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MALIGNANT BRENNER TUMOUR OF OVARY

Pathology

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ABSTRACT

The most common ovarian neoplasms are surface epithelial tumors, including transitional cell tumors. Transitional cell tumors include Brenner tumor and transitional cell carcinoma. While the benign Brenner tumor is well characterized, the malignant counterpart constitutes a rare entity, with relatively few published data to date. Primary management is by surgical excision. Owing to their rarity, the precise regimens of adjuvant chemotherapy and radiation are yet to be established. We report a case of malignant Brenner tumor in a lady who presented with vague abdominal discomfort and inconclusive pre operative work-up, with the definitive diagnosis established by histopathology.

KEYWORDS

Humans, Female, Middle Aged, Brenner Tumor, Non-Smokers,Carcinoembryonic Antigen,Tumor Suppressor Protein p53,Fallopian Tubes, Immunohistochemistry, Carcinoma, Transitional Cell,Urothelium,Biomarkers, Tumor, Menarche THBD protein, human, Thrombomodulin, Salpingo-oophorectomy Colon, Sigmoid, Survival Rate

INTRODUCTION

Brenner's tumor was originally reported in 1907 by Fritz Brenner. This rare entity is presently classified into three: benign, borderline and malignant; with varying implications of each. While Brenner tumor constitutes only 1-2% of ovarian neoplasms, the malignant counterpart forms less than 5%, with lack of clear cut management guidelines are lacking, highlighting the importance of early recognition of this variant. [(1)]

Two clinicopathological entities are defined by some investigators, with malignant Brenner containing a benign or atypical proliferative component, and Transitional cell carcinoma with no such component.

Although usually discovered incidentally, occasional patients with Brenner tumor present with symptoms like palpable mass or pain with predominantly unilateral mass, bilateral lesions occur in 5-14%. (11) Only limited data is presently available primarily as case reports and series; accounting for lack of data regarding management. We report a case of a post menopausal lady who presented to our hospital with abdominal discomfort, and discovered to harbour malignant Brenner tumor on histopathology.

CASE REPORT

A 58 year old lady presented to our hospital, a nodal centre and tertiary care centre in the Himalayan region of northern India with complaints of vague abdominal discomfort. She had been married for 43 years with a parity of three. Menarche was attained at 14 years, menopausal since 6 years.

On examination: General examination was within normal limits. On systemic examination, a per abdominal mass was palpated on the left side, appearing to arise from the pelvis.

Lab investigations: Blood tests were within normal limits. Tumor markers were within normal limits: CA-125: 7.3 U/mL(reference: <30.2 U/mL) and CEA(carcinoembryonic antigen): 2.42(reference : non smokers:<2.5 and smokers:<5.0 ng/ml, index case being a non smoker)
Imaging: Ultrasound revealed a large multiseptate abdominopelvic mass with interspersed solid areas-? malignant ovarian mass.

CT showed a large multilocular abdominopelvic mass with enhancing septate and solid areas within it and abutting the uterus, urinary bladder wall, right iliac vessels and adjoining sigmoid colon: malignant ovarian mass.

She underwent a bilateral salpingo-oophorectomy along with infracolic omentectomy and bilateral pelvic lymphadenectomy; the specimens were sent to the Pathology department.

Gross findings: An already cut open left ovarian mass was received, with attached fallopian tube; the ovarian mass measured 15x12x10cm . Outer surface was smooth and shiny, well encapsulated. Cut surface was grey to tan brown, partly cystic and partly solid, multiloculated with focal papillary excrecenses were seen. Attached fallopian tube was within normal limits. Other ovary with attached fallopian tube were normal. Separately send bilateral pelvic lymph nodes contained fibrofatty tissue with no grossly discernible nodes.

Figure 1: Cut surface revealing partly cystic, partly solid grey to tan brown mass with focal papillary excrecenses

Microscopic examination: The ovarian mass revealed tumor epithelial cells arranged in papillae and sheets with transitional type epithelium, with cytologic atypia, pleomorphism, hyper chromatic nuclei with nuclear grooving, increased mitotic activity and moderate amount of cytoplasm.

