Bilateral Brenner tumor with endometrial adenocarcinoma in a postmenopausal woman

U. Indraccolo[1], *M.D.*; N. Cingolani[2], *M.D.*; S.R. Indraccolo[1], *M.D., Prof.*

[1]Department of Gynaecology, Perinatology and Child Welfare, II Faculty of Medicine and Surgery, "La Sapienza" University, Rome.
[2]Department of Clinical Pathology, Operative Unit of Pathology, ASL 9, Macerata (Italy)

Summary

Brenner tumor is a rare ovarian neoplasm which is generally monolateral, more rarely bilateral, and often associated with endometrial disorders related to oestrogenic production. However, there is no considerable evidence that the possible oestrogenic production of this tumor may be the cause of endometrial disorders.

A case of bilateral Brenner tumor with endometrial adenocarcinoma in a postmenopausal woman is presented and the features are briefly discussed, with the conclusion that hormone-producing Brenner tumors may exert their promoter effect on the development of endometrial carcinoma causing an imbalance in the oestrogen and progesterone ratio rather than producing a large amount of oestrogen.

Key words: Brenner tumor; Endometrial adenocarcinoma; Oestrogen production.

Introduction

Brenner tumor is a neoplasm of the ovary which is usually benign and on the whole unusual [1, 2], consisting of about 1-2% of tumors of the ovary [2, 3]. In about the 90% of the cases it results monolateral [2] and it can produce hormones starting from fibroblasts of its stromal component, which morphologically resemble theca cells of a normal ovary [2]. It has been reported that a Brenner tumor can reveal itself with abnormal uterine bleeding in postmenopause [1, 4] and sometimes it can be associated with endometrial polyposis, hyperplasia and adenocarcinoma [5-10]. However, it is not well understood if these abnormalities could be caused by the oestrogenic hormone activity of hormone-producing Brenner tumors [11]. Finally, there are also Brenner tumor cases associated with other kinds of benign or malignant ipsilateral and/or controlateral tumors of the ovary [5-8].

The case of a benign bilateral Brenner tumor associated with endometrial adenocarcinoma in a perimenopausal woman is reported here.

Case Report

At the age of 48, the patient, a normally menstruating woman, underwent surgery for a mass in her left ovary which was found after a gynecological checkup and subsequent pelvic ultrasound scan. At a combined vaginoabdominal exam, the mass resulted hard, very movable, with the volume of a small lemon and a vaguely irregular outline. On one hand, an ultrasound scan of the pelvis put in evidence a left ovarian cystic formation 5.6 cm x 4.2 cm in diameter, and on the other hand it excluded any aspects of malignancy. The right ovary appeared regular, while the echo-pattern of the uterus appeared dyshomogeneous because of fibromatosis, with a regular endometrium. CA125 was within standard range. In the anamnesis, it was noted that the patient had had two pregnancies with gestational diabetes mellitus and had undergone two caesarean sections. She was an exsmoker, previously obese, and suffered from essential high blood pressure.

At the patient's request, only left salpingo-oophorectomy was performed. Histological examination diagnosed a benign Brenner tumor (2.5 x 2 cm) associated with mucinous cystoadenoma (5 x 4 cm).

Figures 1 and 2 illustrate the microscopic aspect of the Brenner tumor. On the tumorous tissue, P450 aromatase activity was found protruding into the stromal component, while receptors for oestrogens and progesterone were not found.

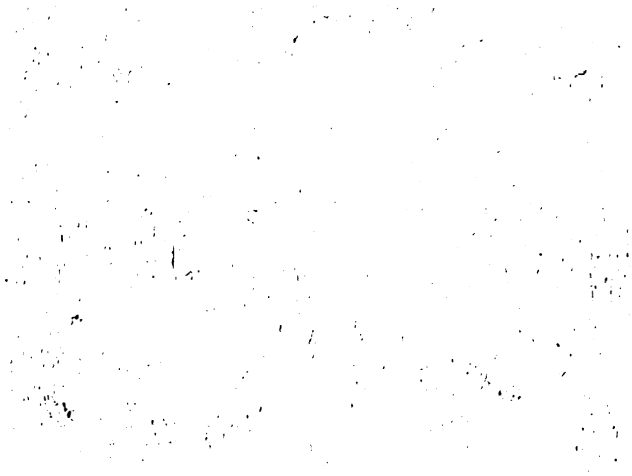
After two and a half years from the operation and after menopause, which had started 16 months before, the patient complained about uterine bleeding, thus urging an endometrial biopsy with the result of endometrial adenocarcinoma. Therefore, she underwent total hysterectomy with right salpingo-oophorectomy. Histological examination confirmed the presence of a well distinguished endometrial adenocarcinoma penetrating the most internal layers of the myometrium (FIGO Stage 1B, G1) and it also revealed a small, benign Brenner tumor in the residual ovary, with P450 aromatase activity penetrating the stromal component.

Discussion

The possibility that hormone-producing Brenner tumors may give rise to endometrial disorders is being discussed. In fact, even if it has been reported that 50% of Brenner tumors might produce hormones [12], Jalůvka *et al.* [9] emphasized that their estrogenic production is not always considerably supported by objective data. Furthermore, even if Sasano *et al.* [11] showed P450 aromatase activity with immunoenzymatic assay in nine out of 23 Brenner tumors, they came to the conclusion that such activity would not be intensive enough to justify endometrial disorders, except in the presence of particularly large tumors.

