RESEARCH COMMUNICATION

# Splenectomy during Secondary Cytoreductive Surgery for Epithelial Ovarian Cancer

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## Abstract

**Splenic metastasis from ovarian cancer is unusual. Most splenic metastases are encountered in the setting of widespread visceral metastases. We present 6 cases of splenic metastasis of epithelial ovarian cancer. Three cases underwent a splenectomy as a part of interval debulking surgery, and the rest received a splenectomy as a surgery for recurrent disease. The splenectomies were well-tolerated in all patients and no serious morbidity or mortality resulted. Only one patient experienced a transient elevation in platelet count.**

**Keywords:** Splenectomy - secondary cytoreductive surgery - ovarian cancer

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## Introduction

Primary cytoreductive (debulking) surgery followed by adjuvant chemotherapy is the mainstay of treatment for advanced epithelial ovarian cancer. Numerous retrospective and prospective studies on prognostic factors have demonstrated the amount of residual tumor is one of the most important prognostic factors for survival of epithelial ovarian cancer patients (Bristow et al., 2002; Wakabayashi et al., 2008). Even in recurrent disease, patients with a prolonged diagnostic to recurrence interval obtain a survival benefit from complete secondary cytoreduction (Janicke et al., 1993; Salani et al., 2007). Therefore, complete cytoreduction should always be the essential context at primary and secondary surgeries for epithelial ovarian cancer. For recurrent epithelial ovarian cancer, to date, no definite consensus has been reached on the optimal strategy for salvage therapy, especially platinum-sensitive patients. Possible strategies include salvage chemotherapy (Pfisterer and Ledermann, 2006) or secondary cytoreductive surgery (Munkarah and Coleman, 2004; Benedetti Panici et al., 2007).

Splenic metastasis occurs rarely in malignant tumors. Based on studies of various tumors, the prevalence of splenic metastasis has been reported as ranging from 2.3% to 7.1% (Koh et al., 2004). The exact incidence of splenic metastasis from ovarian cancer is hard to determine. An autopsy study of 428 patients with various histologic types of ovarian cancer in 1989 noted that splenic metastasis in ovarian cancer to be as high as 20% (Rose et al., 1989).

Nowaday, a splenectomy is still an uncommon component of cytoreduction of ovarian cancer, especially during secondary cytoreduction. This procedure as a part of cytoreduction may be associated with severe morbidity, and their effects on clinical outcomes have been evaluated by previous authors. However, most evidences come from case (s) reports with only a few studies. To add more information on this unusual procedure in the context of secondary cytoreduction of epithelial ovarian cancer such as clinical efficiency and safety, we report a series of 6 cases of epithelial ovarian cancer patients who had a splenectomy as a part of secondary cytoreductive procedures, performed at the Saitama Medical University International Medical Center in Japan.

## Materials and Methods

Approval to conduct this study was obtained from the local ethics committee of the Saitama Medical University International Medical Center. The medical records of all patients who underwent a splenectomy as a part of secondary cytoreductive surgery for epithelial ovarian cancer between April 2007 and May 2009 were reviewed. All data in the patients' medical records including demographic data, surgery reports, perioperative complications, pathology reports, and follow up information were evaluated.

## Results

Between April 2007 and May 2009, we found 6 cases of epithelial ovarian cancer patients who had a splenectomy

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**Table 1. Patient Characteristics and Clinicopathological Outcomes in the Interval Debulking Group**

| Case | Age | Stage | Histology | Prior CMT (n) | CA 125, CA 199 (U/ml) | Splenic lesion | Residual tumor | Adjuvant CMT | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 61 | IIIc | Serous | PTX + CBDCA (5) | 11.1, 2.6 | Parenchyma | N | PTX + CBDCA | NED 4 m |
| 2 | 59 | IIIc | Adenocarcinoma; undetermined | PTX + CBDCA (6) | 10.7, 2.3 | Parenchyma + Capsule | Y (0.5 cm) | PTX + CBDCA | AWD 15 m |
| 3 | 79 | IV | Serous | PTX + CBDCA (5) | 31.7, 3.2 | Parenchyma + Hilum | Y (2 cm) | PTX + CBDCA | AWD 15 m |

