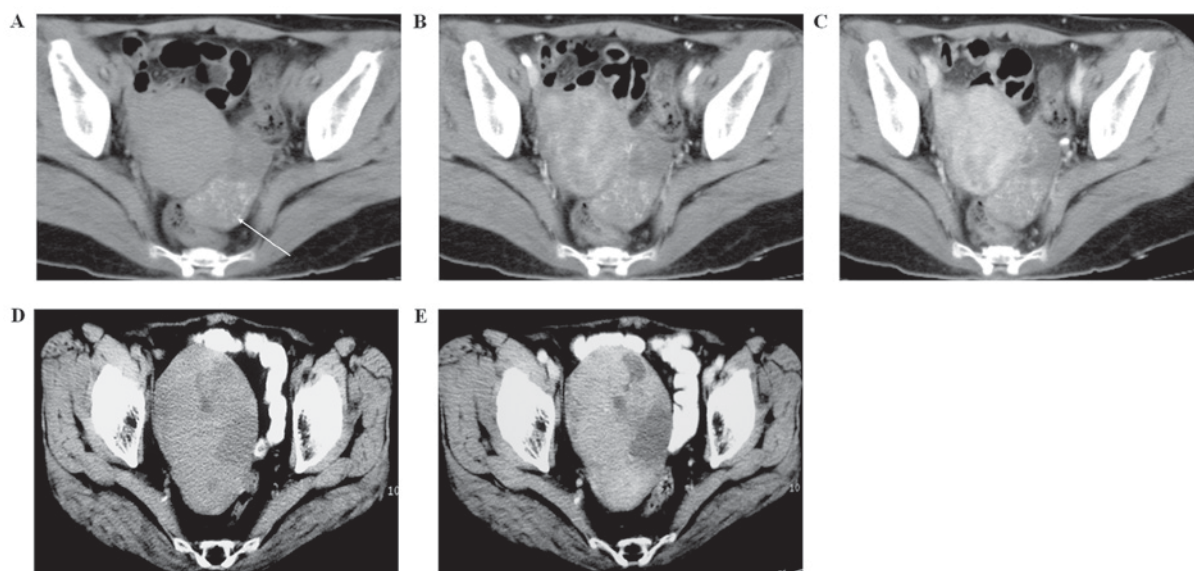


Figure 1. Bilateral ovarian Brenner tumor. (A-C) Left ovarian Brenner tumor. Round-like solid mass with clear border and multiple scattered amorphous calcification focus inside (indicated by the arrow). Moderate enhancement was observed following contrast medium administration. (A) Plain scan; (B) Arterial phase following enhancement; (C) Venous phase following enhancement. (D,E) Right ovarian Brenner tumor. Mass with cystic solid changes and oval shape. Moderate enhancement was observed following contrast medium administration in the solid part, but not in the cystic mass. (D) Plain scan; (E) Enhanced scan.

Table I. Clinical features of the 9 cases of ovarian Brenner tumor.

Characteristics	No. of patients (n=9)
Postmenopausal	2
Postmenopausal bleeding	2
Abdominal swelling pain	2
Uterine leiomyomas	3
The mean age of patients was 57.2 years (range, 24-80 years).	

Pathological examination. Pathological samples were stored in 4% paraformaldehyde solution at 4°C overnight, dehydrated through a series of graded ethanol solutions (70, 90, 95 and 100% ethanol and each for 5 min at room temperature), cleared in xylene (3 times for 5-10 min each), embedded in paraffin and cut into 5 μ m thickness sections. Sections were then stained with hematoxylin (1% w/v; 1-2 min at room temperature) and eosin (0.5% w/v; 2-5 sec at room temperature) for general examination under a Leica microscope (Leica DMI3000 B; Leica, Solms, Germany; x100 magnification). All the pathological sections were reviewed by a senior pathologist for diagnosis confirmation. The following histological parameters were recorded on the basis of histological analysis and review of the original pathologic reports: Gross configuration (solid or cystic); tumor size (in centimeters); gross tumor color; microscopic calcifications; and the presence of coexisting ovarian neoplasms or tumor-like lesions.