Revised manuscript accepted for publication November 27, 2006

Fig. 1



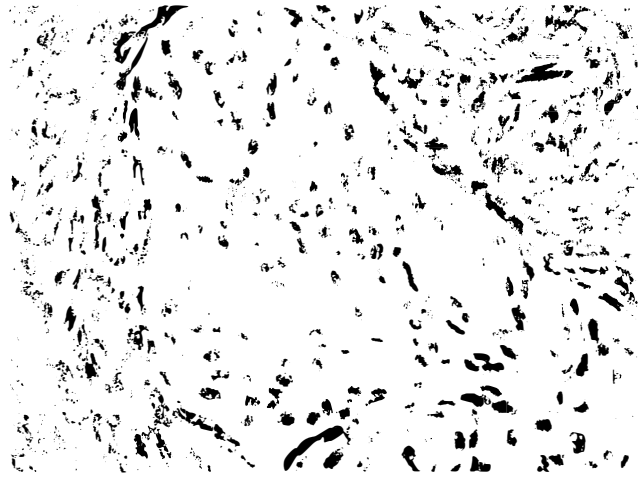


Fig. 2

Figure 1. — Solid nests of epithelial cells histologically resembling transitional epithelium (urothelium) surrounded by an abundant, prominent stromal component of dense, fibroblastic nature (original magnification x 10).
Figure 2. — Characteristic collection of closely packed epithelium with clear cytoplasm and oval nuclei with a small but distinct nucleolus and longitudinal grooves (original magnification x 20).

In the case reported here, it is not obviously possible to come to the conclusion that the endometrial adenocarcinoma could have been caused by the hormone production of the two Brenner tumors, besides being small in size. In fact, other elements of risk for the outbreak of endometrial carcinoma, different from hyperestrogenism, were surveyed anamnestically. However, it can be supposed that, if there was tumoral estrogen production, it could have caused the development of endometrial adenocarcinoma between the premenopausal period, which preceded the first operation, and the postmenopausal one. Those periods were probably lacking in the luteal phase and occurred in a woman with many risk factors for endometrial cancer.

Therefore, it could be hypothesized that hormone-producing Brenner tumors cause an imbalance in the oestrogen and progesterone ratio rather than produce a large amount of oestrogen. Such behaviour appears to be the same as reported for some controlled high-risk conditions for endometrial neoplasms [13] and could result to be particularly dangerous in patients with more risk factors for endometrial adenocarcinoma.

References

[1] Woolf N. Anatomia Patologica. Napoli, EdiSES s.r.l., 2001, 752.
[2] Crum C.P.: "Robbins pathologic basis of disease". The Female Genital Tract. In: Cotran R.S., Kumar V., Collins T. (eds.). Philadelphia, WB Saunders , 1999, 1035.
[3] Cuello F.M.A,. Pomés C.C., Brañes J.Y., Barrena G.N., Mayerson D.B., Wild R.A.: "Tumor ovarico en la postmenopausia. Consideraciones sobre su manejo actual". *Rev. Chil. Obstet. Ginecol.,* 2003, *68,* 97.
[4] Hiroi H., Osuga Y., Tarumoto Y., Shimokama T., Yano T., Yokota H. *et al.*: "A case of estrogen-producing Brenner tumor with a stromal component as a potential source for estrogen". *Oncology,* 2002, *63,* 201.
[5] Jorgensen E.O., Dockerty M.B., Wilson R.B., Welch J.S.: "Clinicopathologic study of 53 cases of Brenner's tumors of the ovary". *Am. J. Obstet. Gynecol.*, 1970, *108,* 122.
[6] Silverberg S.G.: "Brenner tumor of the ovary. A clinicopathologic study of 60 tumors in 54 women". *Cancer,* 1971, *28,* 588.
[7] Ehrlich C.E., Roth L.M.: "The Brenner tumor. A clinicopathologic study of 57 cases". *Cancer,* 1971, *27,* 332.
[8] Piscioli F., Polla E., Reveanne P., Dal Rì P., Franzini M.: "Lesions of the genital system associated with brenner tumor". *Minerva Ginecol.,* 1980, *32,* 893.
[9] Jalůvka V., Kratzsch E.: "Hormone activity of various Brenner tumors". *Gynakol. Rundsch.*, 1982, *22,* 1.
[10] Adamian R.T.: "Hyperplastic processes and endometrial cancer in patients with hormone-producing ovarian tumors". *Vopr. Onkol.,* 1991, *37,* 48.
[11] Sasano H., Wargotz E.S., Silverberg S.G., Mason J.I., Simpson E.R.: "Brenner tumor of the ovary. Immunoanalysis of steroidogenic enzymes in 23 cases". *Hum. Pathol.*, 1989, *20,* 103.
[12] Balouet P., Von Theobald P., Herlicoviez M., Mandard J., Lévy G.: "Brenner tumor. Apropos of 3 recent cases". *Rev. Fr. Gynecol. Obstet.,* 1990, *85,* 263.
[13] Hale G.E., Hughes C.L., Cline J.M.: "Endometrial cancer: hormonal factors, the perimenopausal "window of risk," and isoflavones". *J. Clin. Endocrinol. Metab.*, 2002, *87,* 3.

Address reprint requests to:
U. INDRACCOLO, M.D.
Località Montagnano, 16
62032 Camerino (MC) Italy