# Brenner or non-Brenner's?: A diagnostic challenge!!

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## ABSTRACT

Ovarian tumors are broadly classified into surface epithelial, germ cell, sex cord, and stromal tumors and other rarer special categories under the WHO scheme. The Brenner tumors of the surface epithelial group pose a diagnostic challenge in special context of its histogenesis. We present a case of 46-year-old female with an ovarian mass and ascitis. The surgico-pathological evaluation of gross and microscopic features suggested a malignant Brenner tumor. Transitional cell carcinoma (non-Brenner) was kept as a diagnostic differential and a challenging pitfall.

Key words: Brenner, histiogenesis, non-Brenner, ovarian tumor, transitional cell

# **INTRODUCTION**

Brenner tumor has been classified by the purists as benign Brenner tumor, intermediate Brenner tumor, and malignant Brenner tumors on histopathology.<sup>[1]</sup> Brenner tumors constitute between 1% and 2% of all ovarian neoplasms. The average age at presentation is approximately 50 years, about 70% of the patients being over 40 years of age. Among the Brenner, neoplasms with borderline or malignant tendencies are reported to be <2%.

No other ovarian tumor has provoked much hypothesis as far as the cell of origin goes as has the Brenner group of tumors. Most authors currently favor for the origin of the Brenner tumor as a kind of metaplastic change occurring in the surface epithelial lining of the ovary or the cysts derived from the ovarian surface epithelia.<sup>[2]</sup> This particular case report is of a rare malignant variant of Brenner tumor presenting as an unilateral ovarian mass in a 46-year-old female with abdominal lump and bleeding per vagina.

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# **CASE REPORT**

The patient gives a history of gradually increasing abdominal mass for past 6 months. She has attained menopause 8 months back. She now presents with 15 days history of bleeding per vagina with pain in abdomen. She has past history of left-sided ovary with cyst, for which she underwent an ovariectomy.

Per-abdominal examination revealed a firm to cystic mass of 18 to 20 wks size arising in the pelvis. Per-speculum examination shows cervix deviated to the left, pulled up. Per-vaginal examination revealed cervix high up, posterior as well as right fornix hard mass felt. CT abdomen with contrast was carried out employing spiral axial scans of abdomen in venous and arterial phase. CT reports suggested a large solid to cystic mass with irregular thickened wall, measuring  $10.1 \times 11.8 \times 12$  cm seen in right lumbar region, extending up to the pelvis [Figure 1]. The CT impression comprised of a differential between ovarian cyst/ mesentric cyst with ascitis and peritoneal metastasis.

On explorative laparotomy, a firm whitish-yellow, solid to cystic approximately  $11 \times 12 \times 13$  cm mass, partially encapsulated, was seen completely replacing the right ovary and enveloping the posterior wall of the uterus as well as the cervix. The mass was also firmly adherent to the intestine (descending colon) along with multiple nodularity in the mesentery. Ascitic fluid was drained. Warthim's

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hysterectomy was done, and part of mesentery with the adherent segment of the descending colon was also excised.

The resected specimen was sent for surgical pathology examination. The histopathological evaluation was carried out. Grossly, a specimen of uterus cervix with ovarian mass (right side) was received along with part of mesentery and peritoneum as well as part of the descending colon. The ovarian mass was of size 10.5  $\times$  12.5  $\times$  13 cm externally, partially capsulated with bosselations, firm to soft (cystic) in consistency. Cut section showed variegated areas, whitish-yellow solid areas with multiloculations forming cystic areas containing greenish-yellow mucin-like material. Microscopically, there was presence of sheets of malignant-appearing transitional cells forming papillary projections at places [Figure 2]. The malignant epithelial cells were also seen, infiltrating the serosa of the uterus as well as involving the endocervical area [Figure 3]. The mesenteric nodules and the lymph nodes excised showed evidence of metastatic deposits of epithelial malignancy. Final histopathological impression was of a malignant Brenner tumor with widespread metastasis. However, considering that there were severely atypical Brenner cell rests in the neoplastic tissue, the term of non-Brenner tumor (transitional cell carcinoma) was kept reserved. The patient has been put on chemotherapy with cisplatin, adriomycin, and cyclophospamide for 5 cycles. She has tolerated the first cycle well.

### DISCUSSION

The researchers have always made many a claim, debate, and speculation regarding the origin of Brenner tumor. The most prominent amongst the theories is of the origin of the tumor cells from the urinary tract epithelium, i.e. either from the embryonic remnants of the mesonephric duct left in the ovary or there is an element of metaplastic change in the ovarian germinal epithelia, resulting in Brenner tumors closely resembling the transitional cell carcinoma of the urinary bladder.<sup>[3]</sup>

Benign Brenner tumors microscopically appear to show unremarkable solid urothelial or transitions cell rests (nests). With multiple cystic components and abundance of mucin secretions, the tumor is better designated as metaplastic Brenner. If at all there is presence of long papillary fronds along with nuclear atypia, then the lesion is termed as proliferating Brenner's. With greater evidence of atypia, but no stromal infiltration, the tumors are better known as borderline Brenner tumor. In case of evidence of infiltration by malignant epithelial cells into the stroma, the tumor is called as malignant Brenner tumor.<sup>[4]</sup> The malignant Brenner tumor are the ones, in which besides the presence of malignant transitional cells,



Figure 1: CT contrast abdomen with ovarian mass



Figure 2: ×40 view of H and E malignant urothelial cells papillary formations



Figure 3:  $\times40$  view of H and E stained slide showing groups of infiltrating malignant transitional cells

there is still elements of benign-appearing urothelial cell rests, suggesting the origin of malignant transformation from these rests. Besides these categories, there is a total separate entity, known as the primary transitional cell carcinoma of the ovary, often referred to as non-Brenner type transitional cell carcinoma. The characteristic of these non-Brenner tumors is that they exist without the presence of the so-called benign urothelial cells rests in the same tumor tissue.

The Austin and Norris<sup>[5]</sup> hypothesis suggests that the prognosis of patients with malignant Brenner tumor is better as in comparison to transitional cell carcinoma (non-Brenner type).<sup>[6]</sup> However, the fact that even the immunohistochemistry seems to be rather unreliable in confirming whether the tumor mass is a primary transitional cell carcinoma (non-Brenner type) or is a malignant Brenner as the cytokeritins and uroplakin have been inconsistent and variable in their results on both subsets of tumors.<sup>[7]</sup> The only suggestion and recommendation for the same could be to practice extensive histopathological sectioning of the tumor mass.

This particular case reignites the histogenetic debate, as the microscopic details of the tumor tissue revealed extensive high-grade transitional cell carcinoma in majority of the tumor mass with coexisting well-demarcated rests of severely atypical transitional epithelia (grade II), with no evident benign urothelial rests. Keeping the authors in dilemma in due consideration to the Austin Norris hypothesis.

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