CASE REPORT

Borderline Brenner tumors associated with ovarian cyst – case presentation

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Abstract

Borderline Brenner tumors represent quite a rare entity of ovarian tumors (about 2%) that develop from the surface ovarian epithelium. They are formed from papillary structures made of fibrovascular conjunctive axes covered by a transition epithelium, similar to the urinary bladder epithelium. According to the WHO classification, Brenner tumors present the following forms: benign, borderline and malignant. The benign ones are the most frequent, representing about 95%, the borderline represent about 5%, and the malignant ones less than 1%. We present the case of a 64-year patient who was diagnosed with right ovary cyst. The histopathological examination highlighted the presence of a borderline Brenner tumor at the same time with the cystic lesion, on the same ovary. The surgical treatment led to a complete cure of the patient, so that the yearly ultrasound reexamination did not trace the presence of any tumoral relapse.

Keywords: Brenner tumors, borderline ovarian tumors, transitional cell tumors, immunoprofile.

Introduction

Brenner tumors, also known as transitional cell ovarian tumors, are rare tumors, representing between 2 and 5% of the ovarian tumors [1, 2]. Uzan et al. (2012) stated that until now, there have been described approximately 30 cases of borderline Brenner tumors, all characterized by the absence of stromal infiltration and, by definition, associated with a benign component [3].

The experts of the World Health Organization (WHO) classified Brenner tumors into three categories: benign, borderline (atypic proliferative) and malignant [3]. The benign ones are the most frequent, representing about 95%, the borderline represent about 5%, and the malignant ones less than 1% [4].

They are tumors that have their origin in the surface ovarian epithelium, and the microscopic characteristics are close to those of the extrarenal urinary ways epithelium (urothelium).

Borderline Brenner tumors are epithelial tumors that appear as cellular islands or irregular epithelial masses that predominate in the cystic areas, differentiated by a dense conjunctive tissue at the periphery. Malignant Brenner tumors are characterized by cytological atypia and stroma invasion. Both borderline Brenner tumors and malignant Brenner tumors may co-exist together with benign Brenner tumors, which led some researchers to consider that borderline and malignant forms develop from the benign Brenner tumors [5]. Other authors consider that borderline Brenner tumors develop directly from the surface ovarian epithelium where there exist urothelial cells only from a benign Brenner tumor [6, 7].

We present a case of borderline Brenner tumor associated with an ovarian cyst, which caused problems of clinical diagnosis, positive and differential, because only the histopathological examination specified the diagnosis and allowed a therapeutic approach after surgery.

Case presentation

In the Clinic of Obstetrics and Gynecology of the “Prof. Dr. Panait Sirbu” Clinical Hospital of Obstetrics–Gynecology, Bucharest, Romania, in June 2013, there was admitted a patient IS (No. 11784/12.06.2013), aged 64 years old, living in Bucharest, who presented pains in the right iliac fossa and in the hypogastrium. The pains started insidiously about six months before, progressively intensifying, thus determining the patient to ask for a specialized consultation. The clinical examination showed a patient with normal height and weight (66 kg, 1.71 cm) with normal systems and organs. In the right iliac fossa and in the hypogastrium there was palpated a tumoral formation with an average consistence, sensitive, slightly...
mobile. The gynecological examination (vaginal touch and colposcopic examination) highlighted a closed cervix, lesion-free, normal sized uterus, non-sensitive, surrounded posteriorly and to the right by a tumoral formation of about 9–10 cm in diameter, elastic, sensitive, with low mobility. The left adnexal area was elastic, non-sensitive, with a normal aspect.

The abdominal pelvic examination highlighted a fibromatous nodule in the uterus of about 2.1/1.6 cm, and in the right annex a trisonic formation of 7.5/7 cm with hypererechogenic septa inside.

The paraclinical examinations (hemoglobin, glycemia, urea, uric acid, creatinine, transaminases, urine) had normal limits. Anti-HIV (human immunodeficiency virus) and VDRL (Venereal Disease Research Laboratory) antibodies, anti-Trachomonas pallidum antibodies were negative and the CA125 antigen was within normal limits (19 U/mL). The lung X-ray did not identify any changes of the lungs, and the CA125 antigen was within normal limits (19 U/mL).

There was observed that the tumoral stroma presented a dense network of blood vessels; cytokeratins CK7 (clone M7018, Dako, 1:50 dilution) and CK19 (clone RC2K108, Dako, 1:50 dilution) for highlighting the vascular endothelium cells; cytokeratins CK8 (clone N1520, Dako, 1:100 dilution), CK14 (clone QBEn10, Dako, 1:50 dilution) and CK20 (clone Ks20.8, Dako, 1:50 dilution) for the phenotype characterization of tumoral cells.

The microscopic study highlighted the presence of a solid tumor composed of islands of epithelial cells with a transitional type epithelium, surrounded by an abundant fibromatous stroma rich in conjunctive cells and collagen fibers (Figures 1 and 2). Sometimes, the papillary eminences were tall, with a well-developed axis; other times, the tumoral papillae were well sketched (Figure 3). The tumoral cells had round, oval or polygonal shapes, with pale cytoplasm, slightly acidophil, with ovalary nuclei, sometimes crenelated. Nuclear atypia and cellular mitoses were rarely highlighted (Figure 4).

The evaluation of the KI-67 cellular proliferation index showed a low multiplication rhythm of tumoral cells, less than 5% of the cells being positive to this antigen (Figure 5). Instead, using the immunomarking with PCNA showed an intensely positive reaction in the stromal cells and a moderately positive one in the tumoral epithelial cells (Figure 6).

The p53 protein reaction was a negative one (Figure 7), thus proving that gene TP53 was not affected.

