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► **To cite this version:**

P.-F. Montoriol, C. Hordonneau, C. Boudinaud, I. Molnar, C. Abrial, et al.. Benign Brenner tumour of the ovary: CT and MRI features. *Clinical Radiology*, 2021, 76 (8), pp.593-598. 10.1016/j.crad.2021.03.018 . hal-03346105

HAL Id: hal-03346105

<https://hal.science/hal-03346105>

Submitted on 2 Aug 2023

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Benign Brenner tumour of the ovary: CT and MRI features

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ABSTRACT

AIM: To evaluate the computed tomography (CT) and magnetic resonance imaging (MRI) features of benign Brenner tumours (BBT) of the ovary.

MATERIAL AND METHODS: This was a retrospective two-centre study comprising 35 female patients with a definitive diagnosis of BBT at histology in whom CT and/or MRI examinations had been performed were identified. Two experienced radiologists reviewed the CT and MRI features of 39 ovarian BBT retrospectively with consensus reading. The morphological appearance and size of each tumour were recorded. The

presence or absence of calcifications within the solid portion was noted at CT. The reviewed characteristics at MRI included qualitative assessment of the signal intensity of the solid portion on diffusion sequence and contrast enhancement, compared to that of the myometrium.

RESULTS: CT and MRI images were available for 27 and 28 lesions, respectively. Sixteen patients had both CT and MRI examinations. BBT were unilateral in 89% of patients, and 49% of lesions were solid and 51% were mixed. Calcifications were depicted at CT in 70.4% of lesions. When present, the cystic portion was multilocular in 85% of cases and corresponded to a mucinous lesion in 74% of cases. Enhancement of the solid portion at MRI was inferior or equal to that of the myometrium in 89% of cases and signal on high b-values diffusion images was deemed low or moderate in 93% of cases.

CONCLUSION: The combined CT and MRI findings of a unilateral fibrous ovarian mass containing punctate calcifications often associated with a multilocular cyst suggest the diagnosis of ovarian BBT.

INTRODUCTION

Initially described in 1907 by German pathologist Dr Fritz Brenner, Brenner tumours (BT) are uncommon epithelial ovarian lesions, accounting for 1–2% of all ovarian neoplasms. They are often incidentally discovered at surgery, pathology, or imaging in women between their fifth and seventh decades of life [1].

According to the latest World Health Organization classification of ovarian cancer [2], they are no longer known as “transitional cells tumours of the ovary,” but are now simply entitled “Brenner tumours”. Three subtypes are described: the benign Brenner tumour (BBT), which is by far the most common; the borderline form, also called

atypical proliferating Brenner tumour; and the malignant variant. Borderline and malignant forms are exceedingly rare as they account for <10% of Brenner tumour cases [3] and have a higher age range [1].

Histologically, they are composed of nests of epithelial cells resembling urothelium surrounded by a dense fibrous stroma. Foci of calcifications within the stroma have been reported in about 50% of cases [4]. BT are believed to derive from the ovarian surface epithelium that undergoes metaplasia; a more recent study raised evidence that BT may derive from the fallopian tube epithelium that has undergone transitional-type metaplasia and has seeded to the ovary [5].

On imaging and histopathology examination, Brenner tumours are predominantly solid, but purely cystic and mixed solid and cystic forms are described in cases of association to another surface epithelial lesion on the same ovary, mostly mucinous tumours, which can occur in up to 30% of cases [1]. Numerous case reports and a few larger studies have already reported the imaging features of Brenner tumours of the ovary in the English literature. The aim of the present study is to review the CT and MRI appearances of ovarian BBT on a larger population with a special focus on the presence of calcifications at CT, a feature that had been previously reported at ultrasound [6].

