

Case Report

# Primary ovary transitional cell carcinoma after renal transplantation

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## Abstract

Transitional cell carcinoma (TCC) of the urinary tract is the most frequent malignancy following renal transplantation reported in Taiwan. A 67-year-old female underwent bilateral nephroureterectomy and bladder cuff excision because of bilateral hydronephrosis 5 years after cadaveric renal transplantation. The pathologic report was only atrophied kidney. Pelvic sonography and abdominal computed tomography showed a pelvic mass 8 years after transplantation. After gynecological surgery, the pathologic report of the left ovarian tumor was TCC, high grade, stage IIA. The patient then underwent four cycles of postoperative chemotherapy with carboplatin and gemcitabine. TCC of the ovary is a rare, recently recognized subtype of ovarian surface epithelial cancer. We present the first case of primary ovarian TCC following renal transplant. Copyright © 2011 Elsevier Taiwan LLC and the Chinese Medical Association. All rights reserved.

**Keywords:** Kidney transplantation; Ovary; Transitional cell carcinoma

## 1. Introduction

Renal transplant (RTx) recipients have a marked increase in cancer risk at a wide variety of sites. Malignant tumors developed in 15–20% of recipients 10 years after RTx.<sup>1</sup> In different geographic areas, the prevalence and characteristics of post-transplant malignancy show considerable differences. The predominant malignant tumors after RTx in Western countries are lymphomas, post-transplant lymphoproliferative disorders and carcinomas of the skin and lips, followed by cancers involving the genitourinary system.<sup>2</sup> Recently, several studies in Taiwan have demonstrated a markedly increased incidence of urinary tract transitional cell carcinoma (TCC) in RTx recipients, with an incidence rate of 4.1%.<sup>3,4</sup> Primary TCC of the ovary is a recently recognized subtype of epithelial cancer, with an incidence of 1–2%.<sup>5,6</sup> The common symptoms of this tumor include

abdominal pain, abdominal swelling or distention and weight loss. Herein, we present a case of post RTx TCC of the ovary found by routine sonography. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by postoperative chemotherapy.

## 2. Case report

A 67-year-old postmenopausal woman presented with bilateral native kidney hydronephrosis 5 years after cadaveric RTx. Bilateral native nephroureterectomy and bladder cuff excision were performed. The pathologic report was only atrophied kidney and no malignancy was observed. The post-operative course was uneventful. Unfortunately, routine follow-up abdominal sonogram 8 years after RTx disclosed a 4.6 cm cystic and hypochoic lesion over the left pelvis, possibly arising from the left ovary. Physical examination did not show any pelvic palpable mass because of ovoid abdomen of the patient. Computed tomography disclosed a pelvic mass measuring 5.6 × 5.2 × 4.0 cm (Fig. 1). There was no evidence of abnormal lymphadenopathy. The liver and graft kidney were unremarkable. Routine blood and

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Fig. 1. Abdominal computed tomography shows a complex adnexal mass measuring  $5.6 \times 5.2 \times 4.0$  cm.

biochemical test results were all within normal ranges. Initial investigation of tumor markers before surgery showed mildly elevated serum CA125 (35 U/mL; normal, 0–30 U/mL), but other markers including CA153, carcinoembryonic antigen and CA199 were all within normal ranges.

The patient underwent surgery under the impression of malignant ovarian tumor. The consistency of the white tumor was rubbery-firm, and it measured  $6.5 \times 5.5 \times 4.0$  cm in size. On section, the mass was solid and ill-defined; a cyst measuring  $4.3 \times 2.9 \times 1.2$  cm was identified within the compressed ovarian tissue. The cystic surface was intact and smooth with no rupture. After resection, there was approximately 150 mL of tan-colored cystic fluid in the cystic content. Grossly, several mural nodules, with the largest one about 0.6 cm, were noted on the inner surface of the cyst. Parasurgical frozen-section biopsy of the mural nodules demonstrated the presence of an ovarian malignancy. There was no enlargement of the paraaortic lymph node on palpation. Therefore, surgical staging procedures including total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic lymph node dissection were performed. The ascites was also sent for cytologic examination.

