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Transitional Cell Carcinoma of the Ovary: A Case report and Review of the Literature

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ABSTRACT

Introduction: Transitional cell carcinoma (TCC) of the ovary resembles urothelial rather than ovarian surface epithelium. The histopathology pattern is diagnostic. Ovary TCC typically shows undulating, diffuse, insular, and trabecular growth patterns. **Case presentation:** A 72-year-old postmenopausal woman presented with progressive enlargement of abdominal girth and diffuse pain in October 2008. Abdominal ultrasound showed a pelvic mass with homogeneous echogenicity. Routine biologic test results were all within normal ranges; CA-125 below upper limit (35 mUI/l). Surgical staging procedures including total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and pelvic lymph node dissection were performed. The final diagnosis was TCC of the ovary, grade 3, FIGO stage IIIC. The patient underwent six cycles of chemotherapy with carboplatin and paclitaxel. She was disease-free for 10 months. At progression, liposomal doxorubicin was initiated. At new progression, reintroduction with carboplatin and paclitaxel plus bevacizumab was administered. She had complete response documented by positron emission tomography-computed tomography (PET-CT) scan. **Conclusion:** Primary TCC of the ovary is a rare subtype of epithelial ovarian cancer. Surgical resection remains the primary therapeutic approach, followed in some cases by adjuvant chemotherapy. It is sensitive to platinum-based combinations. The prognosis of these tumors is better than for other types of ovarian cancers. (J CANCEROL. 2014;1:32-5)

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INTRODUCTION

Among the gynecological malignancies, ovarian cancer is the leading cause of mortality in developed countries, with an estimated 225,500 new cases and 140,200 deaths annually worldwide[1]. Ovarian neoplasms consist of several histopathological entities; treatment depends on the specific tumor type. Epithelial ovarian cancer comprises the majority of malignant ovarian neoplasms (about 90%); however, other less common pathologic subtypes may occur[2]. The major histological subtypes of epithelial ovarian cancer include: serous, mucinous, endometrioid, clear cell, undifferentiated, and unclassified[3].

Transitional cell carcinoma (TCC) of the ovary, a recently recognized subtype, resembles urothelium rather than ovarian surface epithelium (mesothelium). Therefore, accurately diagnosing TCC of the ovary as the primary or metastatic lesion is important because the appropriate treatment choice could differ depending on the initial diagnosis[4]. Ovary TCC was initially defined by Austin and Norris in 1987[5]. It has been described as a primary ovarian carcinoma in which definite urothelial features are present, but no benign, metaplastic, and/or proliferating Brenner tumor can be identified. These investigators reported a group of patients who had ovarian tumors presenting with histologic features similar to those observed in a malignant Brenner tumor, but the tumors lacked the associated benign Brenner tumor component. Pure TCC of the ovary was thus distinguished from malignant Brenner tumor[6]. In addition to not having a benign Brenner tumor component, TCC of the ovary lacks the prominent stromal calcification. It arises directly from the pluripotent surface epithelium of the ovary and from cells with urothelial potential, rather than from a benign or proliferative Brenner tumor precursor[7].

We present a case of TCC of the ovary, managed by total abdominal hysterectomy and bilateral salpingo-oophorectomy with infracolic omentectomy and pelvic lymph node dissection followed by postoperative chemotherapy.

CASE PRESENTATION

A 72-year-old postmenopausal female with a family history of diabetes mellitus, ischemic heart disease, and gastric cancer. She smoked cigarettes for 30 years (four packs per year). She was diagnosed with hypertension. Surgical hypothyroidism secondary to multinodular goiter surgery and resection of colon polyps. Actual medications: levothyroxine 100 mcg daily, atenolol 50 mg daily, and acetaminophen/tramadol 325/37.5 mg three times per day as needed.

