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Pure Transitional Cell Carcinoma of Ovary- A Rare Case Report in a Premenopausal Woman

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Abstract

Transitional cell carcinoma of ovary is a rare subtype of ovarian surface epithelial tumors, pure forms comprising of only 1% of all epithelial ovarian cancers. It is defined as a primary ovarian tumor in which urothelial features are present histologically resembling malignant brenner tumor with absence of benign, metaplastic or proliferating brenner tumor components. A 48 year old premenopausal female presented with abdominal pain and distention since 3 months duration. Patient had no significant past medical, surgical or family history. On per-abdominal examination, a firm to hard mass (12x10cm) was noted in the right iliac region. CA-125 levels were raised. Abdominal computed tomography scan was suggestive of a large septated lesion in the right adnexa. A provisional clinical diagnosis of malignant right adnexal mass was made. Total abdominal hysterectomy with right salpingo-oophorectomy and pelvic lymph node clearance was performed. The patient received chemotherapy with carboplatin and cyclophosphamide every three weeks for four cycles. Mainstay of treatment is surgical resection followed by standardized chemotherapy. Clinically it is indistinguishable from other types of ovarian carcinomas. It is important to correctly diagnose this tumor because of its rarity, favorable response to chemotherapy and a better patient outcome therefore histopathological examination plays a pivotal role.

Keywords: Transitional cell carcinoma, Pure, Urothelium. Epithelial Ovarian Carcinoma.

Introduction

Brenner tumor of ovary is classified as benign, borderline or malignant as per the WHO classification (2004).[1] It comprises of <5% of all epithelial ovarian carcinomas. Malignant brenner tumor accounts for only 2% of all brenner tumors of ovary.[2]

Transitional cell carcinoma (TCC) of ovary is a rare subtype of ovarian surface epithelial tumors, pure forms comprising of only 1% of all epithelial ovarian malignancies.[3,4,5,6]

Pure TCC was first described by Austin and Norris in 1987.[7] It is defined as a primary ovarian tumor in which urothelial features are present histologically resembling malignant brenner tumor with absence of any forms of (benign, metaplastic or proliferating) brenner tumor component as well as lacking stromal calcification.[9]

It originates directly from the pluripotent surface epithelium of ovary with cells having urothelial potential.[8] Therefore the tumors are called as pure TCCs. Incidence of TCC of ovary still remains unknown and it was put forth that they should be identified as a separate entity. However the recent WHO classification does not classify TCC ovary as a separate entity and suggest that entity and suggest that in the absence of Brenner component, a high grade serous tumor with transitional cell differentiation should be thought of.[9]

It is important to correctly diagnose this tumor because of its rarity, favorable response to chemotherapy and a good survival rate.[10]

Case Summary

A 48 year old premenopausal female presented with abdominal pain and distention since 3 months duration. Patient had no menstrual irregularities. Patient had no significant past medical, surgical or family history. On per-abdominal examination, a firm to hard mass (12x10cm) was noted in the right iliac region. Per vaginal examination revealed a hard mass in the right adnexal region, which was felt through all the fornices and was non-tender and had restricted mobility. Pouch of douglas and rectal fossa were free with no nodularity. All routine hematological and biochemical investigations were within normal limits. CA-125 levels were raised. Carcinoembyronic antigen (CEA) and CA-199 were within normal ranges. On ultrasonography, a right ovarian mass was noted with homogeneous echogenicity, having solid and cystic areas. Other abdominal and pelvic organs were normal. There was no evidence of lymphadenopathy or ascites. Abdominal computed tomography scan was suggestive of a large septated lesion in the right adnexa with irregular solid foci as well as cystic spaces. The uterus was found to be enlarged with multiple small fibroids. Based on these findings, a provisional diagnosis of malignant right adnexal mass was made. Total abdominal hysterectomy with right salpingo-oophorectomy and pelvic lymph node dissection was performed and the specimen was sent for histopathological examination. On gross examination the tumor mass was lobulated, measured 12x10x8cm. On cut section, multiple solid areas along with few cystic areas were noted. Microscopic examination showed tumor arranged in solid sheets and papillae lined by transitional epithelium. Cells were separated by prominent fibrovascular stroma. Individual tumor cells showed pleomorphism, had round to ovoid nuclei, vesicular chromatin, prominent nucleoli and granular to vacuolated cytoplasm. 6-8 mitotic figures per high power field were noted. Additionally, there was endometrial hyperplasia along with leiomyomata in the uterus. Immunohistochemical studies showed that the tumor was positive for WT1, cytokeratin 7 and negative for cytokeratin 20. On the basis of these features, a diagnosis of pure primary TCC of right ovary was rendered. The patient received chemotherapy with carboplatin and cyclophosphamide every three weeks for four cycles. The patient is currently under follow-up period and has been disease free for one year.