MATERIAL AND METHODS

Patients

This retrospective study was conducted in two tertiary referral hospitals (a university hospital and an anti-cancer institute). Study ethics approval was obtained on 30 March 2020 and informed consent was obtained from all included patients. A computerised search of the pathology records of both institutions from January 2008

to April 2019 was performed and allowed identification of 57 patients with a histological diagnosis of BBT of the ovary. A second search was then conducted on the picture archiving communication system (PACS) of both institutions to identify patients who underwent a computed tomography (CT) and/or magnetic resonance imaging (MRI) examination prior to surgery. Thirty-nine patients were recorded but four were excluded because of the absence of a measurable lesion at imaging. Eventually, 35 patients with 39 lesions in total were included. Sixteen patients benefited from both imaging techniques preoperatively. Twenty-eight lesions were evaluated at MRI and 27 lesions could be studied at CT. The patient flow diagram is illustrated in Fig. 1.

Imaging analysis

All CT and MRI images were interpreted in consensus by two radiologists with experience in gynaecological oncology imaging (9 and 6 years, respectively) with knowledge of the final histological diagnosis. Examinations were performed on various 1.5 or 3 T systems with heterogeneous protocols; however, for each patient, axial T2-weighted sequences, unenhanced T1-weighted sequences, and T1-weighted sequences following intravenous injection of gadolinium chelates were at least available.

For each lesion, the laterality, morphological appearance (i.e., cystic, solid, or mixed-solid and cystic) and largest dimension of the solid portion (representing the “true” Brenner tumour) were recorded. In cases of mixed lesions, the aspect of the cystic lesion was also noted (unilocular, multilocular, presence of papillary projections). When present, histopathology findings of associated lesions adjacent to the Brenner tumour were also notified.

At CT, the presence or absence of calcifications within the solid portion was noted. When present, calcifications were classified into two categories: coalescent or punctate .

At MRI, qualitative assessment of the signal intensity (low, moderate, high) on high b values diffusion-weighted imaging (DWI) sequence (b=700–1000 depending on the MRI system) and enhancement of the solid portion following intravenous injection of gadolinium chelates compared to that of the myometrium (inferior, equal or superior) was reported. In patients with previous inter-adnexal hysterectomy, appreciation of lesion enhancement and signal intensity on DWI images was not performed.

Statistical analysis

Statistical analysis was performed using the 3.6.1 version of the R software (R-Project, GNU GPL, <http://cran.r-project.org/>). Qualitative data are expressed as percentages. Quantitative data are shown as mean \pm standard deviation.

RESULTS

In total, 39 ovarian BBT were reviewed among the 35 included patients, with a mean age at diagnosis of 65 years (range: 31–91). Lesions were unilateral in 31 patients (89%) and bilateral in four (11%). CT and MRI images were available for 27 and 28 lesions, respectively. The mean size of the solid portion was 50 mm (range: 12–140 mm).

The overall morphological findings at imaging were an entirely solid mass in 49% of cases ($n=19$) and a mixed lesion in 51% ($n=20$). No case of entirely cystic BBT was encountered. When a cystic portion was present, it appeared as a unilocular cyst in

two cases (10%), a multilocular cyst in 17 cases (85%), and a multilocular cyst containing papillary projections in just one case (5%).

Pathological findings of associated cystic lesions on the same ovary were as follows: benign mucinous cystadenoma in 14 cases (70%), borderline mucinous cystadenoma in three cases (15%); in three cases, the cysts corresponded to a borderline serous cystadenoma (5%), Struma ovarii (5%), and paraovarian pseudocyst (5%). Overall, mucinous lesions represented 85% of all associated cysts in cases of mixed lesions and were found in 36% of all BBT.

Calcifications were seen at CT in 19/27 lesions (70%) and were classified as punctate in 89% of cases (17/19) and coalescent in 11% (2/19).

At MRI, diffusion sequence was available for 18 lesions but three patients with unilateral lesions had undergone hysterectomy. Thus, 15 lesions were eventually evaluated. Signal intensity on b=800 images was deemed low or moderate in 93% of cases (14/15) and high in just one case (7%). Gadolinium-enhanced T1 sequences were performed in all but one patient who benefited from MRI, but seven of them had a previous history of hysterectomy, one of them with bilateral lesions. Overall, enhancement at MRI was evaluated for 19 lesions and was deemed inferior or equal to that of the myometrium for 17 of them (89%) and superior in only two cases (11%).

