

Ultrasonographic and clinicopathologic features of benign Brenner tumors of the ovary*

Shuyu Wang (✉), Xiaomei Zhou

Department of Ultrasound, Zigong First People's Hospital, Zigong 643099, China

Abstract

Objective The aim of this study was to summarize and analyze the ultrasonographic and clinicopathologic features of benign brenner tumors of the ovary.

Methods Forty-six patients with brenner tumors of the ovary were included, and the imaging and pathologic features of the tumors were analyzed.

Results Thirty-eight cases were unilateral, while eight cases were bilateral. The tumors were located only in the left ovary in 32 patients and in the right ovary in six patients. The median diameter of the tumors was 62 mm, and the diameter ranged from 15 to 270 mm. Vascular tumors were not observed. Most of the tumors (22/46) showed micro-perfusion, while 16 tumors showed no blood flow signal. Acoustic signal shadows after the cysts were observed in 26 tumors, accounting for 57% of all brenner tumors. Fourteen patients showed unilocular or multilocular tumors with no distinct characteristics on ultrasonography. Sixteen masses showed a multilocular solid structure, accompanied by calcification and a post-mass shadow; the solid structure showed mild-to-moderate vascularization on Doppler examination. Sixteen masses showed a pure solid structure, accompanied by calcification, resulting in an acoustic shadow behind the tumor; the solid structure showed mild-to-moderate vascularization on Doppler examination.

Conclusion Some ultrasonographic features, including calcification with shadow, poor blood circulation of solid components, and mass localization, are helpful in the diagnosis of benign brenner tumors.

Key words: brenner tumor; ovary; clinicopathologic features

Received: 11 November 2021
Revised: 10 December 2021
Accepted: 28 December 2021

Brenner tumors are a type of ovarian epithelial tumor first reported by Fritz *et al.* in 1907. They often occur in women aged 50–70 years [1]. Brenner tumors are benign transitional cell tumors of the ovary but have the potential for malignancy. They account for approximately 3% of all ovarian epithelial tumors [2]. Careful histologic examination should be performed in clinics to exclude small malignant tumors that may involve brenner tumors [3]. Benign brenner tumors lack specific clinical symptoms and are mostly detected incidentally during routine physical examination or ultrasonography. Borderline and malignant brenner tumors can manifest as abdominal pain, vaginal bleeding, urinary retention, and ascites [4] owing to maladjustment of estrogen levels. Complete preoperative ultrasonography is important for differentiating between benign and malignant adnexal tumors and formulating further treatment plans. However, although the International Organization for Ovarian Tumor Analysis

has formulated imaging standards for detecting ovarian cancer, the ultrasonographic features of brenner tumors overlap with those of typical ovarian cancer, causing serious difficulties in image interpretation [5]. Therefore, this study retrospectively analyzed and summarized the ultrasonographic and clinicopathologic features of histologically confirmed benign brenner tumors in our hospital to provide a basis for the ultrasonographic diagnosis of affected patients.

Materials and methods

Study subjects

Forty-six patients with brenner tumors of the ovary treated in our hospital between January 2002 and January 2021 were included in the study. The inclusion criteria were as follows: (1) abnormal ovarian ultrasonographic findings with or without elevated CA125 levels

✉ Correspondence to: Shuyu Wang. Email: taoyoujianghwy@163.com

*Supported by a grant from the Medical Research Project of the Sichuan Medical Association (No. s19332).

© 2022 Huazhong University of Science and Technology

and nonspecific abdominal symptoms; (2) ovarian abnormalities detected for the first time; (3) history of surgical treatment; and (4) benign brenner tumor diagnosed on postoperative histopathology. Baseline data, such as age at diagnosis, menopause, serum CA125 level, risk of malignancy index, clinical symptoms, and histologic findings, were collected from the electronic medical record system of our hospital. The average age of the 39 patients was 43.6 ± 7.8 years, including 5 patients with lateral ovarian mucinous cystadenoma, four with hysteromyoma, four with ovarian serous cystadenoma, two with adenomyosis, and one with endometrial polyp. Only seven patients had elevated serum CA125 levels, and the median CA125 level was 19 IU/L.