Discussion

TCC of the ovary is a rare subtype of ovarian surface epithelial ovarian carcinomas. It was first described by Austin and Norris in 1987. TCC of ovary has close

morphologic resemblance to TCC of bladder and behaves more aggressively as compared to malignant brenner tumor, so they concluded that TCC arises directly from pluripotent surface epithelial cells of ovary with urothelial potential rather than from a benign or proliferative Brenner tumor component .[7] Transitional cell tumors account for about 2% of all ovarian tumors. Pure forms of TCC of ovary represent only 1% of surface epithelial tumors.[5] However true incidence of TCC of ovary is still unknown.

Mean age of presentation is 59 years and most are postmenopausal.[11] In our case patient was premenopausal.

CA-125 is a useful serum marker for detecting progression and recurrence.[11] In our case patient had drastically reduced levels after first cycle of chemotherapy. According to a study done by Eichhorn and Young, TCC ovary typically shows a diffuse undulating thick bands, trabecular growth pattern along with numerous micro-cystic spaces of varying sizes followed by large blunt papillae, necrosis, slit-like fenestrations, bizarre giant cells, gland like spaces, squamous differentiation and psammoma bodies. In our case, undulating bands and diffuse patterns were noted as well as many slit-like fenestrations and micro-cystic spaces were also seen. Areas of necrosis and tumor giant cells were also seen.[12]

Silva et al reported that thick papillary proliferations, a smooth luminal border and projection into empty spaces are the prerequisites for diagnosis of TCC.[5]

Immunohistochemically, these tumors have a different profile as compared to brenner tumors and TCC of urinary tract.[13] Both Brenner tumor and ovarian TCC express CK7 but lack expression of CK20 unlike other urinary tract urothelial tumors. Ovarian TCCs are negative for CK20, thrombomodulin and Uroplakin III as opposed to bladder TCCs.[9,12] Ovarian TCC are often positive for vimentin, CA-125 and wilms tumor protein unlike TCC of bladder.[12] Also ovarian TCCs are strongly positive for estrogen receptors, a feature that helps in differentiating it from papillary urothelial carcinoma metastatic to ovary.[14] In our case, tumor was immunoreactive for WT1, CK7 and negative for CK20.

Its histogenesis has been suggested from multipotent coelomic epithelium either at the ovarian surface or from epithelial inclusion cysts which can differentiate into several mullerian forms. It was also postulated that walthard nests are considered as precursors for brenner tumors but mostly these are present in the extraovarian tissue and the cells rarely express uroplakins.[13]

Problems can arise in distinguishing undifferentiated carcinoma and poorly differentiated serous carcinoma in cases having extensive slit like spaces and giant cells. Features favoring the diagnosis of primary TCC of ovary include transitional cells, papillae, thick bands of transitional epithelium and micro spaces. Absence of benign or borderline and brenner elements ruled out malignant brenner tumor.

According to a study, it was proposed that TCC may be more chemosensitive than other common epithelial tumors of ovary.[16] It was concluded by Gershenson et al that advanced staged ovarian TCC was more chemosensitive and had a better prognosis than poorly differentiated serous carcinoma.[17]

Conclusion

Pure primary TCC is a rare subtype comprising of only 1% of surface epithelial tumors. Clinically it is indistinguishable from other types of ovarian carcinomas. IHC and clinical correlation helps in differentiation from metastatic TCC. Mainstay of treatment is surgical resection followed by standardized chemotherapy. Even in advanced stages prognosis is

considerably favorable as compared to serous carcinoma.[15]

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Legends Figure

Figure 1: Microphotograph showing papillae with fibrovascular cores and undulating thick bands lined by transitional type epithelium resembling urothelium. (H & E stain, 4x).

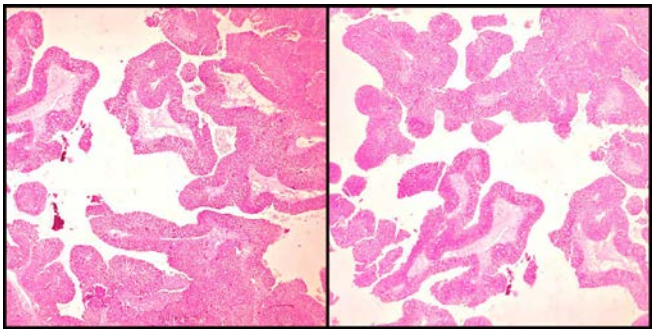

Figure 2: Photomicrograph shows tumor arranged in diffuse sheet pattern. (H & E stain, 4x).