DISCUSSION

General considerations

Even though ultrasound is often the first technique used for the exploration of female pelvis conditions, CT and especially MRI have long proven their efficacy in the characterisation of sonographically indeterminate adnexal masses [7, 8]. Very recently, a specific MRI score (Ovarian-Adnexal Reporting Data System Magnetic

Resonance Imaging or O-RADS MRI) has even been validated for risk stratification of adnexal masses [9].

Numerous case studies on BBT can be found in the English literature, most of them reporting incidental discovery at surgery, pathology, or imaging. A handful of studies, usually including a low number of patients, have also reported the imaging features of BBT at ultrasound [1, 6], CT [1, 10-12], and MRI [3, 10, 11, 13]. To the authors' knowledge, the present imaging-based study includes the largest BBT population to date. The average age of the present patients (65 years) is higher than that reported in some previous studies [1, 14, 15] but similar to some other results [1, 11]; however, the high rate of unilateral lesions (89% in the present study) seems to be a constant feature [11, 15].

Two types of morphological appearance were observed in the present study in almost the same proportion: an entirely solid mass (49% of cases) and a mixed lesion including a solid and a cystic portion (51%). Both entities have been reported in all available imaging studies. The solid and cystic appearance accounts for cases of Brenner tumours, representing the solid portion, coexisting with another epithelial cystic lesion. The association of Brenner tumours with mucinous cystadenoma is well known and is found in approximately 30–36% of cases of BT [1, 3, 14]. The present study showed similar findings with mucinous lesions (benign and borderline forms) found in 36% of BBT. In the study of Roma et al. [14], mucinous epithelium was even found in up to 47% of cases within the Brenner tumour, and a common origin of both components has been suggested, at least when these tumours occur on the same ovary [14].

An entirely cystic appearance had also been reported in one study at CT [11] but this feature concerned only two out of eight BBT and the analysis specified that it also

contained mural nodules with mild enhancement, which would have been classified as a mixed lesion in the present study. Therefore, entirely cystic BBT is a misleading entity as it is likely to represent a cystic epithelial neoplasm associated with a microscopic or infra-radiological Brenner tumour component.

To the authors' knowledge, diffusion imaging at MRI has only been studied in one case of malignant Brenner tumour [16]. Interestingly, in the latter article, the benign component within the tumour displayed low signal intensity on high b-values at DWI. A low to moderate signal intensity was noted at DWI for the majority of the lesions analysed in the present study (Fig. 2).

Similarly, no specific study has been conducted yet for evaluation of enhancement of BBT, especially at MRI. In the present study, enhancement at MRI was inferior or equal to that of the myometrium in all but two cases (Fig. 3). Both low signal on high b-values on diffusion images and mild enhancement following intravenous injection of gadolinium chelates are not surprising findings and simply reflect the dense fibrous stroma found in BBT, as reported in other ovarian fibrous tumours, such as fibromas/fibrothecomas or cystadenofibromas (CAF) [17-19]. Unfortunately, due to the lack of available data, no analysis was performed regarding the dynamic contrast enhancement (DCE) pattern of BBT. It would be interesting to perform a dedicated comparative study in the future.

One of the major objectives of the present study was to assess the presence at CT of calcifications within BBT, which were found at a significant rate (70%), mostly with punctate, scattered pattern (Fig. 4). This relatively high frequency has been specifically mentioned at CT and ultrasound in some previous studies, usually comprising a small number of patients, with reported rates ranging from 56–86% [1, 6, 10, 11, 20]. Even if calcifications are common in ovarian surface epithelial tumours

[4] and non-specific, they could represent a key imaging feature when present and in the appropriate setting, i.e., within a unilateral, fibrous ovarian tumour associated or with an ipsilateral cystic neoplasm and without signs of extra-ovarian extension (Fig. 5). As small calcifications are very hard to depict at MRI and CT does not accurately assess the fibrous nature of a solid mass, this study also highlights the importance of complementary imaging techniques for better characterisation of complex ovarian masses.