Microscopic examination of the ovarian tumor showed high-grade TCC with direct invasion to the wall of the fallopian tube (Fig. 2). Tumor cells resembled those occurring in the urinary tract, and they lacked a benign or borderline Brenner tumor component. There was no metastatic lesion, and the cytology of the ascites was also negative for malignant cells. The final diagnosis was TCC of the left ovary, high grade, stage IIA. Immunohistochemical studies showed that most tumor cells were cytokeratin (CK) 14 positive and CK20 negative (Fig. 3). Furthermore, CK 7 was positive only for tumor cells with glandular differentiation. Mucin stain was also negative for tumor cells.

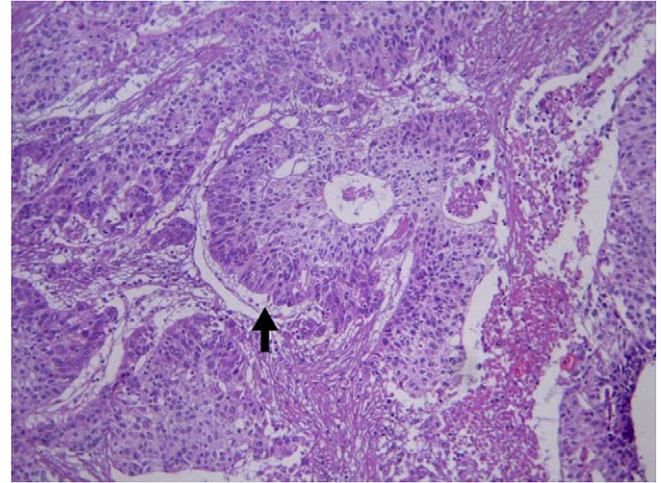


Fig. 2. Section showing transitional cell carcinoma (TCC) in a solid trabecular growth pattern that closely resembles TCC of the bladder. Foci of glandular differentiation are evident (arrow). (Hematoxylin & eosin,  $100\times$ ).

After recovering from surgery, the patient received post-operative chemotherapy with carboplatin ( $300 \text{ mg/m}^2$ ) and gemcitabine ( $1000 \text{ mg/m}^2$ ) every 3 weeks for four cycles. The CA125 level returned to normal range after the first course of chemotherapy. The patient is being regularly followed up at our outpatient department and has been disease-free for 8 months.

### 3. Discussion

TCC of the ovary was first defined by Austin and Norris in 1987.<sup>7</sup> They reported a group of patients who had ovarian tumors presenting with histological features similar to those seen in a malignant Brenner tumor, but the tumors lacked the associated benign Brenner tumor component. In addition to not having a benign Brenner tumor component, TCC lacks the prominent stromal calcification. Because TCC of the ovary has close morphological 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.<sup>7</sup>

Primary TCC is one of the subtypes of epithelial ovarian cancer, with an incidence of 1–2%.<sup>5,6</sup> Thus, when TCC of the ovary is encountered, the main differential diagnoses are primary ovarian TCC, metastasis from the urinary tract and malignant Brenner tumor. The site of origin can be decided by the pattern of distribution of the disease and the immunohistochemical staining. CK7 is expressed in ductal epithelium and transitional cells, and CK20 is expressed in crypt cells and transitional cells.<sup>8</sup> TCC of the urinary tract is virtually always CK7+/CK20+.<sup>9,10</sup> Ovarian TCCs are negative for CK20, thrombomodulin and uroplakin III.<sup>11,12</sup> Based on these findings, the combination of CK7 and CK20 staining showed a very specific pattern for TCC of the bladder and ovary.<sup>13</sup> Our patient had undergone bilateral native nephroureterectomy and bladder cuff excision for bilateral



