CASE REPORT

Multiple visceral resections for pelvic recurrence from surgically treated clear cell ovarian tumor - a case report

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ABSTRACT

Ovarian clear cell carcinoma is a distinct histopathological subtype of epithelial ovarian cancer with a more aggressive biological behaviour and a higher capacity to recur. We present the case of a 47 year old patient diagnosed with a clear cell ovarian tumor invading an ileal loop submitted to radical surgery followed by adjuvant chemotherapy. At one year follow up she was diagnosed with a pelvic recurrence invading the right ureter and the right ileocolon so the patient was re-submitted to surgery. The recurrence was resected en bloc with the right ileocolon and distal ureterectomy. The continuity of the digestive tract was re-established by ileo-transverse anastomosis while the right ureter was re-inserted in the urinary bladder. The postoperative course was uneventful.

Key words: clear cell ovarian tumor, pelvic recurrence, multiple visceral resections

INTRODUCTION

Clear cell carcinoma of the ovary is considered as a distinct histopathological type of ovarian tumors accounting for up to 5% of all ovarian epithelial malignancies (1). Patients diagnosed with this tumor subtype usually report a poor prognosis, this histopathological subtype being considered as a more biologically aggressive tumor with minimal chemotherapy responsiveness (2,3,4). Even in cases with limited stage disease treated by surgery and adjuvant chemotherapy recurrence will develop in up to one third of cases (1,5).

CASE REPORT

A 47-year-old patient was initially investigated for pelvic pain and sub-occlusive syndrome. The imagistic studies revealed the presence of a pelvic tumor with possible ovarian origin invading an ileal loop so the patient was submitted to surgery; intraoperatively a large retro-uterine tumor invading the
right adnexa and an ileal loop located at 50 cm from the ileo-caecal valve was found; the tumor was resected en bloc with total hysterectomy, bilateral adnexectomy and segmental ileal resection; the continuity of the digestive tract was re-established by an end to end anastomosis. The histopathological study revealed the presence of a poorly differentiated adenocarcinoma but could not distinguish between a digestive neuroendocrine tumor and a clear cell ovarian carcinoma. The immunohistochemical studies confirmed the presence of diffuse positive Ck7, CA 125 and oestrogen receptors, with negative tests for chromogranine and synaptophysine so the final diagnosis was the one of a poorly differentiated clear cell ovarian tumor. Ki 67 was positive in up to 80% of the tumoral cells. The patient was referred to the oncology clinic where she was submitted to six cycles of adjuvant chemotherapy with platinum salts and taxanes regimens. One year after ending the adjuvant treatment the patient was diagnosed with a pelvic recurrence invading the right colon, the right hypogastric artery, the wall of the right external iliac vein and the right ureter (figures 1, 2). The patient was re-submitted to surgery and the recurrence was resected en bloc with right ileo-colectomy and distal ureterectomy. The right hypogastric artery was ligated while the invaded area of the right external iliac vein was laterally resected and sutured (figures 3-8). The continuity of the digestive tract was re-established by an side to end ileo-transverse anastomosis while the right ureter was re-implanted in the urinary bladder (figure 9). The urinary anastomosis was protected by placing a double J urinary catheter which was removed 3 weeks later. The postoperative course was uneventful, the patient being discharged the 11th postoperative day.

The histopathological study confirmed the presence of a poorly differentiated clear cell adenocarcinoma with ovarian origin.

DISCUSSIONS

Clear cell ovarian carcinoma represents up to 5% of all types of ovarian cancer and is usually associated with a poorer prognosis when compared to the serous subtype (2). At the time of diagnosis most patients present with a pelvic mass while the initial stage at diagnosis widely varies. It has been reported that 57-81% of cases are diagnosed in an early stage of the disease (6-8). In order to better understand the molecular basis of the disease and the most important prognostic factors a group of researchers reviewed the clinical, pathological and therapeutical features of clear cell ovarian carcinoma in 2010 in Vancouver (8). It has been demonstrated that clear cell ovarian carcinoma have the highest rate of PIK3CA mutations among all types of ovarian cancer and has been stipulated that PI3K–AKT–mTOR–HIF (phosphoinositide 3-kinase, v-akt murine thymoma viral oncogene homolog, mechanistic target of rapamycin, and hypoxia induced factor) pathway may be a therapeutically viable target (9-13). Other similarities encountered between
ovarian clear cell carcinoma and clear cell tumors with other locations such as renal or endometrial tumors have been described and therefore possible common therapies have been proposed (14). However, despite many similarities between renal and ovarian clear cell carcinomas, they practically represent different diseases; patients diagnosed with ovarian CCC do not present somatic and germline mutations in the VHL gene while in those with renal CCC these are commonly seen (8).