Nests of benign transitional cells were seen with round to ovoid nuclei, occasional nuclear grooving, and pale cytoplasm surrounded by hyalinized stroma.

Cysts with focal lining by transitional epithelium and fibrovascular cores, with round to oval pleomorphic cells with cytologic atypia & moderate amount of cytoplasm were also seen. Necrosis, hemorrhage, inflammatory cell infiltrate & calcifications were noted.
Attached fallopian tube, opposite ovary & tube were within normal limits. Bilateral pelvic lymph nodes were negative for tumor deposits.
Immunohistochemical examination revealed variable positivity for CK and variable focal positivity for GATA 3. CK7, CK20, uroplakin, EMA, p63, CEA, PAX-8 were negative.

Post operative period was uneventful, and the patient was referred to the regional cancer centre of our hospital for further management by chemotherapy.

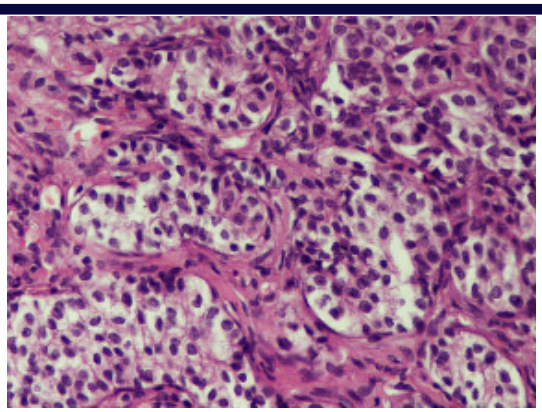

Figure 2: Photomicrograph showing nests of benign transitional cells were seen with round to ovoid nuclei, occasional nuclear grooving, and pale cytoplasm surrounded by hyalinized stroma. (H& E, 400X)

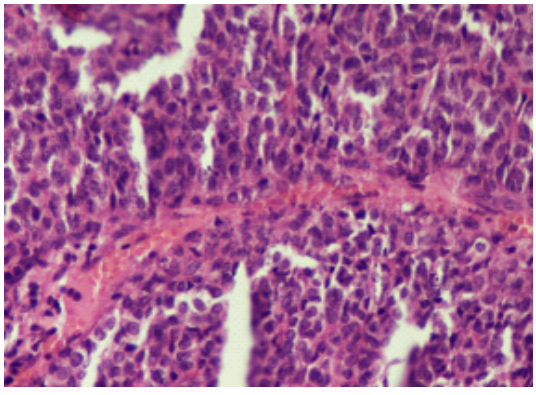

Figure 3: Photomicrograph showing sheets of tumor cells with transitional type epithelium, cytologic atypia, pleomorphism, hyperchromatic nuclei with nuclear grooving, increased mitotic activity and moderate amount of cytoplasm. (H&E, 400X)

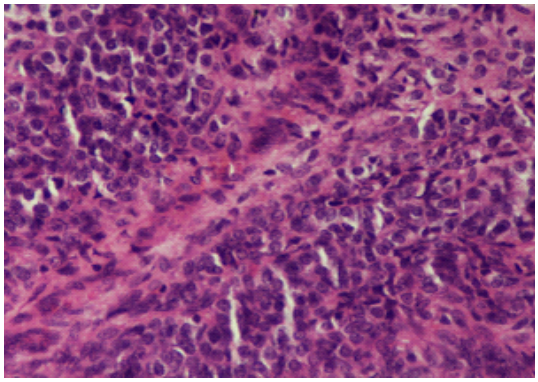

Figure 4: Photomicrograph showing tumor cells arranged in papillae with fibrovascular core. (H& E, 400X)