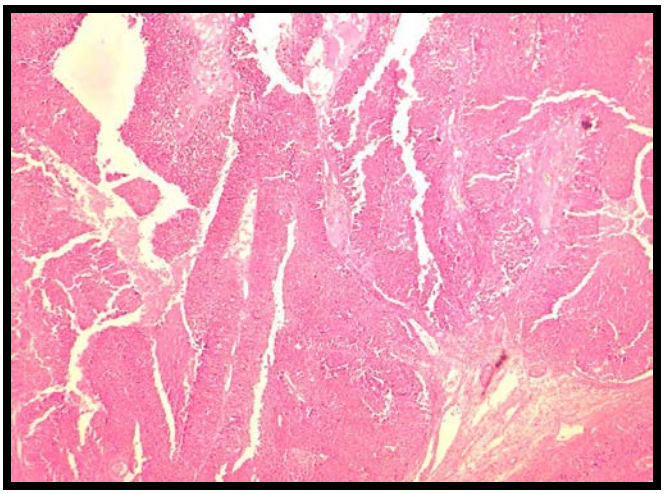

Figure 3: Microphotographs showing slit like fenestrations and numerous intra-epithelial micro-cystic spaces of varying sizes. (H & E stain, 4x and 10x).

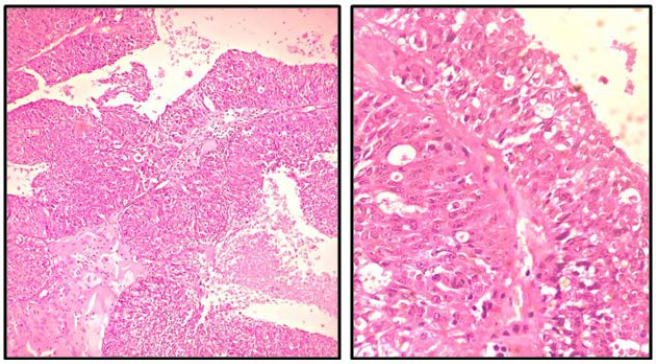

Figure 4: Areas of necrosis was also noted. (H & E stain, 10x).

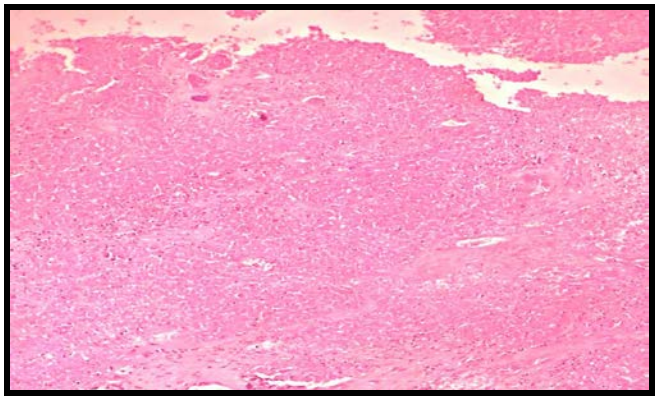

Figure 5: Microphotographs showing pleomorphic tumor cells with round to ovoid nuclei, vesicular chromatin, prominent nucleoli and granular to vacuolated cytoplasm. (H & E stain, 40x).

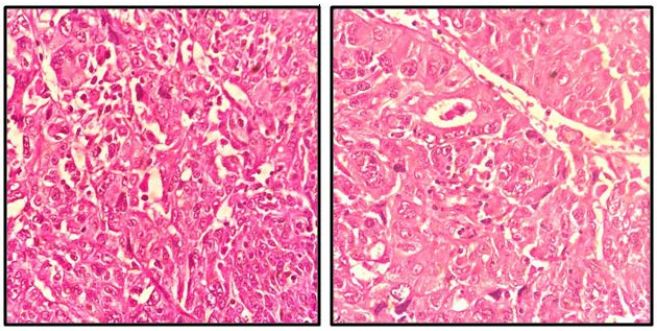

Figure 6: Microphotograph showing bizarre giant cells (Black arrows). (H & E stain, 40x).