Case Report

Malignant Brenner tumor of ovary: A rare entity

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ABSTRACT

Worldwide, ovarian carcinoma continues to be responsible for more deaths than all other gynecologic malignancies. It usually occurs in older women and the average age at presentation is 50 years. Brenner tumor of the ovary is very rare, mostly benign, small, and unilateral. Malignant Brenner tumor is much rarer. These tumors are believed to arise from urothelial metaplasia of ovarian surface epithelium. Malignant Brenner tumor of ovary closely resembles the transitional cell carcinoma of ovary. They must be differentiated because the latter has a worse prognosis. A case of unilateral malignant Brenner tumor in a postmenopausal woman is reported here and its features are briefly discussed.

Key words: Malignant Brenner tumor, ovarian neoplasms, transitional cell carcinoma ovary

INTRODUCTION

Transitional cell tumors of the ovary represent about 2% of all ovarian tumors and according to WHO, depending on the histopathological pattern, they are classified as benign, borderline or malignant Brenner tumors, and transitional cell carcinomas.[1] Brenner tumor is a fibroepithelial tumor composed of transitional epithelial cell nests, similar to bladder epithelium.[2] These tumors have predilection for postmenopausal women.[3] The Brenner tumors are usually small, solid, firm grayish knots up to 2 cm in size, however, they may also be quite big, and in such cases they usually have cystic components as a result of cystic degeneration and necrosis. They are mostly benign and 95% of cases are unilateral. Malignant cases are extremely rare (roughly about 2% of all cases), and so are proliferative Brenner tumors.[2]

CASE REPORT

A 70-year-old female, gravida 7 para 6 presented with pain abdomen and menorrhagia for the last 2 years with progressive weakness. At the time of examination, her vitals were stable, and no abnormality was detected in general and systemic examination except for moderate anemia. On per abdominal examination, a firm to hard, nontender and the mobile lump was palpable in the pelvic region. Per vaginal examination revealed normal size uterus with a 12 cm × 10 cm mobile lump anterior it.

Ultrasonography revealed 14 cm × 13 cm mass in the pelvis and contrast-enhanced computed tomography (CECT) of abdomen and pelvis was advised to confirm the origin of tumor. On CECT, the uterus was normal. There was presence of approximately 17 cm × 15 cm × 11 cm well-defined cystic lesion with peripheral enhancing soft-tissue arising from pelvis and extending up to the umbilical region. Both ovaries were not identified separately from it. A final impression of well-defined pelvic mass lesion, of ovarian origin was made. On laparotomy, a multilobulated ovarian tumor was found on the right side. The uterus, bilateral fallopian tubes, and contralateral ovary were normal. Right-sided salpingo-oophorectomy was done and sent for histopathological examination.

An oophorectomy specimen measuring 14 cm × 12 cm × 8 cm with attached fallopian tube was received. On serial sectioning, the mass was partially cystic and partially solid. Cut surface of solid areas was gray white to gray brown with areas of congestion. The wall of the cystic areas was in continuity with the solid areas. The inner surface of the cysts showed coarse nodularity [Figure 1]. Extensive sampling was done and multiple sections from representative areas were taken.

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Multiple microsections examined showed cyst wall lined by dysplastic transitional like epithelium [Figure 2a]. The stroma was infiltrated by nests and islands of malignant cells with squamous morphology [Figure 2b]. The tumor cells showed moderate atypia with frequent mitotic figures and large areas of necrosis. Dyskeratosis was present. The tumor was seen to evoke inflammatory host reaction with foreign body giant cell reaction to keratin. Foci of calcification were also present [Figure 3]. The fallopian tube showed normal morphology. All the above features favored the diagnosis of malignant Brenner tumor of the ovary with extensive squamous metaplasia.

The postoperative period was uneventful. She was advised six cycles of chemotherapy with serum cancer antigen-125 (CA-125) levels every 3 months. Chemotherapy included intravenous cyclophosphamide, doxorubicin hydrochloride, and cisplatin.

DISCUSSION

The term Brenner tumor was introduced by Robert Meyer in 1932, referring to a tumor described by Fritz Brenner 25 years previously.[4] It is very rare. The most common site is ovary, however, it has also been described in other organs such as testis and epididymis.[2] It has been reported that Brenner tumor can reveal itself with abnormal uterine bleeding in postmenopausal females and sometimes may be associated with endometrial polyposis, hyperplasia, and adenocarcinoma. Brenner tumors are also known to be associated with other benign or malignant ipsilateral and/or contralateral tumors of the ovary.[4]

This is a relatively uncommon ovarian tumor and constitutes 1.4–2.5% of all ovarian neoplasms. Most of the Brenner tumors are benign. Only 2–5% are malignant.[5] It is characterized by varying numbers of rounded nests of transitional or squamous cells and glandular structures of cylindrical cells within abundant fibrous nonepithelial tissue. The malignant components of the tumor, which shows heterogeneous epithelial growth and atypia with intervening stroma, consist of transitional cells, squamous or undifferentiated carcinoma or an admixture of these types.[3]

By definition, transitional cell carcinoma of the ovary and malignant Brenner tumors are composed of epithelial cells morphologically resembling urothelium. At matched stage, transitional cell carcinoma of the ovary has a worse prognosis compared to malignant Brenner tumor, therefore, transitional cell carcinoma of ovary should be differentiated from malignant Brenner tumors.[6] In addition to not having a benign Brenner component, transitional cell carcinoma lacked the prominent stromal calcification common in most benign and malignant Brenner tumors. Transitional cell carcinoma is sufficiently different from malignant Brenner tumor in that it is reasonable to suppose that ovarian transitional cell carcinoma arises directly from pluripotential surface epithelium of the ovary and from cells with urothelial potential, rather than from a benign or proliferative Brenner tumor precursor.[7] Thus, extensive tumor sampling is needed to make an accurate diagnosis.