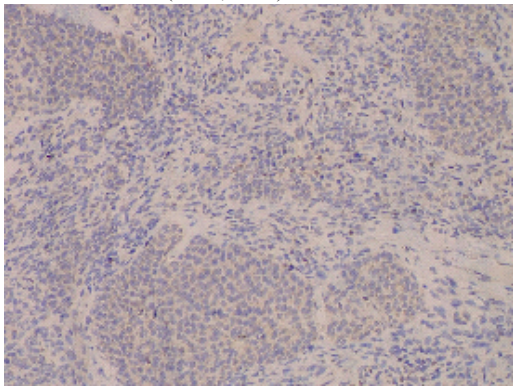

Figure 5: Photomicrograph showing variable focal positivity of tumor cells for GATA-3(IHC, 400X)

DISCUSSION:

Brenner tumor js a rare epithelial neoplasm,accounting for less than 2% of ovarian malignancies. (2) The malignant form is particularly rare, accounting for less than 5% of all Brenner tumor; the other subtypes being benign and borderline variants. [(1)(2)]

The transitional epithelium resembles urothelium, with a relatively uniform population of stratified cells, with grooved ovoid nuclei; hence named so. [(3)]

The pathogenesis remains unclear. Despite demonstrating a transitional type differentiation, a urothelial tract derivation is not favored. While initial reports suggested a ovarian surface epithelial derivation, recent reports favor origin from Walthard cell nests, foci of transitional cell metaplasia within adnexa. [(7)(8)]

Non specific clinical findings are present, such as pelvic or abdominal pain and a mass; with a mean age of 63 years, befitting our case of a 58 year old lady with abdominal discomfort. The size of the tumor varies unto 25cm, with a mean of 14cm. [(4)]

Clinical utility of CT and MRI are unclear, as malignant Brenner tumor does not have pathognomic imaging features; it's utility lies more in assessing tumor location, size, burden and surgical planning. Thus the primary diagnostic modality is histopathological examination. [(1)]

On microscopy, the malignant form is diagnosed when a benign or atypical proliferative component is identified within or is contiguous with the tumor. [(3)]

Thick, blunt elongated papillary fold are the characteristic feature, with fibrovascular cores and a transitional epithelial lining resembling urothelium. Half of cases show a solid pattern. [(4)]

Majority show microspaces, large cysts and necrosis. (4) Less than 20% show focal squamous or glandular differentiation. Stromal invasion occurs as haphazard infiltrative growth at base of papillae, or as extensive solid areas, or as solid tumor similar to the benign component; but more angulated and a disorderly growth pattern. (3) About half show slit like fenestrations. [(4)]

Prominent cytologic atypia and mitotic activity is seen, corresponding to grade 2 or 3 papillary transitional cell carcinoma of urinary tract. (3) The primary differential remains transitional cell carcinoma. [(3)]

Published data on immunohistochemistry is limited presently.(3) Immunohistochemistry reveals positivity for CK7, WT1, p16, P53, with negativity for CK20, in contrast to transitional cell carcinoma and a minority being positive for CEA, CA 19-9, urothelial markers uroplakin 3 and thrombomodulin. (3)(5)(6) In our case however, variable positivity for CK and only focal positivity for GATA-3 was seen. Thus histopathology remains key in the accurate diagnosis of this tumor.

No reliable tumor markers have yet been identified for malignant Brenner tumor. In our case major tumor markers were all within normal limits. Although CA-125 has a low sensitivity (50-62%) and moderate specificity (94-98.5%), it is the most widely used serologic marker in patients with surface epithelial tumors. (9) Considering that malignant Brenner tumor belongs to this family, it seems sensible to follow up with this marker for recurrence post resection. [(1)]

The prognosis depends on the FIGO stage, with a 5 year disease specific survival rate of 94.5% and 51.3% for disease confined to ovary and extra ovarian disease respectively. (10)(12) This case highlights the clinical presentation of this rare neoplasm, the diagnostic utility of histopathological examination as a primary tool and the immunohistochemical findings .

CONCLUSIONS:

Early recognition of the clinical and radiological findings of malignant Brenner tumor combined with the primary diagnostic modality, histopathology aids in accurate diagnosis and timely initiation of therapy. Owing to the rarity of malignant Brenner tumor, sufficient data regarding the same are currently lacking. Equally important is differentiating it from transitional cell carcinoma. This case brings to light the presentation of such a case, and the histopathological features of the same.

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