Instruments and methods

Prior to the examination, the patients were asked to empty their bladder and take the lithotomy position. The Mairui DC_ Type 8 color Doppler ultrasound diagnostic instrument and transvaginal (5–8 MHz) and transabdominal probes (3.5–5 MHz) were used. The uterus, pelvic cavity, and bilateral attachments of the patients were carefully scanned through the vagina, and patients with large tumors were scanned repeatedly using a transabdominal probe. The scanning focused on the size, boundary, envelope, relationship with surrounding tissues, internal echo, and blood flow of the masses.

Results

Histologic examination

Microscopically, the tumors were composed of well-defined and uniform epithelial islands located in dense fibrous stroma. The epithelial cells had characteristic coffee bean-like nuclei with longitudinal grooves and a pale cytoplasm (Fig. 1).

Ultrasonographic examination

Thirty-eight (82.7%) tumors occurred in the unilateral ovary and eight in the bilateral ovaries. Brenner tumors were diagnosed simultaneously. Two patients had ascites; their serum CA125 level increased, and no pleural effusion was found. The tumors were located only in the left ovary in 32 patients and in the right ovary in six patients. The median diameter of the tumors was 62 mm, with the diameter ranging from 15 to 270 mm, and the diameter of the largest solid structure was 40 mm (range: 0–85 mm). Thirty-six tumors contained solid components (Fig. 2a and 2b), and only 14 (30%) tumors contained pure cystic components. The cystic fluid was anechoic in 28 patients (Fig. 2c) and hypoechoic in two patients. The Doppler color signal was between NO and moderate, and no rich vascular tumors were found. Acoustic signal shadows after the cysts were observed in 26 tumors (Fig.

2d).

Difference between the ultrasonographic and clinical diagnoses

The tumors in 14 patients were unilocular or multilocular without distinct characteristics on ultrasonography and were correctly diagnosed as benign masses. Sixteen masses showed a multilocular solid structure, accompanied by calcification and a post-mass shadow; the solid structure showed mild-to-moderate vascularization on Doppler examination. Sixteen masses showed a pure solid structure, accompanied by calcification resulting in an acoustic shadow behind the tumor; the solid structure showed mild-to-moderate vascularization on Doppler examination. At the first diagnosis, the doctors performing the ultrasonography misdiagnosed four cases of benign brenner tumors as malignant. The median diameter of the four brenner tumors was 96 mm, and the maximum diameter was 270 mm, which was generally greater than the median

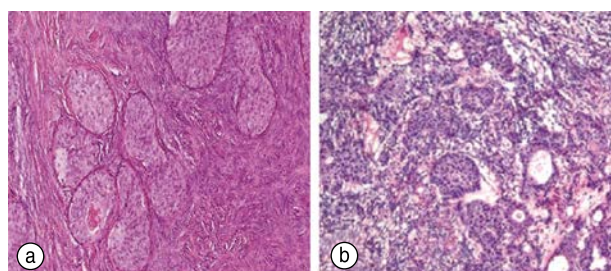


Fig. 1 Microscopic view of a benign Brenner tumor. (a) Large nuclei (HE staining $\times 200$); (b) Interstitial fibrous hyperplasia of the tumor (HE staining $\times 400$)