She started with progressive enlargement of an abdominal girth and diffuse pain in October 2008. There were no changes in bowel movement or urinary habit. Abdominal ultrasound showed a pelvic mass with homogeneous echogenicity. Routine biologic test results were all within normal ranges; CA-125 below upper limit (35 mUI/l). In March 2009, surgical staging procedures including total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and pelvic lymph node dissection were performed. The final diagnosis was bilateral TCC of the ovary, grade 3, FIGO stage IIIC; left ovary tumor of 11 cm and right ovary tumor of 4 cm (Fig. 1, 2 and 3). She received adjuvant chemotherapy with carboplatin AUC 6 and paclitaxel 175 mg/m^2 every three weeks for a total of six cycles. Surveillance started in September of 2009 and she was disease-free for 10 months.

In May 2011, recurrence of disease was documented via PET-CT. A second line of chemotherapy was started with liposomal doxorubicin (50 mg/m^2) until progression, but it was suspended secondary to adverse effect grade 4 (hand-foot syndrome).

In February 2012, progression of disease was documented, and carboplatin AUC 6 and paclitaxel

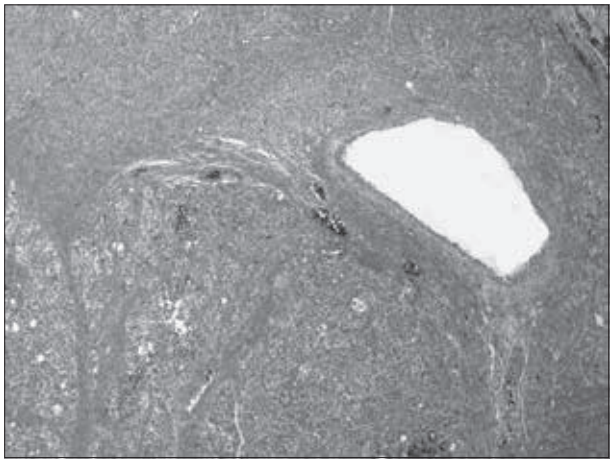

Figure 1. In this photomicrograph, ovarian stroma is infiltrated by a malignant epithelial neoplasm in nests growth pattern.

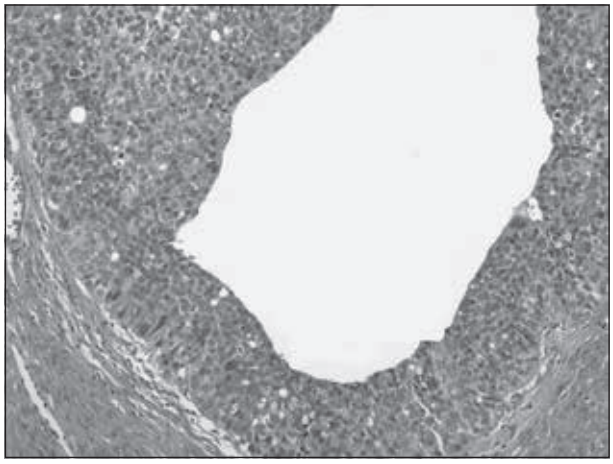

Figure 2. On closer examination, the neoplasia has trabecular growth pattern and remembers the urothelium.

175 mg/m^2 was reintroduced every three weeks with the addition of bevacizumab 7.5 mg/kg every two weeks. After six cycles, the patient achieved complete response documented by PET-CT.

DISCUSSION

The true incidence of TCC of the ovary remains unknown. At present, clinical studies focusing on TCC of the ovary are somewhat impractical due to the limited incidence. In a study by Silva, et al., focal or diffuse TCC of the ovary pattern was seen in 88 of 934 ovarian cancers. They reported that the estimated five-year survival rate after surgery for 88 patients was 37%, whereas for patients who received chemotherapy, it was 41%[8].

The common presenting symptoms of TCC of the ovary are abdominal pain, abdominal swelling or distension, and weight loss. Some of these symptoms were present in our patient. Occasionally, the

