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Case Report

Pathology Section

Transitional Cell Carcinoma of the Ovary: Case Series and Review of Literature

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ABSTRACT

Transitional cell carcinoma (TCC) of the ovary is a recently recognized, subtype of ovarian surface epithelial cancer; the pure form accounting for only 1% of surface epithelial tumors. It has been described as a primary ovarian carcinoma with definite urothelial features but no benign, metaplastic and/or proliferating Brenner tumor (BT) identified. Recognition of such tumours is important because of its rarity, favorable response to chemotherapy and an improved patient survival. A case series of primary TCC of the ovary (3 cases) with brief review of literature is being presented.

Keywords: Brenner tumor, Ovarian carcinoma, Surface epithelial tumors, Urothelial tumors

CASE SUMMARY

A series of 3 cases of Transitional cell carcinoma of the ovary are presented here. Case details are summarized in [Table/Fig-1].

DISCUSSION

TCC of the ovary is a rare subtype of ovarian surface epithelial cancer classified under transitional cell tumors along with benign, borderline and malignant Brenner tumor [1]. It was first defined by Austin and Norris in 1987. They reported a group of patients who had ovarian tumors presenting with histologic features similar to those seen in a malignant Brenner tumor, but the tumors lacked associated benign Brenner tumor component and thus was distinguished from malignant Brenner tumor. In addition, TCC lacks the prominent stromal calcification. Because TCC of the ovary has close morphologic similarities to TCC of the bladder and it behaves more aggressively than malignant Brenner tumor, Austin and Norris concluded that ovarian TCC arises directly from the pluripotential surface epithelium of the ovary and from cells with urothelial potential, rather than from a benign or proliferative Brenner tumor precursor. The clinical presentation is indistinguishable from other types of ovarian carcinoma [2].

TCC of the ovary has been described as a primary high grade carcinoma in which definite urothelial features are present but no benign, metaplastic and/or proliferating Brenner tumor can be identified. The pure form of TCC accounts for only 1% of surface epithelial tumours, mixed carcinomas with a minor TCC component comprise 3% and those with a predominant TCC component make up 5% [3]. These tumors have a immunohistochemical profile that is different from ovarian Brenner tumors and TCC involving the urinary tract. It has been proposed that ovarian TCC may represent a high grade serous carcinoma with morphologic features of transitional cell differentiation rather than being a distinct tumor type [4]. Recognition of such tumors is important because of a favorable response to chemotherapy and an improved patient survival [3,5].

Eichhorn and Young found a variety of histologic features that, in aggregate, produced a distinctive appearance. The patterns included, in order of frequency; undulating, diffuse, insular, and trabecular. Punched out microspaces, large cystic spaces, and large, blunt papillae were also common. The tumor cells tend to be relatively monomorphic with typically pale and granular cytoplasm, although occasionally it is clear or oxyphilic. The round to oblong nuclei have a large, single nucleolus or a longitudinal groove. Although nonspecific, slit-like fenestrations and bizarre tumor giant cells, two features of high-grade serous carcinoma, are frequently seen in TCC of the ovary [6]. In present study [Table/Fig-2a, 2b], all three cases showed presence of papillae [Table/Fig-2c] and tumor giant cells [Table/Fig-2d]. Squamous metaplasia was observed in a single case (case 1).

The histogenesis of Brenner tumor is thought to be from multipotential celomic epithelial cells, either at the surface of the ovary or from epithelial inclusion cysts, which can differentiate into several mullerian forms. It has also been suggested that Walthard nests are precursor lesions for Brenner tumors but this is a problematic theory as most Walthard nests are found in extraovarian tissue and the cells rarely express uroplakins. There are little data relevant to the histogenesis of TCC, but it is suggested to be a variant of high-grade serous carcinoma [4].

The immunoprofile of TCCs is similar to that of other surface epithelial carcinomas. Both Brenner tumor and ovarian TCC express CK7 but lack expression of CK 20 unlike urinary tract urothelial neoplasms. Most ovarian TCCs are immunoreactive for Wilms tumor protein (WT1) and, in contrast to Brenner tumors and extraovarian urothelial tumors, they typically lack reactivity for uroplakin III and thrombomodulin. p63, another urothelial differentiation marker, has been demonstrated in benign and borderline Brenner tumors but not in ovarian TCC [4,6-9]. Unlike bladder TCCs, ovarian TCCs are often positive for vimentin, CA-125 and WT [1]. Croft et al., concluded that almost all of the ovarian TCCs marked strongly for estrogen receptors (ERs), a characteristic that may help to differentiate these lesions from papillary urothelial carcinoma metastatic to the ovary [10]. In present study, immunohistochemistry for ER showed weak nuclear positivity in all three cases [Table/Fig-2e,f,g].