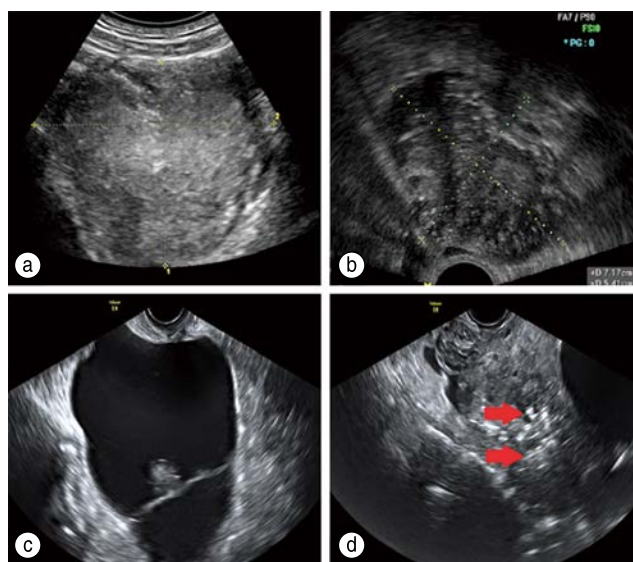


Fig. 2 Ultrasonographic features of a brenner tumor. (a, b) The tumor body contains solid components; (c) There is no echo in the cystic fluid of the tumor; (d) Post-cyst signal shadow



Fig. 3 Ultrasonographic image of a brenner tumor misdiagnosed as a malignant tumor

diameter of all tumors. Further, all four brenner tumors contained anechoic cystic components (Fig. 3).

Discussion

Brenner tumors usually occur in postmenopausal women, and most patients have no symptoms. Although the imbalance of estrogen activity can manifest as vaginal bleeding, only five patients in this study had abdominal pain or ascites, and the proportion of symptomatic patients was very low. Ovarian masses and elevated serum CA125 levels usually suggest malignant processes in postmenopausal women^[6]. Studies have evaluated the correlation between the CA125 level and malignancy of ovarian tumors and found that the detection of tumor marker CA125 alone is not suitable for distinguishing between benign and malignant adnexal masses^[7]. In this study, only two patients had elevated serum CA125 levels.

Dierickx *et al.* reported that experienced ultrasonography doctors failed to describe the unique ultrasonographic features of brenner tumors, and no other studies found unique images of brenner tumors^[8]. Many benign brenner tumors show a complete solid structure on ultrasonography, while some may show cystic components, with or without a solid structure. In our study, color Doppler imaging showed poor vascularization of the solid components. In the literature, the calcification rate of brenner tumors based on ultrasonographic findings is approximately 50%. Researchers have found calcification in 15 patients with benign brenner tumors and 13 other patients on ultrasonography^[9]. In this study, 32 brenner tumors containing solid components showed a sound shadow caused by calcification. Therefore, we conclude that the multiple calcifications observed on ultrasonography may be a key feature in the diagnosis of brenner tumors.

The laterality of brenner tumors varies greatly in different studies^[10]. In this study, 82% of the brenner tumors occurred on the left side of the ovary. This is consistent with the findings reported by Dierickx *et al.*, indicating that brenner tumors are more common in

the left ovary than in the right ovary. Only 18% of the brenner tumors in this study were bilateral; this rate is slightly higher than the range reported in the literature (5–14%)^[11]. Brenner tumors are often associated with the risk of a second ovarian tumor. It has been reported that 30% of brenner tumors can be accompanied by other ovarian tumors. In this study, there were 13 patients with benign tumors, 5 patients with lateral ovarian mucinous cystadenoma, 4 patients with hysteromyoma, and 4 patients with ovarian serous cystadenoma. The sonogram of a brenner tumor can show a cystic, cystic solid, or solid mass. The cystic part can be separated, and blood flow signals can be detected during separation. The solid part is mostly hypoechoic, and the hypoechoic part is mostly accompanied by a strong echo formed by uncertain calcification, followed by attenuation. Brenner tumors have a certain misdiagnosis rate in most literature reports, which shows that it is difficult to distinguish between benign and malignant simple ovarian tumors on ultrasonography^[12].