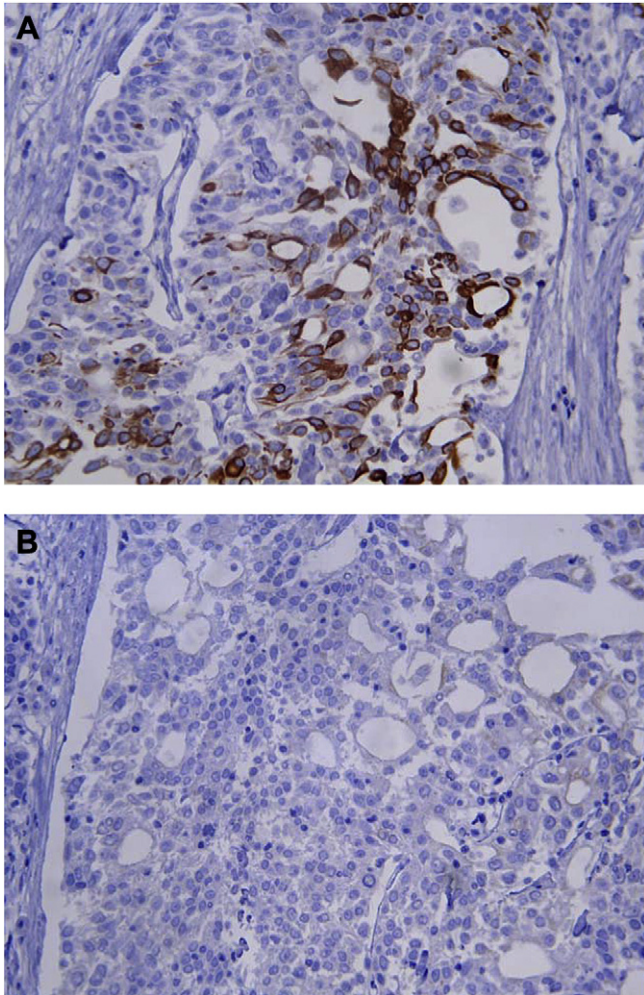


Fig. 3. Immunohistochemical staining for: (A) CK7 is focally positive in glandular differentiated areas (200 $\times$ ) and (B) CK20 is negative for tumor cells (200 $\times$ ).

hydronephrosis. The pathological report only noted atrophied kidney and no malignancy. The graft kidney was also unremarkable on computed tomography. Routine cystoscopy revealed no abnormality. The left resected ovary also disclosed CK7 positive and CK20 negative immunohistochemical staining. Therefore, the diagnosis was primary TCC of the left ovary.

Austin and Norris reported surgery alone for 14 patients with stage  $\geq$  stage II. None of the patients presented free of disease within 5 years.<sup>7</sup> TCC of the ovary is reported to be as sensitive to cisplatin-based chemotherapy as urinary tract TCC and has a better prognosis than other types of common epithelial tumors of the ovary. Gershenson et al. concluded that advanced-stage ovarian TCC was significantly more chemosensitive and associated with better prognosis than poorly differentiated serous carcinoma.<sup>14</sup> Kommos et al. also documented that patients with ovarian TCC had better prognoses compared to patients with all other types of ovarian carcinomas after standard chemotherapy.<sup>15</sup> An interesting characteristic of cancers among renal transplant recipients is their aggressiveness, which is increased as compared with the remainder of the

population that has not received transplantation. The role of immunosuppressive drugs as related to this aggressiveness should be taken into account. Therefore, the lowest possible dose of immunosuppressive agents in RTx recipients with developing cancers is recommended.

RTx recipients in Taiwan are at extremely high risk for TCC of the urinary tract. The development of TCC in RTx recipients is likely multifactorial and cumulative.<sup>3</sup> It is difficult to understand a cause/effect relationship between kidney transplantation and the development of TCC. Whether or not the development process of ovarian TCC has the same pathophysiological mechanism of urinary tract TCC after RTx warrants further research.

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