Case Report

A Rare Case of Grade 1 Endometrioid Adenocarcinoma of the Uterus With Omental Metastasis with Brenner Tumor of the Ovary in a Postmenopausal Female

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ABSTRACT

Early-stage endometrial cancer may have microscopic omental metastases which is associated with a poor prognosis. There are no standard guidelines for omentectomy in early-stage endometrial cancer without risk factors. Brenner tumor is a rare ovarian tumor which is usually benign, but rarely, it may be malignant. Some Brenner tumors are endocrinologically active. Various studies have shown an association of Brenner tumor with endometrial hyperplasia, polyp, or early-stage carcinoma, probably due to its estrogen-secreting nature. We report a rare case of well-differentiated endometrioid adenocarcinoma of the uterus with <50% myometrial invasion with omental metastases associated with benign Brenner tumor of the ovary in a postmenopausal female.

KEYWORDS: *Brenner tumor, omental metastases, well-differentiated endometrial cancer*

INTRODUCTION

Omental metastasis of endometrial cancer implies peritoneal spread of carcinoma and is regarded as advanced (Stage IVB) endometrial cancer.[1] The prevalence of omental metastases has been reported as approximately 3%–8% in patients with clinical Stage I endometrial cancer.[2] Neither omentectomy nor omental biopsy is included in the standard staging procedures for endometrial cancer. Brenner tumor is a rare neoplasm accounting for 1.5%–2.5% of all ovarian neoplasms. About 7.5% of Brenner tumors are estrogen producing which increases the risk of endometrial hyperplasia and endometrial malignancy.[3] Since the incidence of Brenner tumor with endometrial cancers is quite rare, there are no definitive data to comment on whether such endometrial cancers present in an advanced stage with worse outcome and whether omentectomy or omental biopsy should be done in them for prognostication and early detection of occult metastasis. We hereby report a patient with well-differentiated endometrioid adenocarcinoma of the uterus with Brenner tumor of the right ovary with omental metastases.

CASE REPORT

A 63-year-old multiparous postmenopausal female with hypertension, type 2 diabetes, and hypothyroidism (all controlled with medications) presented to our gynecology outpatient department with a complaint of postmenopausal bleeding for 1 month. The bleeding was fresh red, and the amount ranged from spotting to requiring a pad occasionally. Her previous cycles were regular, and

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there was no history of menorrhagia before menopause. Her family history was negative for breast, colorectal, and gynecological cancers. On general examination, her vital signs were normal, general condition was good, and body mass index was 23 kg/m^2. There was no palpable abdominal mass or ascites. Speculum examination showed normal-looking cervix and vagina, and minimal bleeding was seen coming from the external cervical os. On bimanual examination, the uterus was of 6–8 weeks size, and there was a firm, smooth, mobile mass in the right adnexa of 4 cm size. There was no nodularity in the posterior fornix. Papanicolaou smear showed atypical glandular cells of unknown significance. On ultrasound, the uterus was bulky with diffusely thickened endometrium of 11 mm. The right ovary showed a unilocular solid mass (4 × 4 cm) with minimal flow on color Doppler. The left ovary was normal. Office endometrial aspiration biopsy was collected which showed atypical hyperplasia with focal areas of well-differentiated endometrioid adenocarcinoma. Magnetic resonance imaging pelvis revealed endometrial widening with T2-hyperintense mass lesion with <50% myometrial invasion. No parametrial involvement or lymphadenopathy was seen. In addition, there was a 4 cm × 4 cm T2-hypointense lesion with peripheral rim of postcontrast enhancement suggestive of a solid ovarian tumor. The left ovary was normal; there was no ascites or any other intra-abdominal pathology [Figure 1a]. Her CA125 was raised (355 IU/L). She was diagnosed to be a case of carcinoma endometrium associated with a solid ovarian tumor, possibly a granulosa cell tumor or synchronous/metastatic epithelial ovarian tumor. Serum inhibin level was normal. At laparotomy, there was no ascites, and peritoneal cytology was obtained for malignant cells. The uterus was enlarged to 8 weeks' size with a small anterior subserous fibroid (2 cm × 1 cm). The right ovary was replaced by a gray-white solid tumor, 4 × 4 cm with intact capsule, and no surface excrescences. The left ovary and both fallopian tubes were normal. There were no palpable pelvic or para-aortic lymph nodes or any intraperitoneal tumor deposits. The omentum was grossly normal. Extrafascial hysterectomy with bilateral salpingo-oophorectomy, infracolic omentectomy, and pelvic lymph node dissection was performed. Peritoneal fluid cytology showed metastatic adenocarcinoma. Histopathological examination of the hysterectomy specimen revealed a well-differentiated endometrioid adenocarcinoma with <50% myometrial invasion. Lymphovascular emboli were seen. The cervix, bilateral fallopian tubes, left ovary, and lymph nodes were free of tumor. The right ovary revealed nests of transitional cells embedded in fibroconnective tissue suggestive of Brenner tumor [Figure 1b], and omentum showed multiple microscopic metastatic deposits of adenocarcinoma [Figure 1c]. The tumor cells of endometrioid adenocarcinoma showed strong nuclear positivity of estrogen receptor (ER) and progesterone receptor (PR) and were negative for p53. Microsatellite instability markers (immunohistochemistry [IHC] for MLH1, PMS2, MSH2, and MSH6) showed retained expression. Transitional cells of Brenner tumor were negative for ER and PR; however, surrounding fibrous tissue showed strong nuclear positivity for ER and PR. Transitional cells of the Brenner tumor also showed positivity for Cyclin D1 and p63 and were negative for epidermal growth factor receptor (EGFR), Ki-67, and p53 [Figure 1d]. Thus, a final diagnosis of Stage IVB endometrial cancer with Brenner tumor (benign) of the right ovary was made which has a poorer prognosis than what was anticipated. At present, the patient is receiving combination chemotherapy (carboplatin and paclitaxel) which is planned for six cycles.

