

Prolonged overall survival in Stage IV patient with malignant transformation from ovarian mature cystic teratoma by combination therapy including radiotherapy: a case report and the review of literature

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Summary

Background: The prognosis of Stage IV disease of malignant transformation from mature cystic teratoma (MT-MCT) of the ovary in is extremely poor, and there has been no standard therapy established for MT-MCT. A case with Stage IV tumor that achieved disease-free survival of 19 months treated with radiotherapy, in addition to surgery and chemotherapy is reported, with a review of the literature. **Clinical case:** A 57-year-old Japanese woman, gravida 3, para 2, received total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph nodes biopsy, and Hartmann's operation. Although tumors in the pelvis were completely resected, residual tumor was present in liver. The pathological findings revealed squamous cell carcinoma (SCC) arising from MCT, and her diseases were diagnosed as Stage IV MT-MCT. Postoperatively she received one cycle of combination chemotherapy of paclitaxel and carboplatin (TC). Then stereotactic radiation therapy (SRT, 48 Gy/four fractions) for liver metastasis and additional five cycles of TC was conducted, and the liver metastasis achieved complete response. After 19 months of disease-free interval, relapsed tumors in para-aortic nodes were observed, and radiation therapy (50 Gy/27 fractions) was administered. Although the lesions achieved partial response, recurrence was observed after eight months, and the patient died of disease after achieving overall survival of 30 months. **Conclusion:** Radiotherapy could be an effective procedure for advanced SCC from MCT, even when the tumors are metastatic or recurrent.

Key words: Ovary; Malignant transformation; Mature cystic teratoma.

Introduction

Mature cystic teratoma (MCT) is the most common ovarian germ cell tumor, which accounts for 10-25% ovarian neoplasms [1, 2]. The frequencies of malignant transformation (MT) in MCT are reported to be less than 2% [1-4]. Among them, more than 80% of MT tumors are squamous cell carcinoma (SCC) [5, 6]. The prognosis is extremely poor when disease spreads beyond the ovary [7]. Particularly, there are very few reports of cases who survive more than two years in Stage IV patients. The authors report a rare case of SCC from MCT in Stage IV that achieved overall survival of 30 months using chemotherapy and radiotherapy, with a review of the literature.

Case Report

A 57-year-old Japanese postmenopausal woman, gravida 3, para 2, was referred to the present hospital for the treatment of a large pelvic tumor. Computed tomography (CT) and magnetic resonance imaging (MRI) showed a simple cystic tumor with fat and solid lesions in the lower abdomen. There was also single liver metas-

tasis, which was 2.4 cm in diameter (Figure 1). Serum levels of SCC and CA125 were elevated: 43.8 ng/ml of SCC and 116.3 U/ml of CA125. Preoperatively, she had massive bleeding from tumor directory invading her rectum. The patient received total



Figure 1. — MRI of the patient. A) T2-weighted image of ovarian tumor. A simple cystic tumor with fat and solid lesion with a diameter of 19 cm is observed in the pelvis. B) Fat-suppression gadolinium-enhanced MRI of the patient. The tumor shows fat lesions and wall thickness.

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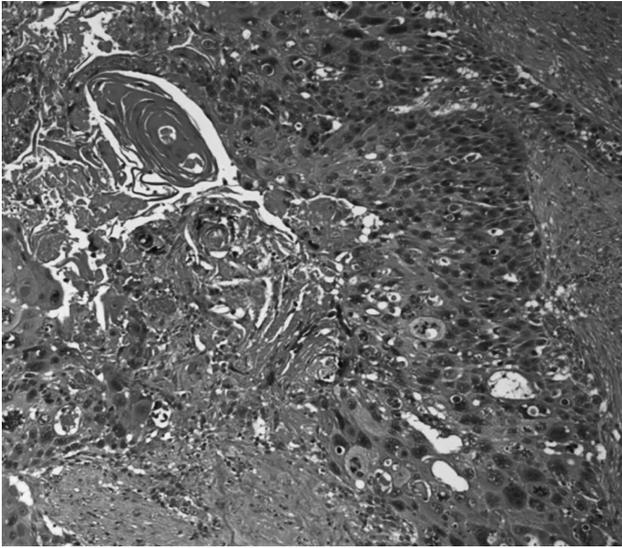