First case of malignant Brenner tumor was described in 1945 by von Numbers.[8] The criteria proposed by Hull and Campbell in 1973 for diagnosis of malignant Brenner tumor are as follows:[9]

- Frankly malignant histological features must be present
- There must be an intimate association between the malignant element and a benign Brenner tumor
- Mucinous cystadenoma should preferably be absent or must be well separated from both benign and malignant Brenner tumor
- Stromal invasion by epithelial elements of malignant Brenner tumor must be demonstrated.

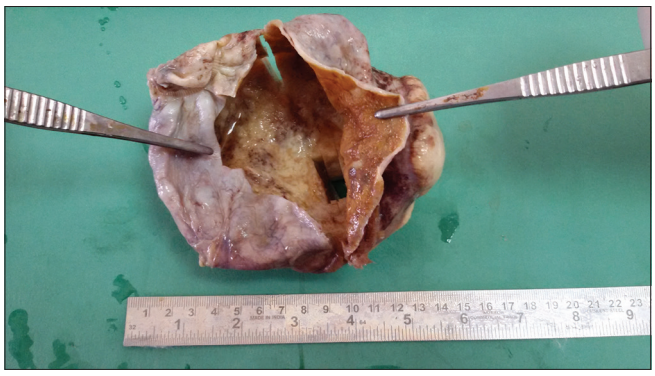

Figure 1: Gross specimen showing cystic and solid areas with coarse nodularity of the inner surface of the cyst

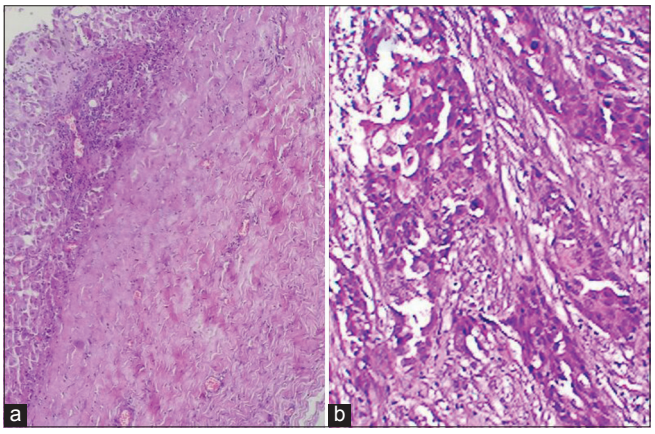

Figure 2: (a) Photomicrograph showing dysplastic transitional lining of cyst representing the borderline component of the tumor (H and E, ×100). (b) Photomicrograph showing stroma infiltrated by nests and islands of malignant cells with squamous morphology along with mitosis (H and E, ×200)

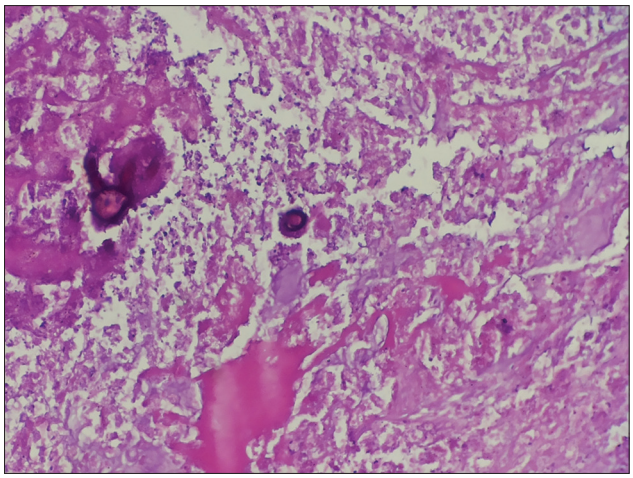

Figure 3: Photomicrograph showing extensive necrosis along with foci of calcification (H and E, ×400)

The present case fulfilled all the criteria described above.

Most Brenner tumors are candidates for surgical resection. Malignant Brenner tumors may affect surrounding tissue and metastasize into other structures, but this is so rare that a standard treatment has not been developed. Even malignant Brenner tumors, if diagnosed early, are candidates for complete surgical resection.[10]

Adjuvant therapy to surgery for epithelial ovarian cancer varies according to the stage of the disease, but, in most cases, will consist of chemotherapy.[11] Adjuvant platinum-based chemotherapy improves survival in early (stage I/IIa) epithelial ovarian cancers. Chemotherapy is advised for all women with stages II-IV disease following surgery. The standard regimen is paclitaxel and carboplatin given intravenously every 3 weeks for six cycles. Intraperitoneal chemotherapy may be used as an alternative, and evidence suggests it may be more effective.[12]

New biological therapies (targeted therapy) are being developed and undergoing trials as understanding of the molecular biology of the types of ovarian cancer has advanced.[13] CA-125 may be used to monitor the efficacy of treatment, and to monitor for recurrence every 3 months.[12]

CONCLUSION

Ovarian tumors are fairly common neoplasms. However, the incidence of Brenner tumors is very rare (1.4–2.5%) of which only 2–5% are malignant. Malignant Brenner tumor of ovary closely resembles the transitional cell carcinoma of the ovary. They must be differentiated because the latter has a worse prognosis. Histopathological examination remains the gold standard for diagnosis of this entity.

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