Results

Patient demographical data. Details of the demographical data of these 9 patients are listed in Table I. The mean age of patients

were 57.2 years, range, 24-80 years. The clinical manifestations were as follows: 2 cases were postmenopausal and presented with irregular vaginal bleeding; 2 cases presented with abdominal swelling pain; 3 cases exhibited uterine leiomyomas; and 2 were detected at the time of physical examination.

Clinical features of ovarian Brenner tumors. All 9 cases of ovarian Brenner tumor were unilateral lesions with clear borders (Table II). Among these cases, 3 were located to the right and 6 were located to the left. Seven cases presented with round- or oval-shaped tumors, and 2 cases presented with irregular- and lobulated-shaped tumors. The largest and smallest size of lesions was 8.1x7.2x3.2 and 1.5x1.2x0.8 cm, respectively, and the mean size was 4.3 cm. Upon morphological analysis, 2 cases presented with uterine enlargement and endometrium thickening, 3 were combined with uterine leiomyomas, 1 with uterine leiomyomas and endometrium thickening, 2 combined with an adeno-cystic mass, and 1 combined with an ovarian cyst.

CT manifestation. The masses were classified according to the cystic and solid ratio inside the lesion as follows: i) 5 cases were solid mass (Fig. 1). A small amount of low-density necrosis region was observed inside the lesions. Multiple scattered or dot-like calcification with evident enhancement was observed in 3 cases of lesions. ii) Cystic-solid lesion in 3 cases (Fig. 1). Similar ratios of the cystic and solid component were observed in these cystic-solid mixed lesions. The CT value of the cystic part was 18-20 HU and no enhancement was identified following contrast medium administration, whereas moderate enhancement was observed in the solid part. iii) Cystic lesion in 1 case (Fig. 2). The CT manifestations included single cystic lesion with papillary projections and slight enhancement was observed following contrast medium administration. The detailed CT features of each case of ovarian Brenner tumor are listed in Table II.

Table II. Detailed clinical features and computed tomography manifestation of the ovarian Brenner tumor.

Patient no.	Age (years)	Location	Morphology	Size (cm)	Type	CT value of the solid mass (HU)			Calcification	Comorbidity
						Plain scan	Arterial	Venous		
1	54	Left	Oval	6.5x5	Solid	55	64	73	Multiple and scattered shape	Intramural and subserous uterine leiomyomas combined with adenomyosis
2	51	Right	Round	1.5x1.2x0.8	Solid	48	67	86	None	Uterine leiomyomas
3	80	Left	Oval	6x5x4.5	Solid	50	89	90	Dot-like shape	Intramural leiomyomas, post menopausal endometrial hyperproliferation response
4	48	Left	Lobulated	4.5x3.8x2.7	Solid	53	75	83	Multiple and scattered shape	Uterine adenomyosis and endometrial hyperplasia
5	81	Right	Oval	8.1x7.2x3.2	Cystic-solid	56	80	91	Dot- and disk-like shape	Endometrial hyperproliferation response
6	41	Left	Oval	6.1x5.3x4.7	Cystic-solid	46	68	73	None	Left ovarian mucinous cystic adenoma
7	24	Right	Lobulated	3.7x2.2x2.0	Cystic-solid	52	69	78	Dot-like shape	Ovarian simple cyst
8	66	Left	Oval	7.5x3.2x4.4	Cystic	30	38	60	None	Right ovarian mucinous cystic adenoma
9	70	Left	Oval	6.2x4.2x3.8	Solid	45	63	81	None	Intramural uterine leiomyomas combined with adenomyosis

HU, Hounsfield unit.