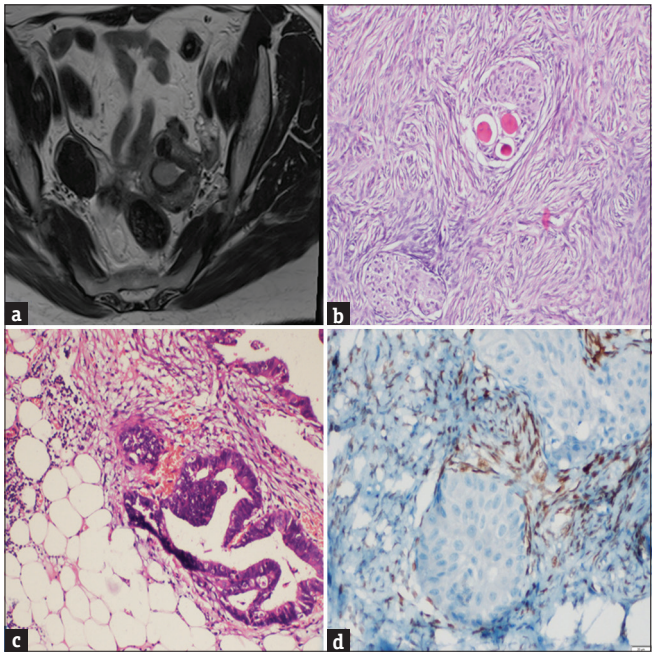

Figure 1: (a) T2-weighted axial image on magnetic resonance imaging shows hyperintense mass lesion in the endometrial cavity (white arrow); in addition, there is well-defined hypointense ovoid lesion seen in the right adnexa (black arrow). (b) Nests of urothelial cells with coffee bean nuclei present with abundant fibrous stroma indicating benign Brenner of the ovary (H and E ×40). (c) Omentum showing metastatic adenocarcinoma in a case of endometrioid adenocarcinoma (H and E ×40). (d) Immunohistochemistry for estrogen receptor showing nuclear positivity only in fibrous stroma of ovarian Brenner tumor (immunohistochemistry ×40)

Discussion

Endometrioid adenocarcinoma of the uterus accounts for ≥90% of endometrial cancers and usually occurs in the background of unopposed estrogen exposure. They are mostly low-grade tumors and are associated

with good prognosis. While the indications for lymphadenectomy in endometrial cancers are now well established after the ASTEC trial,[4] the role of omentectomy in endometrial cancers, especially in Stage I is still an issue of debate.