With optimal surgical resectability and standardized chemotherapy TCCs have a significantly better prognosis as compared to all other types of ovarian carcinomas. A propensity for micronodular rather than macronodular extraovarian spread and better surgical resectability due to lesser degree of diffuse infiltrative growth of TCC might contribute to the survival benefit [11]. Hence, prognosis of patients with TCC is considerably better than those with the more common serous carcinoma, even in advanced stage [5].

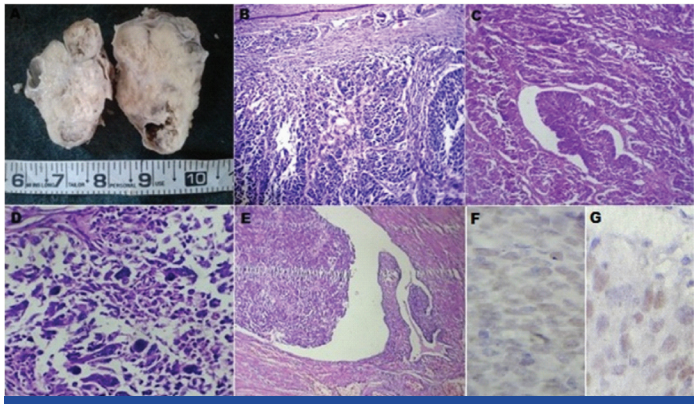
DIFFERENTIAL DIAGNOSIS

Primary TCC can be closely mimicked by metastatic disease [12]. The usual clinical, gross, and microscopic criteria for differentiating primary from secondary ovarian tumors are helpful in this differential diagnosis; immunohistochemical staining may also be of assistance. Urinary tract tumors of this type have been shown to be reactive for CK20 and thrombomodulin, in contrast to primary ovarian TCC [7-9].

A more common problem is distinguishing moderate to high-grade TCCs from other poorly differentiated surface epithelial carcinomas, particularly poorly differentiated serous carcinomas and undifferentiated carcinomas. Such tumors have a greater tendency to grow in diffuse masses; when they have a pattern simulating that of papillary TCCs, it is much more often caused by

	Case 1	Case 2	Case 3
Presentation	Pain abdomen & h/o incomplete evacuation of urine	Pain abdomen	Pain abdomen
Ultrasound findings	Solid mass with degenerative changes in pelvis; probably subserosal fibroid or right ovarian mass	Right Ovarian mass, solid and cystic with moderate ascites	Right ovarian mixed density mass
Other investigations	Cystoscopy – Base of bladder neck, trigone completely bulge touching anterior wall; Mucosal congestion & ulceration	Not Available	CT Abdomen – Right ovarian tumor measuring 10.5x7cm and minimal fluid in the uterine cavity
Surgical Procedure	Total abdominal hysterectomy with left salpingooophorectomy, right salpingectomy & excision of right ovarian tumor & right internal iliac artery ligation	Right salpingoooporectomy with sub-daiphragmatic and pelvic lymph node dissection	Total abdominal hysterectomy with right salpingo-oophorectomy
Gross			
Size of ovarian mass	8.5x5x3cm	8x7x6cm	6x4x3cm
Surface & Consistency	Solid bosselated mass adherent to the posterior uterine wall	Solid and cystic mass with irregular nodular surface. Tumor extending beyond the capsule at one area.	Irregular, nodular solid mass.
Cut section	Gray white, nodular areas with tiny cystic spaces and areas of haemorrhage	Mainly solid with few cystic spaces & areas of necrosis & haemorrhages	Grayish white solid areas with areas of haemorrhage, necrosis & few cystic spaces [Table/Fig-2a].
Microscopy	Transitional cells in large papillae with fibro-vascular core, sheets and acini [Table/Fig-2b, 2c]. Bizzare cells with few giant cells and necrosis also noted. Focal squamous metaplasia seen	Solid sheets, nests and cords of malignant transitional cells, multinucleate giant cells [Table/Fig-2d] with large areas of haemorrhage & necrosis. Few papillary structures lined by transitional cells seen within cystic spaces	Cords, sheets and papillae of pleomorphic transitional cells with large areas of necrosis. Tumor giant cells & multiple mitoses (6-8/10 HPF) noted.
Extent	Infiltration into posterior uterine wall	Infiltration into ipsilateral fallopian tube	Infiltration into ipsilateral fallopian tube [Table/Fig-2e].
Immunohistochemistry	Weak nuclear positivity for ER [Table/Fig-2f].	Weak nuclear positivity for ER	Weak nuclear positivity for ER [Table/Fig-2g].

