



Malignant Brenner Tumor- A rare case of ovarian carcinoma

Shikha M. Toshniwal¹, Saunitra A. Inamdar², Himanshi D. Agarwal³, Sakshi R. Sharma⁴

¹Junior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical college, Datta Meghe Institute of medical sciences(Deemed University), Sawangi Meghe, Wardha, Maharashtra, India; Email: shikhatoshniwal802@gmail.com

²Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical college, Datta Meghe Institute of medical sciences (Deemed University), Sawangi Meghe, Wardha, Maharashtra, India; Email: saunitrainamdar56@gmail.com

³Junior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical college, Datta Meghe Institute of medical sciences(Deemed University), Sawangi Meghe, Wardha, Maharashtra, India; Email: hagarwal2701@gmail.com

⁴Junior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical college, Datta Meghe Institute of medical sciences(Deemed University), Sawangi Meghe, Wardha, Maharashtra, India; Email: s.sakshisharma22@gmail.com

Article History

Received: 12 August 2020

Reviewed: 13/August/2020 to 17/September/2020

Accepted: 17 September 2020

E-publication: 25 September 2020

P-Publication: September - October 2020

Citation

Shikha M. Toshniwal, Saunitra A. Inamdar, Himanshi D. Agarwal, Sakshi R. Sharma. Malignant Brenner Tumor- A rare case of ovarian carcinoma. *Medical Science*, 2020, 24(105), 3550-3554

Publication License



This work is licensed under a Creative Commons Attribution 4.0 International License.

General Note



Article is recommended to print as color digital version in recycled paper.

ABSTRACT

Ovarian cancer are a heterogenous group of tumors, involving a variety of histological tissue ranging from epithelial tissue, connective tissues, specialized hormone secreting cells to germinal and embryonal cells. Brenner Tumor' (BT) is a rare epithelial ovarian tumor accounting for about 1-2% of all ovarian neoplasms. Malignant Brenner tumor (MBT) is much rarer. Although asymptomatic, they can presents as abdominal discomfort, abdominal pain or abnormal uterine bleeding. On gross appearance, it

resembles fibroma of ovary with cut section appearing gritty and yellowish grey. On histological examination, solid and cystic nests of urothelium-like cells surrounded by abundant dense, fibrous stroma are seen. It closely resembles to transitional cell carcinoma of ovary, latter having worse prognosis and needs to be differentiated from Brenner tumor. Currently, most accepted treatment is primary surgical resection with or without lymph node dissection followed by platinum based chemotherapy. We herein review a case of MBT in a postmenopausal woman with abnormal uterine bleeding with emphasis on clinical features, investigations and primary treatment and discuss the current state of the literature and standards of practice regarding this malignancy.

Keywords: ovarian carcinoma, Malignant Brenner tumor, Transitional cell carcinoma

1. INTRODUCTION

Brenner tumor is a rare epithelial ovarian carcinoma, accounting for less than 2% of ovarian neoplasms. In 1907, it was identified by Fritz Brenner. Brenner tumor are classified into benign, borderline (proliferative) or malignant subtypes. Brenner tumor is a tumor of fibroepithelial origin. It is composed of transitional epithelial cell nests, similar to bladder epithelium. These tumors have propensity for postmenopausal women. Malignant Brenner tumor clinically presents as abdominal distension, pelvic discomfort or postmenopausal bleeding (Gezginç et al., 2012). The Brenner tumors are usually small, solid, firm grayish knots upto 2 cm in size; however they may also be quite big, typically having cystic components as a result of cystic degeneration and necrosis. Mostly they are benign and 95% of cases are unilateral. Malignant cases are extremely rare accounts roughly about 2% of all cases, and so are proliferative Brenner tumor (Jodha and Garg, 2017).

2. CASE REPORT

A 65 year old female P4L3D1 with a past medical history of diabetes mellitus type 2 since 4 years presented for gynecologic consultation due to post menopausal bleeding and pelvic mass found on ultrasonography. She further complained of abdominal fullness with increasing urinary pressure and frequency. Pelvic ultrasonography revealed a solid large cystic pelvic mass, showing lot of internal vascularity malignant ovarian mass of size 14.1x7.2 mm seen in right adnexa abutting the uterus, could not be separated and left ovary could not be seen. Pre-operative CA-125 measured 227 U/ml (normal range- 0-35 U/ml).

The patient underwent total abdominal hysterectomy and bilateral salphingo-opeectomy. During surgical exploration, a large solid, cystic mass was present on the right side of the ovary of around 15 x 7 cm in size and is adherent to anterior aspect of uterus and on the left side a mass of size 4 x3 cm was seen. There was also a small cystic mass on the posterior surface of urinary bladder and posterior surface of cervix of size 3 x 3 cm. A small neoplastic growth of size 1 x 1 cm size was present in POD which was adherent to rectum along with omental thickening and ascites.

Pathologic examination revealed an ovarian mass having features suggestive of Surface Epithelial Tumor, a biphasic proliferation of epithelial cells along with areas of solid, well formed nests immediately juxtaposed with regions of infiltrative cord like and single cell growth (image 1).