CMT, Chemotherapy; Serous, Serous cystadenocarcinoma; PTX, Paclitaxel; CBDCA, Carboplatin; AWD, Alive with disease; NED, No evidence of disease

**Table 2. Patient Characteristics and Clinicopathological Outcomes in the Recurrence Group**

| Case | Age | Stage | Histology | Recurrence free interval | CA 125, CA 199 (U/ml) | Solitary | Splenic lesion | Residual tumor | Adjuvant CMT | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 40 | Ic | Clear cell | 10 m | 41.5, 10.9 | Y | Parenchyma | N | PTX + CBDCA | NED 10 m |
| 2 | 48 | IV | Serous | 10 m | 99.9, 4.8 | N m | Parenchyma + Hilum | N | PTX + CBDCA | NED 11 |
| 3 | 65 | IIIC | Clear cell | 33 m | 5.4, 5.3 | Y | Capsule + Hilum | N | CPT-11 + CDDP | NED 2 m |

CMT, Chemotherapy; Clear cell, Clear cell carcinoma; Serous, Serous cystadenocarcinoma; PTX, Paclitaxel; CBDCA, Carboplatin; CDDP, Cisplatin; CTX, CPT-11; NED, No evidence of disease

as a part of secondary cytoreductive procedures at the Saitama Medical University International Medical Center. During the study period, of 6 splenectomies, 3 had undergone a splenectomy as a part of interval debulking, and the rest had undergone a splenectomy as a part of surgery for recurrent disease. No patient had received a splenectomy as a part of primary cytoreductive surgery in this period. Histological examinations showed tumor involvement in all cases.

The median age of the 6 patients was 60 years (range, 40-79). All patients had a Gynecological Oncology Group (GOG) performance status of 0. Most had advanced stage tumors of serous histology. Of the 3 in the interval debulking group, 2 had a residual tumor ≥ 0.5 cm, with evidence of disease at the most recent follow up. Their characteristics and clinicopathological outcomes are summarized in Table 1. Of the remaining 3 patients, all of recurrence status, one had an extra-splenic lesion with inguinal lymph node metastasis. The other two had isolated splenic metastasis. Table 2 presents the characteristics and clinicopathological outcomes of the 3 recurrence patients. None of the 6 patients in this series had received preoperative pneumococcal vaccine.

The splenectomy was well-tolerated in all patients with no serious morbidity or mortality. One patient experienced a transient elevation in platelet count. To date, 2 of 6 patients have persistent disease; however, there are limitations in trying to assess the outcomes of this procedure in our series given the short to-date follow up time.

## Discussion

Splenic metastasis from epithelial ovarian cancer is uncommon. Most patients with splenic metastasis already have widespread systemic disease. When splenic metastases are found, the splenic capsule is usually involved with intraperitoneal seeding. On the other hand, isolated splenic parenchymal lesions are rare. A literature search performed through Pubmed yielded reports of 30 similar cases (Farias-Eisner et al., 1993; Klinger et al., 1998; Gemignani et al., 1999; Ushijima et al., 1999; Lauro et al., 2002; Yano et al., 2002; Koh et al., 2004; Tserkezoglou et al., 2005; Manci et al., 2006; Otrock et al., 2006; Furukawa., 2007; Alloni et al., 2008; Yoshioka et al., 2008). Several studies have proposed different hypotheses to explain this phenomenon, most notably suggesting that the splenic capsule acts as a shield, the contractile properties of the spleen may be involved, perhaps it results from poor development of afferent lymphatics in the spleen, or perhaps the tortuosity of the splenic artery, or rhythmical splenic contractionsor, or local splenic immunomechanisms are involved. Among isolated splenic metastasis, isolated splenic parenchymal lesions are rare and represent hematogenous spreading (Koh et al., 2004; Furukawa., 2007; Alloni et al., 2008). In this study, one of the three recurrence cases had isolated parenchymal splenic metastasis. Previous studies found that the prognosis of ovarian cancer patients who had a splenectomy in cases of solitary splenic metastasis was good (Lauro et al., 2002; Furukawa, 2007; Yoshioka et al., 2008). One prior study concluded that patients with splenic metastasis from ovarian cancer had a less favorable prognosis and should be attributed an International Federation of Gynecology and Obstetrics (FIGO) stage classification of IV (Nicklin et al., 1995). Other studies found that ovarian cancer patients with splenic metastasis tended to have poorer prognoses than those without splenic metastasis, but the difference was not statistically significant (Ayhan et al., 2004; Eisenkop et al., 2006).