The main differential diagnosis that should be considered in cases of entirely solid BBT is ovarian fibroma or fibrothecoma (OF). These benign tumours belong to the category of sex-cord stromal tumours of the ovary and may secrete oestrogens. Ascites or pleural effusion may be present (Meigs's syndrome). OF also presents as a well-delineated, fibrous mass with low signal intensity on T2 images, no diffusion restriction, and poor blood supply [17, 21]. To the authors' knowledge, the presence of calcifications has not yet been investigated regarding these tumours; however, in the authors' experience, even if gross calcifications may be present in larger, degenerative forms of OF, they are uncommon.

Regarding the solid and cystic form of BBT, the differential diagnosis is mainly represented by CAF, which is an uncommon subtype of surface epithelial tumour of the ovary containing prominent fibrous stroma. The benign variant is the most frequent and typically presents as a multilocular cystic mass with a T2-dark signal intensity solid component containing small cystic locules, the other common aspect being a multilocular cystic mass with T2-dark signal diffuse or partial thickening of the cyst wall [22, 23]. Again, in available studies, the presence of calcifications within the solid portion of CAF has not been specified. In the authors' experience, in cases of BBT associated with a mucinous tumour, the BBT is mostly nodular in shape, as

opposed to a more “spiculate” appearance of the fibrous stroma of CAF, and this feature could enable differentiation of both entities.

There are several limitations to this study. First, its retrospective nature necessarily implies a selection bias. Second, as tertiary referral centres, the examinations reviewed are performed in other hospitals with various imaging systems, imaging protocols, and contrast media, which results in lack of homogeneity, especially regarding DWI sequences. On the other side, the present study is the first to report the BBT features at DWI in a significant population. Third, the present study was a qualitative, and therefore subjective, analysis of the DWI signal on high b-values at MRI; it would be interesting to conduct a study specifically focusing on the dynamic curves of BBT at DCE imaging and to compare apparent diffusion coefficient (ADC) values with other similar fibrous ovarian lesions (such as CAF and OF) on a larger population. It could also be of interest to evaluate the presence and/or type of calcifications as a way to differentiate BBT from OF and CAF in dedicated comparative studies.

As mentioned earlier, CT and MRI are not in competition with one another for the characterisation of ovarian masses, but are complementary techniques. The combined imaging findings detailed above should help radiologists in confidently suggesting a diagnosis of BBT in the appropriate settings. Even if factors governing resection do not tend to be limited to imaging appearance alone, this could be of interest in patients at high surgical risk, as a more conservative approach could be considered (i.e., simple clinical and/or imaging follow-up).

In conclusion, the combined CT and MRI findings of a unilateral fibrous ovarian mass containing punctate calcifications often associated with a multilocular cystic neoplasm on the same ovary is suggestive of the diagnosis of ovarian BBT.

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Fig. 1. Patient flow diagram.

Fig. 2. Diffusion imaging of BBT of the left ovary. (a) Axial T2 image shows a mixed lesion with a large fibrous component representing the BBT (asterisk) and a multilocular cystic mass representing a mucinous cystadenoma (mc). (b) BBT

(delineated) displays low signal intensity on the corresponding diffusion image ($b = 800$), as does the associated cystic lesion (b).

Fig. 3. Typical enhancement pattern of a solid BBT at MRI. (a) Axial T2 image displays an entirely solid BBT of the right ovary (arrow); note the haematometrium (h) secondary to a chronic cervical os stenosis in this patient. (b) Enhancement after intravenous injection of gadolinium chelates is moderate, slightly inferior to that of the adjacent myometrium (m).

Fig. 4. Examples of typical calcifications within BBTs at CT. (a–c) Axial CT images showing diffuse punctate calcifications within BBTs (arrows) associated to mucinous cystadenomas (borderline form in a)

Fig. 5. Typical aspect of a BBT with associated mucinous cystadenoma at CT and MRI. (a) Axial T2 images shows a mixed right ovarian mass composed of a BBT (asterisk) and a septate cystic lesion corresponding to a benign mucinous cystadenoma. (b) Punctate calcifications can be seen within the BBT on the corresponding CT image. (c,d) Axial fat-saturated enhanced T1 image displays moderate enhancement of the BBT, slightly inferior to that of the myometrium (m)