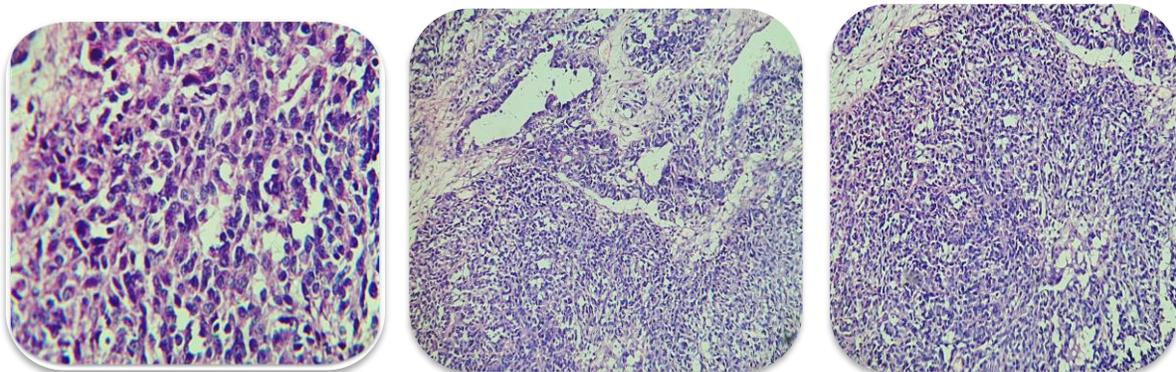


Image 1 (By Dr. Samarth Shukla)- Section stained with Hematoxylin and Eosin(H & E) stain (low power view : 10x and high power view : 40x) show histopathological features of Malignant Brenner tumor. Section shows solid nests of urothelium- like cells surrounded by abundant dense, fibrous stroma. Cells are moderately pleomorphic with polygonal shape, pale cytoplasm and distinct nucleoli.

Ascitic fluid cytology revealed isolated intermediate to little large sized epithelial cells, a few small disschesive groups of epithelial cells and rare small groups of pseudogranular placement. The cells carry hyperchromatic nuclei with nuclear enlargement and mild pleomorphism. Nuclei show granular uneven chromatin and infrequent nucleoli. Cytoplasm is modest and few show vacuoles. Background shows mesothelial cells, lymphocytes, macrophages, cell debris and haemorrhage material present. Cytomorphology is suggestive of infiltrate of adenocarcinoma. Post-operately her CA-125 was 1000 U/ml. The patient was discussed at a multidisciplinary tumor board, which recommended 6 cycles of Injection carboplatin AUC-5 and Injection Paclitaxel 175 mg/m² AUC-5 (image 2). At the time of writing she has received 2 cycles of chemotherapy.



Image 2 Sectioned surface of bilateral ovaries containing soft tan areas with small sized cysts as well as firm white areas

3. DISCUSSION

In 1932, Robert Meyer introduced the term Brenner tumor, referring to a tumor described by Fritz Brenner 25 years previously (Pagrut et al., 2016). Relatively it is uncommon ovarian tumor and constitutes 1.4-2.5 % of all neoplasms of ovaries. In 1945, von Numbers described the first case of Malignant Brenner tumor (Numers, 1945). The most common site of Brenner tumor is ovary. Interestingly, it has also been described in other organs such as testis and epididymis. Malignant Brenners Tumor, although asymptomatic, can presents as abdominal discomfort, abdominal pain, bulk symptoms and relative vague symptomatology (Gezginç et al., 2012). In <10% of patients, it can present with ascites (Driss et al., 2010). While generally not hormone secreting, estrogen secreting malignant Brenner tumors have been reported causing abnormal uterine bleeding, such as menstrual irregularity or postmenopausal bleeding (Joh et al., 1995).

Diagnostic features

Malignant Brenner tumors (MBT) are not associated with findings consistent with hemorrhage or necrosis; however, typically other malignant epithelial ovarian tumors have these features along with a thick irregular wall, thick septa and papillary projections. This difference would indicate that if hemorrhage or necrosis is noted on imaging, there should be higher suspicion for non-MBT malignant epithelial neoplasms. As MBT do not have pathognomic imaging features, the clinical utility of CT and MR imaging is unclear. However, Imaging contributes to the assessment of tumor location, size, and burden as well as with surgical planning (Moon et al., 2000).

Hull et al. established the histologic criteria to diagnose the MBT which requires the concomitant presence of malignant as well as benign/ borderline BT with clear stromal invasion by the malignant epithelial components. In addition, associated tumor types (most commonly mucinous cystadenoma) must either be absent or geographically distinct from the MBT (Hull and Campbell, 1973). The transitional-type differentiation essential for the diagnosis of BT/MBT is characterized by the presence of nuclei with distinct nuclear grooves (so-called "coffee-bean" shape) along with immune-histochemical demonstration of the urothelial marker expression such as GATA3, uroplakin-III, thrombomodulin, and p63. CA125 is elevated in some patients with MBT, but was not correlative to stage or tumor burden. Despite the low sensitivity (50–62%) and even moderate specificity (94–98.5%) of CA125, it is the most widely used serologic marker in patients with epithelial ovarian cancer. Given that MBT is a member of this neoplastic family, it is recommended to check pre-operative CA125 in these patients and to use it as a marker of recurrence if a raised CA125 returns to normal after treatment (Sölétormos et al., 2016).