The varying ultrasonographic features and low incidence of brenner tumors of the ovary make ultrasonographic diagnosis more difficult. There are no special ultrasonographic features that can characterize benign brenner tumors. However, it is worth noting that some ultrasonographic features, including calcification with shadow, poor blood circulation of solid components, and tumor location, may be signs of benign brenner tumors and even help experienced ultrasonography doctors to preliminarily determine the benign and malignant nature of lesions. However, this study was a single-center study with a small sample size. In the future, a multi-center study with a larger sample size may draw a more convincing conclusion.

Acknowledgments

Not applicable.

Funding

This study was supported by a grant from the Medical Research Project of the Sichuan Medical Association (No. s19332).

Conflicts of interest

The authors indicated no potential conflicts of interest.

Author contributions

Not applicable.

Data availability statement

Not applicable.

Ethical approval

Not applicable.

References

1. Tamás J, Vereczkey I, Tóth E, et al. Mixed ovarian tumor composed of Brenner tumor and adult-type granulosa cell tumor: a case report of a very rare mixed ovarian tumor and a review of the literature. *Int J Surg Pathol.* 2018;26(4):382-387.
2. Lin DI, Killian JK, Venstrom JM, et al. Recurrent urothelial carcinoma-like FGFR3 genomic alterations in malignant Brenner tumors of the ovary. *Mod Pathol.* 2021;34(5):983-993.
3. Pfarr N, Darb-Esfahani S, Leichsenring J, et al. Mutational profiles of Brenner tumors show distinctive features uncoupling urothelial carcinomas and ovarian carcinoma with transitional cell histology. *Genes Chromosomes Cancer.* 2017;56(10):758-766.
4. Simons M, Simmer F, Bulten J, et al. Two types of primary mucinous ovarian tumors can be distinguished based on their origin. *Mod Pathol.* 2020;33(4):722-733.
5. López MM, González PL, Domingo ÁG, et al. Tumor de brenner benigno asociado a tumor mucinoso borderline de ovario en paciente postmenopáusica. *Clínica e Investigación en Ginecología y Obstetricia.* 2021;48(2):156-160.
6. Bazot M, Thomassin-Naggara, Daraï E. CT and MR imaging of ovarian adenocarcinoma (serous/mucinous/endometrioid). *Ovarian Neoplasm Imaging.* 2013.243-262.
7. Stukan M, Badocha M, Ratajczak K. Development and validation of a model that includes two ultrasound parameters and the plasma D-dimer level for predicting malignancy in adnexal masses: an observational study. *BMC Cancer.* 2019;19(1):564.
8. Dierickx I, Valentin L, Van Holsbeke C, et al. Imaging in gynecological disease (7): clinical and ultrasound features of Brenner tumors of the ovary. *Ultrasound Obstet Gynecol.* 2012;40(6):706-713.
9. Patel-Lippmann KK, Sadowski EA, Robbins JB, et al. Comparison of international ovarian tumor analysis simple rules to society of radiologists in ultrasound guidelines for detection of malignancy in adnexal cysts. *AJR Am J Roentgenol.* 2020;214(3):694-700.
10. Ordóñez NG, Mackay B. Brenner tumor of the ovary: a comparative immunohistochemical and ultrastructural study with transitional cell carcinoma of the bladder. *Ultrastruct Pathol.* 2000;24(3):157-167.
11. He B, Gong S, Hu C, et al. Obscure gastrointestinal bleeding: diagnostic performance of 64-section multiphase CT enterography and CT angiography compared with capsule endoscopy. *Br J Radiol.* 2014;87(1043):20140229.
12. Buscail L, Bournet B, Cordelier P. Role of oncogenic KRAS in the diagnosis, prognosis and treatment of pancreatic cancer. *Nat Rev Gastroenterol Hepatol.* 2020;17(3):153-168.

DOI 10.1007/s10330-021-0533-3

Cite this article as: Wang SY, Zhou XM. Ultrasonographic and clinicopathologic features of benign brenner tumors of the ovary. *Oncol Transl Med.* 2022;8(3):146–149.