Using the immunomarking with anti-cytokeratins antibodies for the phenotype characterization of tumoral cells allowed us to observe that these were intensely positive to CK8 and CK19 (Figures 8 and 9). Immunomarking with CK7 showed that the tumoral cells were moderately positive in this antibody, the most reactive ones being the cells of the basal stratum; the rest of the tumoral cells presented a low reactivity, more intense in the ectoplasm and the subplasmalemmal area (Figure 10). The immunohistochemical reaction of tumoral cells to CK20 was a negative one (Figure 11).

For evaluating the tumoral microvasculatization, there was used the anti-CD34 antibody. There could be observed that the tumoral stroma presented a dense network of blood capillaries, intensely reactive to the anti-CD34 antibody (Figure 12).
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Figure 1 – Island of tumoral cells with a transitional epithelium characteristic, surrounded by an abundant fibromatous stroma. GS trichrome staining, ×100.

Figure 2 – Brenner tumor with a microcystic aspect. HE staining, ×100.

Figure 3 – Area of Brenner tumor with tall papillae. HE staining, ×100.

Figure 4 – Tumoral papillae with clear cytoplasm cells and rare nuclear atypias. GS staining, ×200.

Figure 5 – Area of Brenner tumor with a small number of tumoral cells positive to Ki-67. Anti-Ki-67 antibody immunostaining, ×200.

Figure 6 – Image of Brenner tumor with stromal cells strongly positive to PCNA. Anti-PCNA antibody immunostaining, ×200.
We present a case of borderline Brenner tumor associated with a right ovary cyst, in a menopause woman, who had non-specific symptoms and posed problems of clinical and imagistic diagnosis. According to the references we consulted, we believe that it is the first case of a borderline Brenner tumor ever published in Romania. Also, we believe, that the incidence of this tumor is high, although lots of cases were not published or were confused with other types of ovarian lesions, tumoral or non-tumoral ones.

The reduced clinical symptoms lead to a difficult clinical or imagistic diagnosis of these tumors. Most of the tumors manifest by moderate pains in the small hip area, with a tumoral formation in the pelvis; other times,
the tumors have no symptoms at all [8], being discovered by chance when performing an abdominal echography or other imagistic investigations.

Ovarian Brenner tumors have a low incidence, with an unclear etiopathology until now. According to some studies, Brenner tumors emerge from the tubular epithelial cells by a process of transitional metaplasia [1, 9], while other studies support the idea that the tumoral cells originate from the multipotent cells of the coelomic epithelium, found either on the ovary surface or in some epithelial cysts [10].

Borderline Brenner tumors are rare; they represent only 4–5% of the total of Brenner tumors [2]. As presented by us, these tumors are solid, usually developed on a single ovary, with an ultrasound expression like a parenchymatous tumoral mass located in the pelvis, without intercrossing the uterus. There were also described cases of bilateral Brenner tumors [11, 12].

Neither ultrasounds nor computer tomography (CT) cannot specify the nature of the tumor, as this tumor presents no imagistic particularities [12, 13]. In the studies on benign Brenner tumors, they are generally similar to other solid ovarian masses, such as fibroma, fibrothecoma and peduncular leiomyoma.

We consider that, in our case, the detection of the Brenner tumor was purely incidental, the clinical symptoms being determined by the presence of quite a large ovarian cyst, well detectable with ultrasounds. The presence of adherences between the tumoral ovary and the surrounding organs, as well as the changed aspect of the ovary observed during surgery, determined the clinician to send the resection piece to the histopathological examination.

In our study, the histopathological and immunohistochemical examinations allowed the establishment of an accurate diagnosis of the lesion. Thus, the tumoral cells were arranged in papillary formations made up of a transitional epithelium, centered on a conjunctive axis and differentiated by an abundant fibromatous stroma at the periphery. The immunohistochemical examinations showed that the tumoral cells were positive to CK7, CK8, CK19 and negative to CK20 and p53. Also, the tumoral cells were poorly positive to Ki-67 and positive to PCNA. Our data are similar to the one found by other authors, who observed phenotype expressions of tumoral cell cytokeratins similar to the ones we found [1, 10, 14].

According to some authors, in 25–36% of the cases, the Brenner tumors coexist with other tumoral lesions, such as cystic mucinous tumor, serous cyst adenoma or the cystic dermoid teratoma [11, 15, 16]. The presence of other tumoral or non-tumoral lesions in the female genital system would be due to the fact the Brenner tumors contain cells with a secretory function producing estrogens, hormones that are responsible for the emergence of various lesions, from endometrial hyperplasia with vaginal bleeding to ovarian tumors [16, 17].

The Brenner tumors develop in premenopause or menopause women. Some studies showed that the average age at which these tumors are diagnosed is 46–63 years [12, 18]. Also, it seems that benign Brenner tumors develop in women aged between 30 and 59 years, while malignant and borderline tumors develop in older women (45–60 years) [19, 20].

Most of the borderline Brenner tumors are detected in the first stage and have a favorable progression after the surgical treatment, with a survival rate of five years in about 99% of cases, and of 10 years in about 97% of cases [21]. There were also reported cases in which the tumor had a relapse [22]. Left untreated, the borderline Brenner tumor may cause local complications by the adherences that it makes with the surrounding organs.

Conclusions

The borderline Brenner tumor diagnosed by us in a 64-year-old patient presented minor and unspecific symptoms. The ultrasound examination highlighted an ovarian cyst, considered to be responsible for the clinical symptoms. The positive diagnosis was done after surgery through the classical histological examination associated with immunohistochemical examinations. The progression after surgery was a favorable one, in the first years after tumor resection there were not detected any abdominal relapses during the ultrasound examination.

Conflict of interests

The authors declare that they have no conflict of interests.

References


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