Figure 2. — Pathological image of the ovarian tumor, showing moderately differentiated squamous cell carcinoma (hematoxyline and eosin, $\times 20$).

hysterectomy, bilateral salpingo-oophorectomy, pelvic lymph nodes biopsy, and Hartmann's operation. The tumor of the left ovary was found to be adhered to the uterus, sigmoid colon, and pelvic wall. Tumors in the pelvis were completely resected, but liver metastasis was not extracted. Pathologically, the tumor was diagnosed as squamous cell carcinoma (SCC) of the ovary arising

from MCT (Figure 2). Subsequently, the patient received one cycle of combination chemotherapy with 175 mg/m^2 of paclitaxel and carboplatin (area under the blood concentration time curve, $\text{AUC}=5$) and stereotactic radiation therapy (SRT, 48 Gy/four fractions) for liver metastasis. The patient underwent five more cycles of chemotherapy with paclitaxel and carboplatin every four weeks, and the liver metastasis completely disappeared seven months after the operation (Figures 3A–C). The patient achieved disease-free survival of 19 months after primary surgery. However, disease relapse was observed in para-aortic nodes, and she was treated with radiation therapy for lymph nodes recurrence (50 Gy/27 fractions), achieving partial remission (PR) (Figures 3D–E). After eight months from the completion of radiation therapy to para-aortic nodes, the para-aortic nodes showed progression, and the patient was treated with combination with gemcitabine and bevacizumab. However, the tumor did not respond to the therapy and the patient died of disease after achieving overall survival of 30 months from primary surgery.

Discussion

MT arising from MCT is extremely rare disease and the incidence is less than 2% of ovarian neoplasms [1–4]. Approximately half of them are diagnosed at early stage: 50% in Stage I, 17% in Stage II, 28% in Stage III, and 4% in Stage IV [7]. Early presentation, being diagnosed at Stage I, was reported to be the most important prognostic factor for MT from MCT [7, 8]. Several report indicated that five-year survival rate was significantly worse in Stages II–IV compared with Stage I disease: 75.7% in Stage I, 33.8% in Stage II, 20.6% in stage II, and 0% in Stage IV [9]. Additionally, a report suggested that