[Table/Fig-1]: Case summary



[Table/Fig-2]: A- Gross: Cut section showing solid ovarian tumour with cystic areas and necrosis, B- Transitional cells in sheets (H & E, 10X), C- Papillae lined by transitional cells (H & E, 10X), D- Bizzare giant cells and mitosis (H & E, 40X), E- Infiltration into fallopian tube (H & E, 10X), F&G- Weak nuclear positivity for ER in case 1 & 3 respectively (40X)

the presence of pseudopapillae resulting from necrosis with dropout of necrotic cellular debris. TCCs have broad papillae lined by cells, some of which are recognizable as transitional cells; similar cells form undulating, thick bands. Scattered microspaces, which are often numerous, also favor a diagnosis of TCC [6].

CONCLUSION

TCC of the ovary is a rare and relatively recently established entity. The pure form of TCC accounts for only 1% of surface epithelial tumours. Though currently classified under transitional cell tumors [1], the exact histogenesis of the tumor is unclear. In addition to routine histopathological features, markers like WT-1 and ER are helpful in establishing a diagnosis. The recognition of this tumor holds significance due to its biologic behavior. Patients with TCC have considerably better outcome with optimal resection and standardized chemotherapy as compared to other ovarian neoplasms particularly serous adenocarcinoma.

REFERENCES

[1] Lee KR, Tavassoli FA, Prat J, et al. Tumors of the ovary and peritoneum. In: Tavassoli FA, Devilee P, eds. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. *Lyon: IARC Press*. 2003:113–45.
[2] Austin RM, Norris HJ. Malignant Brenner tumor and transitional cell carcinoma of the ovary: a comparison. *Int J Gynecol Pathol*. 1987;6: 29-39.
[3] Silva EG, Robey-Cafferty SS, Smith TL, Gershenson DM. Ovarian carcinomas with transitional cell carcinoma pattern. *Am J Clin Pathol.* 1990;93: 457-65.
[4] Ali RH, Seidman JD, Luk M, Kalloger S, Gilks CB. Transitional Cell Carcinoma of the Ovary is Related to High-grade Serous Carcinoma and is Distinct From Malignant Brenner Tumor. *Int J Gynecol Pathol*. 2012 Nov;31(6): 499-506.
[5] Gershenson DM, Silva EG, Mitchell MF, Atkinson EN, Wharton JT. Transitional cell carcinoma of the ovary: a matched control study of advanced-stage patients treated with cisplatin based chemotherapy. *Am J Obstet Gynecol.* 1993;168: 1178–85.
[6] Eichhorn JH, Young RH. Transitional cell carcinoma of the ovary. A morphologic study of 100 cases with emphasis on differential diagnosis. *Am J Surg Pathol.* 2004;28: 453-63.
[7] Ordonez NG. Transitional cell carcinomas of the ovary and bladder are immunophenotypically different. *Histopathology.* 2000;36: 433-38.
[8] Soslow RA, Rouse RV, Hendrickson MR, Silva EG, Longacre TA. Transitional cell neoplasms of the ovary and urinary bladder: a comparative immunohistochemical analysis. *Int J Gynecol Pathol.* 1996;15: 257-65.
[9] Logani S, Oliva E, Amin MB, Folpe AL, Cohen C, Young RH. Immunoprofile of ovarian tumors with putative transitional cell (urothelial) differentiation using novel urothelial markers: histogenic and diagnostic implications. *Am J Surg Pathol.* 2003;27: 1434-41.
[10] Croft PR, Lathrop SL, Feddersen RM, Joste NE. Estrogen receptor expression in papillary urothelial carcinoma of the bladder and ovarian transitional cell carcinoma. *Arch Pathol Lab Med.* 2005;129: 194–99.
[11] Kommoss F, Kommoss S, Schmidt D, Trunk MJ, Pfisterer J, du Bois A. Survival benefit for patients with advanced-stage transitional cell carcinomas vs. other subtypes of ovarian carcinoma after chemotherapy with platinum and paclitaxel. *Gynecol Oncol.* 2005;97: 195–99.
[12] Young RH, Scully RE. Urothelial and ovarian carcinomas of identical cell types: problems in interpretation. A report of three cases and review of the literature. *Int J Gynecol Pathol.* 1988;7: 197-211.

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