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Title: MALIGNANT BRENNER TUMOUR ASSOCIATED WITH RESIDUAL OVARIAN SYNDROME – A RARE CASE REPORT.

INTRODUCTION

Ovarian cancer is the fifth most common cause of death among women. It is also the leading cause of death in women with gynaecological cancers. The development of pathology in conserved ovaries is called as Residual ovary syndrome (ROS). It is estimated that 2.85% of patients will develop ROS and will require surgery following hysterectomy.
Now the name “Brenner tumour” was given to acknowledge Dr. Fritz Brenner who described 3 cases in 1907 and named them “oophoroma folliculare,” with the assumption that tumor nests may represent abnormally developed ovarian follicle.
Today Brenner Tumours (3%), a distinct histological subtype of epithelial ovarian tumours are categorized as benign, borderline, or malignant. Malignant Brenner tumors (MBTs) are very rare, and most of them are confined to the ovary, comprising < 5% of all BT.
We herein review a case of MBT associated with ROS with emphasis on primary treatment along with preventive management of recurrent disease, by using adjuvant pelvic radiation.

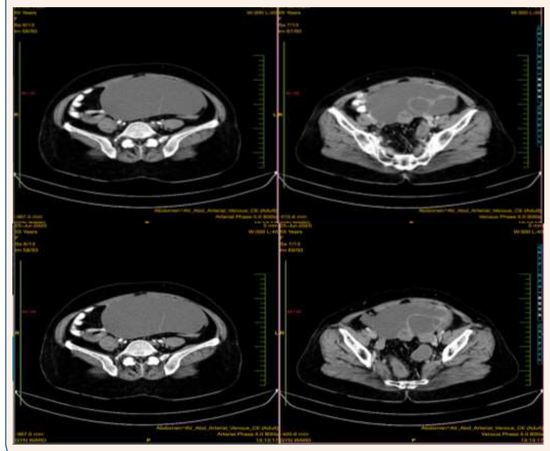
OBJECTIVES

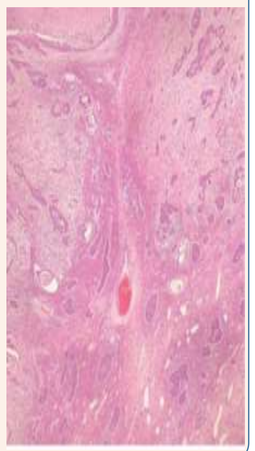
To report and analyse the clinical presentation, diagnostic challenges, and management of a rare case of Malignant Brenner’s tumour (MBT) associated with Residual Ovarian Syndrome (ROS) highlighting its pathological features, treatment approach and outcome.

CASE REPORT

A 55-year-old (P1L1) with history of essential hypertension and class II obesity was referred to consultation at the gynaecological department at JNMC, Wardha on 24th July,2024.
SYMPTOMS : Chronic pelvic pain with palpable mass per abdomen. She reported abdominal fullness with increasing urinary pressure, frequency, and dyspareunia. There was no history of vaginal discharge. She denied any weight loss or change in eating or bowel habits. As a result of the distention of the abdomen and concern for probable gastrointestinal origin of abdominal pathology, a CT scan of the abdomen and pelvis was performed. She gave a history of getting hysterectomy with bilateral subtotal salphingo-opherectomy 15 years back, with the aim to preserve hormonal function.
SIGNS: On examining her, we felt a firm to hard irregular mass, nontender in left suprapubic/iliac fossa extending towards periumbilical area. On per vaginal examination, a mass was felt through vault, smooth in consistency.
On Cect Abdomen + Pelvis– (1) There was e/o multiloculated multiseptated complex solid cystic lesion noted in left adnexa extending into pelvis and infraumbilical region. (2) The septations and nodular solid component show mild to moderate enhancement and is abutting the left ovarian part. The lesion is displacing urinary bladder towards right side. Tumour marker CA-125 done preoperatively was 129.9 U/ML.
Exploratory laparotomy was planned. After the peritoneum was opened, 120 cc of haemorrhagic ascitic fluid was present. On further exploration, 14 x 13 x 5 cms greyish solid cystic mass with irregular surface was found adhered to the omentum, peritoneum along with adnexa. Concurrent paratubal cyst of 2 x 2 cms diameter was coincidently discovered. We consulted with the oncological department and decided to perform complete surgical staging. We found the uterus to be enlarged at 12 weeks of gestation and on further exploration, we also found peritoneal seeding. No pelvic lymph node metastasis was observed. **Grossly**, the mass was a whitish-grey rubbery split cyst. On the cut surfaces, some of the mass was dull and solid, while some was hollow. **Histopathological** examination revealed the diagnosis of left ovarian malignant Brenner tumours that infiltrated the uteri along with peritoneal seeding. The ascitic fluid cytology revealed haemorrhagic fluid with features suggestive of deposits of epithelial malignancy. Background is haemorrhagic probably attributing to the therapeutic procedure.