When it comes to cases diagnosed in an advanced stage of the disease, surgery seems to be the most appropriate therapy especially due to the fact that clear cell ovarian carcinoma is less responsive to chemotherapy and patients who have a poor response to first
The poor response to chemotherapy is mainly related to ovarian CCC's platinum resistance; Sugiyama et al reported that the response rate to platinum and taxanes therapy is significantly lower for patients with CCC when compared to those with epithelial ovarian cancer (91.1% versus 72.5%) (6). Due to this fact cytoreduction should be performed in all cases and ovarian CCC should be managed in the same manner as epithelial ovarian cancer (1, 15-17). However, given the rarity of cases, the role of surgery has not been prospectively evaluated (18).

In order to determine the most important prognostic determinants for patients diagnosed with gynaecological CCC, Rauh-Hain et al conducted a study on 5421 women with ovarian and uterine CCC; patients data were found in 18 SEER registries between 1988-2010. Advanced stage ovarian CCC with regional involvement was found in 398 cases (11% of patients) while distant involvement was seen in 1411 cases (38.9%). Among patients with regional disease, 5-year disease free survival was 65.8% for ovarian CCC; in contrast, the 5 year cancer-specific survival was 57.8% (53.1%-62.8%) for women with uterine CCC (p = 0.01). The Cox proportional hazards model identified an independent association of older age, African-American race, SEER registry location, advanced stage, absence of surgical treatment, and absence of lymph node dissection with cancer-specific mortality. The Cox model demonstrated that the strongest quantitative predictor of death was stage at the time of diagnosis, with more advanced stages associated with higher rates of mortality. Although in univariate analysis patients diagnosed with advanced stage ovarian CCC had a better outcome, in multivariate analysis there was no significant difference in terms of survival between cases with locally advanced ovarian or uterine CCC (19).

In their meta-analysis, Lee et al studied the long term outcomes of ovarian CCC compared to other histological subtypes. When comparing the hazard ratio based on stage I-II and stage III-IV patients with ovarian CCC had a higher hazard arte for death among all stages when compared to those with non-CCC. When focusing on the differences between advanced stage ovarian CCC and advanced stage epithelial ovarian cancer, a poorer outcome was seen in cases with ovarian CCC. When studying the outcomes of CCC compared to each histopathological subtype of epithelial ovarian cancer, a better outcome was observed for endometroid epithelial ovarian cancer; this difference was not maintained when it came to mucinous epithelial ovarian cancer.

When it comes to recurrent ovarian CCC, it seems that it is practically unresponsive to chemotherapy. In the study conducted by Levenback et al involving 51 patients with recurrent ovarian CCC 105 regimens were administrated. At the time of recurrence, among patients with platinum sensitive disease only 9% had partial response to re-treatment and 18% had stable disease while among cases with platinum resistant disease only1% reported a partial response to gemcitabine (20).

In the study conducted by Kajiyama et al regarding post-recurrent oncologic outcome of patients with
ovarian CCC, both overall survival and post-recurrence survival were significantly shorter for patients with ovarian CCC when compared to those with recurrent serous adenocarcinomas (21).

**CONCLUSIONS**

Ovarian CCC represent an aggressive biological subtype of ovarian cancer associated with poor prognosis and low rates of long term survivors. Although due to the paucity of reported cases a standard therapeutic protocol has not yet been established it seems that cytoreductive surgery is the only potential curative solution especially due to the high chemoresistance developed by these patients. When it comes to recurrent tumors, they seem practically unresponsive to chemotherapy, so re-resection is perfectly justified in order to prolong survival.

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