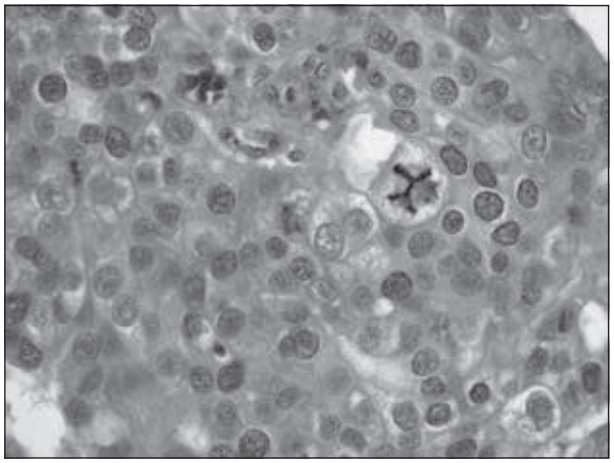

Figure 3. Malignant cells display nuclear atypia, prominent nucleoli, multiple abnormal mitosis, and granular eosinophilic cytoplasm.

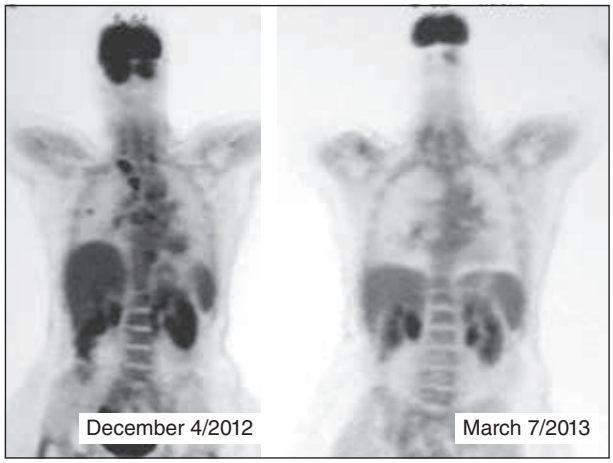

Figure 4. Transitional cell carcinoma of the ovary. Case report and review of literature. Treatment: carboplatin + paclitaxel + bevacizumab.

patient may present with uterine bleeding, back pain, and bowel or urinary symptoms. The clinical presentation is indistinguishable from other types of ovarian carcinoma[9].

The histopathology pattern is diagnostic. Ovarian TCC typically shows undulating, diffuse, insular, and trabecular growth patterns. The tumor cell nuclei are round, often exhibiting nucleoli or longitudinal grooves. The cytoplasm is often pale and granular, rarely clear or eosinophilia[10].

Immunohistochemical markers can help to differentiate the primary ovarian TCC from metastatic lesions: CK7, CK20, thrombomodulin, and uroplakin III. The presence of CK7+/CK20+ always indicates a urinary tract origin; and ovarian TCCs are negative for CK20, thrombomodulin, and uroplakin III. Other immunohistochemical markers include vimentin, CA-125, Wilms' tumor protein (WT1), and various estrogen receptors because these markers are positive in primary ovarian TCC but negative in urinary tract TCC[11].

Ovarian TCC is reported to be sensitive to platinum-based chemotherapy and has a better prognosis than other types of common epithelial tumors of the ovary. Sweeten, et al. suggested that TCC of the ovary may be more chemo sensitive than other common epithelial tumors in the refractory setting. The relative influences of tumor biology and treatment strategies remain undetermined. Patients with TCC of the ovary have better prognoses compared to patients with all other types of ovarian carcinomas following standardized chemotherapy[12]. Further studies confirmed the increased chemo sensitivity of TCC of the ovary, including a series of 62 patients that were matched for stage and residual disease with serous controls[13]. As in the case of our patient, the reintroduction of carboplatin after progression with liposomal doxorubicin resulted in a complete response. Neither of the cases of TCC of the ovary reported in the literature have achieved a complete response with the reintroduction of carboplatin and paclitaxel after progression on second-line therapy. Also, the use of bevacizumab, an anti-vascular endothelial growth factor (VEGF) monoclonal antibody, hasn't been reported in previous cases.

CONCLUSION

Primary TCC of the ovary is a rare subtype of epithelial ovarian cancer. Surgical resection remains the primary therapeutic approach, followed in some cases by adjuvant chemotherapy. The tumors are sensitive to platinum-based combinations, and the prognosis is better than for other types of ovarian cancers. The patient in this study is alive with partial response, and overall survival of four years and eight months. She is asymptomatic and with excellent quality of life.

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