Omental metastases are observed in 2.4%–8.3% of patients with endometrial cancer, and it is associated with a poor prognosis.[5] All guidelines for the treatment of endometrial cancer recommend omentectomy for visible peritoneal dissemination or in cases when the histology is papillary serous, clear cell, or carcinosarcoma.[2] However, omentectomy is not routinely recommended when the histology is endometrioid adenocarcinoma in the absence of macroscopic intra-abdominal metastases. In a recent meta-analysis done to identify risk factors for omental metastases in clinical Stage I endometrioid adenocarcinoma, it was found that positive lymph nodes, adnexal metastases, and appendiceal implants increase the risk of omental metastases.[2] None of these factors were present in the index patient, and hence, the possibility of omental metastases from the adenocarcinoma was less likely.

Omentectomy in the presence of metastases may not improve the outcome as shown by Turan *et al*., who concluded that although omental metastases were associated with a poor prognosis, the effect of omentectomy on survival was controversial.[5] Turan *et al*. performed omentectomy in 811 women with endometrial cancer, and omental metastases were present in 48 patients (5.9%), of whom 26 women had endometrioid carcinoma. Omental metastases were macroscopic in 60% patients and microscopic in 40% of the patients. Although the survival benefit of this procedure was unclear, it helped to diagnose metastatic disease and thereby offered chemotherapy which may improve survival. Omental metastases remained a poor prognostic factor, and two-thirds of patients with omental metastases expired within 2 years. Hence, new treatment modalities are needed in this group of patients to improve their final outcome.

In the present case, omentectomy was performed not as part of surgery for endometrial carcinoma but due to the presence of a coexisting solid ovarian tumor.

Brenner tumor is a rare ovarian neoplasm, out of which only 2%–5% are malignant.[6] It is difficult to diagnose Brenner tumor on imaging due to its nonspecific nature.[7] Histopathological examination remains the gold standard. The criteria proposed by Hull and Campbell for the diagnosis of malignant Brenner tumor are frank malignant features, an intimate association between malignant element and benign Brenner, absent or well-separated mucinous cystadenoma from benign and malignant Brenner tumor, and demonstration of stromal invasion by epithelial elements of malignant Brenner tumor.[8] On IHC, malignant Brenner tumor is negative for p16, p63, Rb, and p53, but strongly positive for EGFR, Cyclin D1, and RAS.[9] IHC in the present case showed positive Cyclin D1 and p63 and were negative for EGFR, Ki-67, and p53. Although positive Cyclin D1 may suggest malignancy, the histopathological picture of Brenner tumor was confirmatory of its benign nature.

Several cases have shown various hormonal activities attributable to this tumor. In a review of 69 patients with Brenner tumor by Ming and Goldman, 26 (37.6%) patients had endometrial hyperplasia and 12 (17.4%) had endometrial carcinoma.[10] However, the stage and grading of endometrial cancers have not been mentioned. A case report of bilateral Brenner tumor with endometrial cancer suggested that hormone-producing Brenner tumors may exert their promoter effect on the development of endometrial carcinoma causing an imbalance in the estrogen and progesterone ratio rather than producing a large amount of estrogen.[11] A similar coexistence was reported by Sharma *et al*., in 2017. She was a 55-year-old nulliparous, postmenopausal female with metabolic syndrome and underwent staging laparotomy with total abdominal hysterectomy, bilateral salpingo-oophorectomy with lymph node dissection. The histopathology report was well-differentiated endometrioid carcinoma, Grade I with unilateral Brenner tumor.[12]

A review of the literature shows that majority of estrogen-producing Brenner tumor are associated with either endometrial hyperplasia or early-stage uterine cancer. However, the number of cases is too small to comment on the prognosis of endometrial cancers existing in the background of Brenner tumor and whether selective omentectomy should be performed in such patients for timely detection and management of occult metastasis. No such report of endometrial cancer with omental metastasis associated with Brenner tumor of the ovary has been reported till date to the best of our knowledge.

Conclusion

Omental metastases are rarely found in well-differentiated endometrioid adenocarcinoma with <50% myometrial invasion. Hence, it is difficult to comment whether the presence of coexistent Brenner tumor worsened the

prognosis and stage of uterine cancer in the present patient. More data are required to determine whether omentectomy should be considered as a part of surgical management in such patients to improve the overall survival.

Informed consent

Written informed consent has been taken from the patient to this case report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Ethical clearance

Ethical clearance was taken from institutional ethics committee.

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Conflicts of interest

There are no conflicts of interest.

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