The primary tumor on the differential diagnosis of Malignant Brenner tumor (MBT) is Transitional Cell Carcinoma (TCC).

MBT	TCC
On imaging and gross examination, calcification is seen.	On imaging and gross examination, it lacks calcification.
Less aggressive. Mostly presents with early stage of disease.	More aggressive. Mostly diagnosed in advance stage.
Well differentiated transitional cell nests.	Frankly malignant features.
Typically negative for WT1, ER and p53. Increase in EGFR, Ras and cyclin D expression with increasing degree of malignancy.	Diffuse expression of WT1, ER and p53

Treatment options

For all epithelial ovarian tumors, surgery is accepted as the standard of care. Recently Nasioudis et al., reported that on a retrospective population based analysis of MBT showing that nearly 98% of patients with MBT have primary surgical resection (Nasioudis et al., 2016). Pelvic and para-aortic lymph node dissections are classical procedures undertaken for malignant ovarian neoplasm for accurate staging (Ngo and Chau, 2020). However, while approximately 50% of patients with surgical tumor excision had concomitant lymph node dissection, only 5% of these patients had evidence of lymphatic spread and therefore lymph node dissection did not confer any disease-specific survival benefit to these patients (Nasioudis et al., 2016). International Federation of Gynecology and Obstetrics (FIGO), has currently recommended the complete lymph node dissection in combination with total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy in these patient population for accurate staging (Heintz et al., 2006).

The effect of platinum-based chemotherapy plus paclitaxel as a post-surgical chemotherapy has showed good outcome. Currently, standard chemotherapy regimen for patients with epithelial ovarian neoplasms is carboplatin plus paclitaxel for 6 cycles (Ozols et al., 2003). Intraperitoneal chemotherapy is suggested to be more effective.

4. CONCLUSION

Brenner tumor is very rare and closely resembles transitional cell carcinoma of ovary, latter having worse prognosis, which makes it mandatory to differentiate between the two. As ultrasonography is difficult to differentiate it from ovarian fibroma, histopathological examination remains the gold standard for its diagnosis. CA-125 should be done to monitor the efficacy of treatment, and to monitor for recurrence 3 monthly. The best treatment strategy, due to rarity of these tumors, will likely to be developed through reporting of clinical experience.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that they have no conflict of interest.

Informed consent

Written and oral informed consent was obtained from participants included in the study.

Data and materials availability

All data associated with this study are presented in the paper.

Peer-review

External peer-review was done through double-blind method.

REFERENCES AND NOTES

1. Driss, Mrad, Dhoub. Ascitic fluid cytology in malignant Brenner tumor: a case report. *Acta Cytol.* 2010;54:598–600.
2. Gezginç, Karatayli, Yazici. Malignant Brenner tumor of the ovary: analysis of 13 cases. *Int. J. Clin. Oncol.* 2012;17:324–329.
3. Heintz, Odicino. Carcinoma of the ovary. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. *Int. J. Gynaecol. Obstet. Off. Organ Int. Fed. Gynaecol. Obstet.* 2006; 95:161-192.
4. Hull, Campbell. The malignant Brenner tumor. *Obstet. Gynecol.* 1973;42:527–534.
5. Jodha, Garg. Brenner tumor of ovary: an incidental finding: a case report. *Int. J. Reprod. Contracept. Obstet. Gynecol.* 2017;6:1132–1135.
6. Joh, Aizawa, Ohkawa. Case report of a malignant Brenner tumor with hyperestrogenism. *Pathol. Int.* 1995;45:75–84.
7. Moon, Koh, Kim. Brenner tumor of the ovary: CT and MR findings. *J. Comput. Assist. Tomogr.* 2000;24:72–76.
8. Nasioudis, Sisti, Holcomb. Malignant Brenner tumors of the ovary; a population-based analysis. *Gynecol. Oncol.* 2016;142:44–49.
9. Ngo XM, Chau TV. An assessment of female ovarian cancer patients' death and survival rates after surgical intervention: Neoadjuvant chemotherapy versus primary debulking surgery. *Medical Science*, 2020, 24(104), 1839-1844
10. Numers, Von. Contribution to the Case Knowledge and Histology of the Brenner Tumor.: Do malignant Forms of the Brenner Tumor also occur? *Acta Obstet. Gynecol. Scand.* 1945;25:114–127.
11. Ozols, Bundy, Greer. Gynecologic Oncology Group, Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a Gynecologic Oncology Group study. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* 2003; 21:3194–3200.
12. Pagrut, Khadse, Khandekar, Mahadani. Malignant Brenner Tumour of the Ovary: A Rare Entity. *Int. J. Biomed. Adv. Res.* 2016;7:479–481.
13. Sölétormos, Duffy, Hassan. Clinical Use of Cancer Biomarkers in Epithelial Ovarian Cancer: Updated Guidelines from the European Group on Tumor Markers. *Int. J. Gynecol. Cancer* 2016;26:43–51.