Secondary cytoreduction has been described in several scenarios, including for interval cytoreduction,

at the time of second look reassessment, recurrence and disease progression. The available data suggest a benefit for complete tumor cytoreduction in selected patients with recurrent ovarian cancer. This needs to be considered in the light of recent data reporting prolonged survival with the use of salvage chemotherapy without surgery. Currently, it is not known if a salvage strategy combining surgery and combination chemotherapy regimens will have a greater survival benefit than chemotherapy alone (Munkarah and Coleman, 2004; Pfisterer and Ledermann, 2006; Benedetti Panici et al., 2007). However, a longer recurrence free interval after primary treatment indicates a tumor that is biologically less aggressive and more chemoresponsive, and therefore, patients who have recurrent disease after a prolonged recurrence free interval might benefit most from a combined approach of complete tumor cytoreduction and chemotherapy. In our series, we performed a splenectomy in 3 patients with platinum-sensitive at the part of surgery for recurrent disease, with no serious complications.

The performance of a splenectomy during secondary cytoreduction was initially reported by Deppe et al. (1983). Since that time, several medical reports have examined performing a splenectomy during secondary cytoreduction, and found that it appears to be a feasible procedure and may be associated with long term survival (Lauro et al., 2002; Manci et al., 2006; Furukawa, 2007; Yoshioka et al., 2008). Bilgin et al. (2005) reviewed a series of 13 epithelial ovarian cancer patients who underwent a splenectomy as part of cytoreducton, seven as part of primary cytoreduction and six for recurrent disease. Three patients (2 in the primary cytoreduction group and 1 in the recurrent group) with suboptimal debulking died of their disease within a short period of time . Manci et al. (2006) reported the results of 24 ovarian cancer patients who had received a splenectomy during secondary cytoreduction. Multiple site disease recurrence occurred in 15 patients, and in their series, overall survival was significantly correlated to residual disease at secondary surgery, disease free survival, consolidation chemotherapy, and type of adjuvant therapy. Another review study by Magtibay et al. (2006) demonstrated that overall survival by residual tumor status did not achieve statistical significance in patients undergoing secondary cytoreduction, although there was a tendency toward improved survival.

Generally, neoadjuvant chemotherapy followed by interval debulking surgery lessens surgical morbidity in advanced epithelial ovarian cancer patients with apparently unresectable bulky tumors or poor performance status. As noted in a recent literature review, there is an apparent benefit of neoadjuvant chemotherapy followed by interval debulking surgery in the subgroup of patients whose primary surgery has not been performed under optimum conditions (Tangjitgamol et al., 2009). In our series, a splenectomy was performed in 3 patients at the part of surgery for interval debulking after neoadjuvant chemotherapy, with no serious complications.

Morbidity associated with splenectomy is reported to be acceptable (Nicklin et al., 1995; Chen et al., 2000). The possible perioperative complications of a splenectomy include hemorrhage, leukocytosis, thrombocytosis, thromboembolic phenomenon, disseminated intravascular coagulation, infection, left sided atelectasis or pneumonia, injury to the pancreatic tail or stomach, and splenic vein thrombosis (Nicklin et al., 1995; Ayhan et al., 2004; Magtibay et al., 2006). The most common complications are left sided atelectasis, a thromboembolic event, and pneumonia (Nicklin et al., 1995; Magtibay et al., 2006). Magtibay et al. reported that of 112 patients, who underwent a splenectomy as a part of cytoreduction, the perioperative morbidity rate was 15% and the mortality rate was 5%, with none of the deaths directly related to the splenectomy (Magtibay PM et al., 2006). In our experience, there was only one small complication, as one of the six patients experienced a transient elevation in platelet count.

In conclusion, solitary splenic metastasis from ovarian cancer is an extremely rare phenomenon. Splenectomy when indicated at the time of secondary cytoreduction is a safe and feasible procedure that can facilitate optimal tumor debulking. A select group of patients with isolated splenic metastasis and a prolonged recurrence free interval may benefit from this procedure.

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