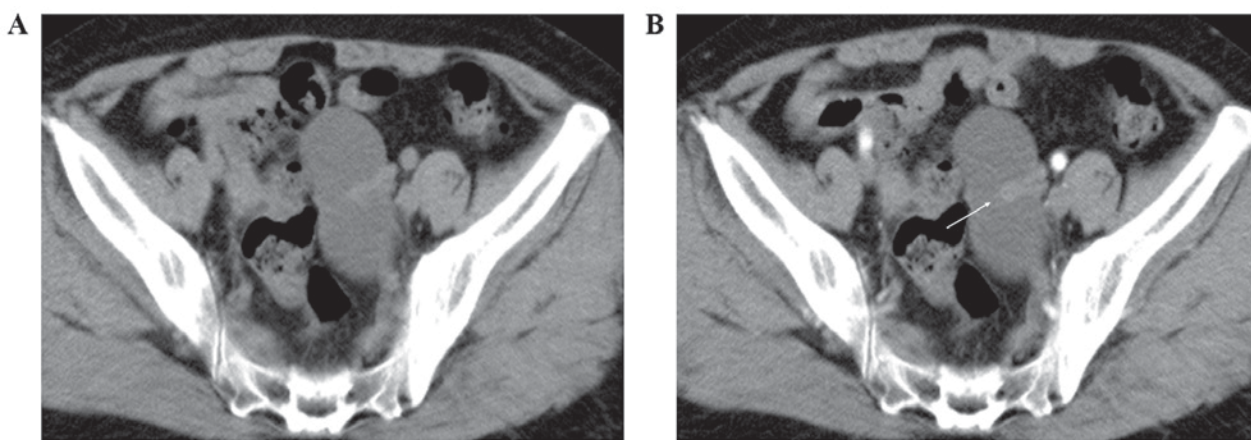


Figure 2. Left ovarian Brenner tumor. Single cystic foci with papillary projections inside and mild nodular enhancement was observed following contrast medium administration (indicated by the arrow). (A) Plain scan; (B) Enhanced scan.

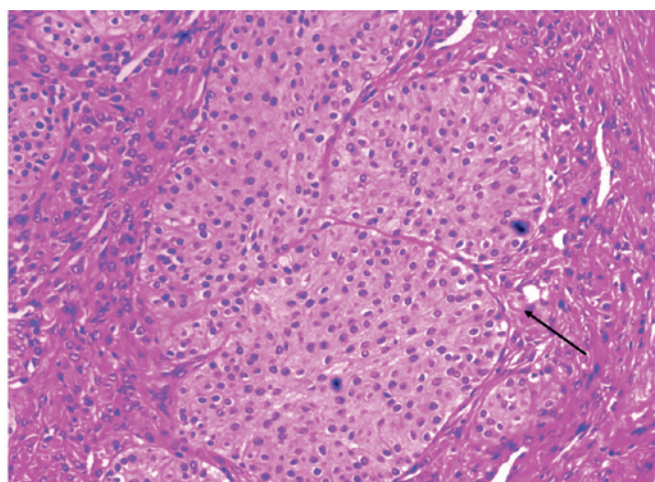


Figure 3. Pathological analysis of a case of ovarian Brenner tumor. Under the microscope, the tumor was identified as urothelial-looking cells composed by an epithelium nest and fibrous stroma. The epithelial nest was merged and closely located to the tumor, exhibiting solid properties and lacking a mesenchyme (indicated by the arrow) (100x magnification).