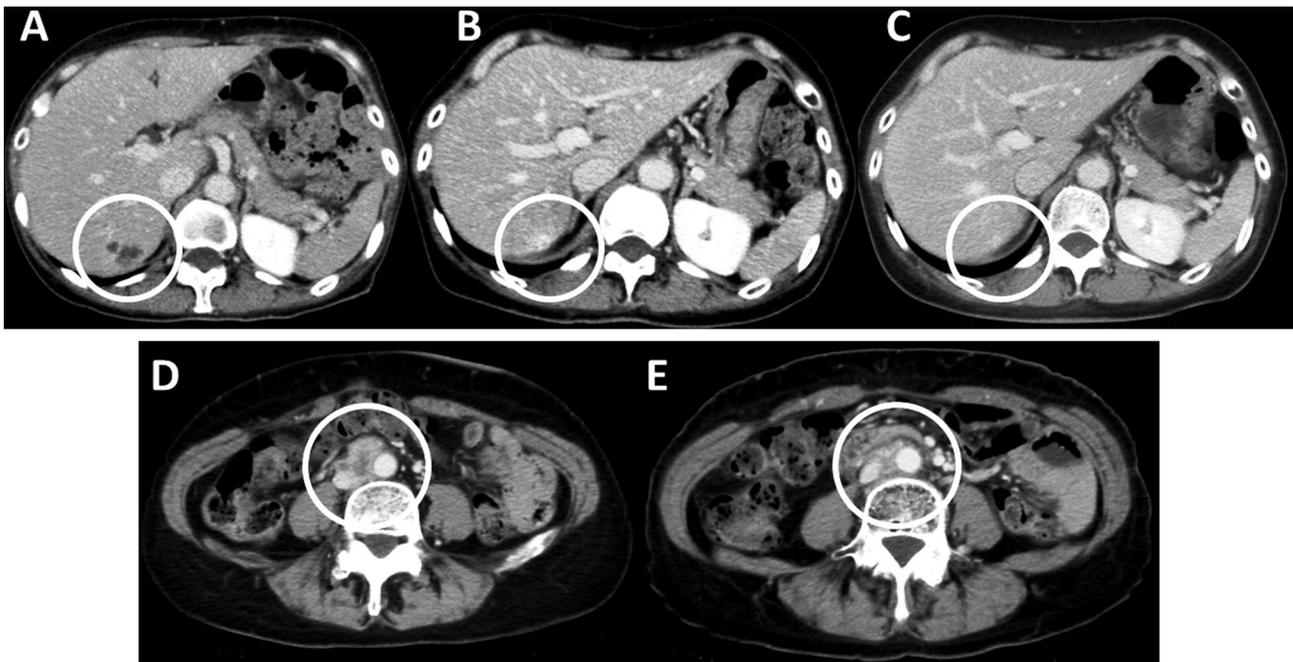


Figure 3. — CT images of the liver metastasis and relapsed para-aortic nodes. A) Single liver metastasis with a diameter of 24 mm is observed before primary surgery. B) The lesion reduced in size after one cycle of paclitaxel/carboplatin chemotherapy and stereotactic radiotherapy. C) The lesion shows a complete response after additional five cycles of paclitaxel/carboplatin chemotherapy. D) Relapse is observed in para-aortic lymph nodes after 19 months from primary surgery. E) Para-aortic lymph nodes shows partial response after completion radiation therapy (50 Gy/27 fractions).

Table 1. — Review of the Stage IV patients with malignant transformation from mature cystic teratoma.

Authors (year)	Number of patients	Treatment	Follow-up (months)	Outcome
Hackethal, <i>et al.</i> (review, 2008) [7]	2	NA	1	DOD
Hackethal, <i>et al.</i> (review, 2008) [7]	3	NA	3	DOD
Hackethal, <i>et al.</i> (review, 2008) [7], Tseng, <i>et al.</i> (1996) [10]	1	RAH+BSO+OMx+B+N, POMP x 4, PI x 3	24	DOD
Sakuma, <i>et al.</i> (2010) [12]	1	BSO+OMx, RT	3	DOD
Koc, <i>et al.</i> (2015) [14]	1	RSO + sigmoid colon resection	3	Discontinued follow-up
Present case (2015)	1	TAH+BSO+H+N TC x 1, liver-RT, TC x5, PAN-RT	30	DOD

NA: not available; DOD: dead of disease; RAH: radical hysterectomy; BSO: bilateral salpingo-oophorectomy; OMx: omentectomy; B: bladder partial resection; N: retroperitoneal node sampling; POMP: cisplatin, vincristine, mitomycin-C, bleomycin; PI: cisplatin, ifosfamide; RT: radiotherapy; TAH: total abdominal hysterectomy; H: Hartmann's operation; TC: paclitaxel and carboplatin; PAN: para-aortic lymph node.

patients with Stage IV tumors were extremely poorer; two-year disease-free survival was 0% in Stage IV [10]. A PubMed search was undergone over three decades using the words: “squamous cell carcinoma”, “mature cystic teratoma of the ovary”, “malignant transformation”, and a review of the patients with Stage IV MT from MCT, as summarized in Table 1. To the best of the present authors' knowledge, this case achieved the longest overall survival in Stage IV MT from MCT.

Although there is no standardized treatment, several studies showed optimal cytoreduction was associated with a significant improvement in survival regardless of stage or adjuvant treatment [9–11]. For postoperative adjuvant chemotherapy, platinum/taxane was suggested a possible beneficial effect [12]. Although effectiveness of radiotherapy for MT from MCT is not determined, some studies supported efficacy of postoperative radiation therapy for this disease [8, 10]. SRT is reported to be an alternative and complementary technique for the treatment of hepatocellular carcinoma and hepatic metastases [13]. The present case clearly demonstrated that SRT was a quite effective treatment modality for metastatic lesion in the patient with MT from MCT.

Conclusion

MT in MCT is extremely aggressive and there is no consensus on a treatment modality for the patients with metastatic lesions. Effectiveness of radiotherapy in combination with surgery and paclitaxel/carboplatin chemotherapy, was demonstrated. Further studies to evaluate the effectiveness of radiotherapy are needed to improve the prognoses of the patients with metastatic lesions of MT from MCT.

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