Right ovary, and omentum were free of malignant cells.
An Institutional tumour board committee advised a **3 cycle Chemotherapy** with carboplatin (576.5mg) + paclitaxel (254mg) under AUC-5; the last cycle being on March, 2021.
Follow-up of the patient was maintained by monitoring CA-125 - (6) monthly and CECT abdomen and pelvis yearly for a 2-year duration.
The patient continued to show no evidence of disease till that period.





DISCUSSION

Currently, according to the 2020 WHO Classification of Female Genital Tumours, the essential criteria for diagnosing MBT by morphology is listed as a “malignant tumour with urothelial differentiation and a benign or borderline Brenner tumour component in the background” (1)
Proposed Histogenesis: - There are several proposed models for how these tumors may develop as the etiopathogenesis and hormonal activity of these tumors are still an enigma. (2)

ORIGIN
- GERM CELLS
- RETE OVARIES
- WALTHARD CELL NESTS
- GONADAL STROMA
- FOLLICULAR STRUCTURES
- GERMINAL EPITHELIUM

Genetic Mutations

ACTIVATING MUTATIONS
- KRAS, PIK3CA , TP53 or CTNNB1 GENE in some MBT.
- Loss of PTEN expression has been reported in some MBT.

Furthermore, genetic mutations are not the only factors involved , Environmental and lifestyle factors, as well as epigenetic changes, can also play a role in tumour formation (3)
Immunohistochemistry profile of MBT
Malignant Brenner tumour does not have any specific tumour marker that can help establish its diagnosis. However, like in our case, the level of tumour markers, specifically CA-125, can be used to assess tumor activity and to better distinguish whether the tumour is malignant or benign. (4)

The immunohistochemical markers that have been studied are :-

POSITIVE IN MAJORITY	POSITIVE IN SOME CASES	NEG OR FOCALLY POSITIVE	VARIABLE EXPRESSION
CK 7	ER,PR,PAX 8,WILMS TUMOUR1	CK 20	CA-125,CD99,ALPHA INH

P53 OVER EXPRESSION IN SOME CASES .It's important to note that the immunohistochemical profile of malignant Brenner tumors can overlap with other ovarian tumors, particularly transitional cell carcinomas and urothelial carcinomas. Immunohistochemistry should be interpreted in the context of other clinical and pathological features to make an accurate diagnosis. (5)
Like in our case, the presence of an ovarian mass associated with squamous cells in peritoneal fluid regardless of the status of nuclear abnormalities is, for all practical purposes, diagnostic of metastatic squamous cell carcinoma.(6)
Similar to other epithelial ovarian carcinomas, surgery with total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and tumour debulking is the mainstay of treatment for MBT. The role of routine lymphadenectomy in the surgical management of MBT remains unclear. In addition, it has been suggested that intensive adjuvant chemotherapy with a platinum-based Taxol regimen may be beneficial in patients post surgically .(7)

CONCLUSION

We herein state that our case was managed effectively with a combination of surgery and an adjuvant chemotherapy with a diligent follow-up. As this represents a singular case of successful treatment, generalizations about treatment protocols cannot be suggested. Lastly, given that randomized studies are not feasible, we propose the establishment of an international tumor registry to collect information on treatment modalities such as lymphadenectomy, chemotherapy administration, recurrence rates and outcome of this rare ovarian tumor.

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