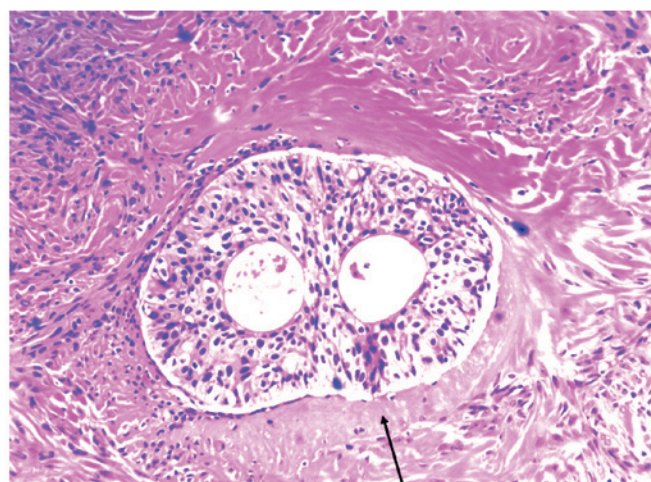


Figure 4. Pathological analysis of a case of ovarian Brenner tumor. Part of the epithelial nest exhibited adeno-like cystic lumen in the center and light pink-stained objects were observed inside the lumen (indicated by the arrow). A clear border without cell mitosis or mesenchyme infiltration was observed on the epithelial nest (100x magnification).

Post-operation pathology features. The post-operation pathology features of the 9 Brenner tumors were as follows: 9 cases with an intact capsule and smooth surface; 5 cases with a hard texture solid mass; 3 with a tenacious solid mass; and 1 with a soft cystic lesion. The cross-section of the mass revealed gray-white or gray-red coloring, and calcification with a gritty texture was observed in some of the mass. Furthermore, different degrees of cystic change and necrosis were observed in these masses. Water- or jelly-like translucent mucous with a coffee-colored cystic liquid and a smooth cystic wall was observed inside the cystic or cystic-solid mass. Furthermore, nodular or papillary projections were observed inside the inner wall of the cystic lumen.

The microscopic observation revealed that the Brenner tumors were epithelial cell nests composed by transitional urothelial-like cells and fibrous stroma, and close or merged epithelial nests with a limited amount of mesenchyme were observed in some of the regions. The epithelial nest exhibited various morphologies, the majority of which were of solid

composition (Fig. 3). Sieve and adenoduct-like morphologies were observed in the center of certain epithelial nests and 5 cases of nests demonstrated an adeno-like lumen (Fig. 4). No nuclear mitosis or mesenchyme infiltration was observed in any case and the histological diagnosis confirmed benign Brenner tumor in all cases.

Discussion

Brenner tumors are uncommon epithelial-stromal tumors that originate from the surface of the ovaries (4) and were first described in detail by Fritz Brenner in 1907 (5). Histologically, Brenner tumors exhibit epithelial cell nests growing in a fibrous stroma (6). These epithelial cells have the similar appearance to urothelial cells, and therefore Brenner tumors were classified as a transitional cell tumor type by the World Health Organization. Brenner tumors are divided into three primary types, including benign, borderline and invasive. Benign Brenner tumors may be found in women of any age,

but are predominantly seen in women aged ~50 years old, while women with borderline or malignant Brenner tumors are typically 10 years older (7). The mean age of patients who participated in the present study was 57.2 years, and all cases were benign Brenner tumors. Almost all Brenner tumors are asymptomatic and discovered by accident. In ~30% of cases, a second tumor is identified in the same ovary, most often a serous or mucinous cystadenoma, or occasionally a teratoma (5,7,8). In the present study, 3 cases were identified with coexisting uterine leiomyomas, 2 with abdominal swelling pain and 2 with postmenopausal irregular bleeding. The post-operative histological examination confirmed 2 cases with differing degrees of endometrium thickening, 3 with uterine leiomyomas, 1 with uterine leiomyomas and endometrium thickening, 2 with ovarian cystadenoma, and 1 with ovary cysts. To the best of our knowledge, no literature has reported an association between ovarian Brenner tumors and coexisting comorbidities. Patients that also present with pleural fluid and ascites are said to have Meigs' syndrome (9). Ovarian Brenner tumors combined with Meigs's syndrome are a common tumor types. Here, no case was identified with pleural fluid and ascites, which was attributed to the limited number of cases investigated.

The CT manifestations of Brenner tumor include adnexal solid or solid-cystic, or cystic masses with a clear border, amorphous in appearance, with round, oval, irregular or lobulated morphologies. Benign Brenner tumors are typically small solid tumors with small cysts (10). Furthermore, grossly visible amorphous calcifications in the solid mass with mild or moderate enhancement are typical CT manifestations. Histologically, minimal cystic changes, necrosis and varying degrees of calcium crystal are often identified in the solid mass (11). In the current study, 5 cases had solid masses, of which 2 were with multiple scattered calcification and 1 with dot-like calcification. In addition, 3 cases were with evident enhancement and 1 with mild enhancement. According to the aforementioned description, borderline or invasive Brenner tumors are characterized by the presence of solid-cystic or cystic structures with papillary structures, and mild or moderate enhancement in the solid mass. In a study by Wang *et al* (12), ovarian Brenner tumors were described as typically unilateral and often accompanied by other tumor components, such as solid tissue in ovarian cancer. When a tumor is of uniform component, the CT imaging often reveals a homogeneous solid tumor with homogeneous or heterogeneous density.

When a tumor is accompanied by other tumor components, it may be solid-cystic or cystic and has partial calcification. Following enhancement, a benign Brenner tumor is slightly enhanced, while the borderline of the Brenner tumor is moderately/highly enhanced. In the present study, following the pre-surgery histology, 3 cases were confirmed as cystic-solid mass, of which 2 were borderline tumors and 1 was an invasive tumor. According to the post-surgery histology, epithelial nest with an intact border had no heterogeneous cell or mesenchyme infiltration. Furthermore, a cystic mass with a papillary nodular shadow (1/9 cases) was revealed on the CT scan. We hypothesized that the residue cystic or necrosis tumor resulted in an artifact shadow, thereby generating a papillary nodular shadow. We concluded that CT scans combined with

a histology should be performed when diagnosing Brenner tumors. The observations of the current study are consistent with the previous description by Wang *et al* (12). Generally, malignant tumors should be considered when a cystic mass of the ovary with enhanced solid nodules is present (13); however, Brenner tumors do not adhere to this rule. Furthermore, the possibility of a Brenner tumor should be considered when there is the presence of combined dot-like calcifications in a cystic-solid lesion. The main CT manifestations of Brenner tumors were as follows: A solid mass in a small sized tumor; cystic-solid mass with multiple cystic changes during tumor growth; and single cystic lesions with a solid border when the presence of increasing degree of cystic changes, necrosis and septa destroy.

The differential diagnosis of Brenner tumor includes fibroma, cystoadenocarcinoma, Krukenberg tumor and leiomyomas. Fibroma presents as a homogeneous solid mass with a smooth border and minimal enhancement, but occasionally involves cystic changes and necrosis calcification (3). Cystoadenocarcinoma presents as an adnexal cystic-solid mass with an unclear border and cystic-solid borderline, an unequally thickened cystic wall with multiple nodules and septa, and is usually accompanied by peritoneal lumen implantation metastasis (14). Krukenberg tumors are usually bilateral with additional findings of primary malignancy, and frequently accompanied by abdominal and pelvic effusion or metastasis (15). Leiomyomas present with a limited amount of dot- or eggshell-like calcification with a similar degree of enhancement as Brenner tumors (16). Furthermore, the difference of blood supplies may be detected between Brenner tumor and leiomyomas (17).

In conclusion, the present study demonstrated that the CT features of benign ovarian Brenner tumors include multiple, scattered calcification focused in the solid component, and we propose that histological examination is necessary. These results aid in improving the understanding of the clinical manifestation, histological and CT features of ovarian Brenner tumors, which may aid in its diagnosis.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

YZ and XM conceived and designed the study; YZ, XM and LY performed the study; YZ, XM LY and JS analyzed the data; YZ and LY contributed reagents/materials/analysis tools; YZ, XM, LY and JS contributed to the writing of the manuscript; XM and JS gave the final approval of the version to be published.

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board or Ethics Committee and written informed consent was obtained from all the patients.

Consent for publication

Written informed consent was obtained from all the patients for the publication of their data.

Competing interests

The authors declare that they have no competing interests.

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