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Carcinosarcoma of the fallopian tube with disappearance of carcinoma cells by neoadjuvant chemotherapy: case study

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Summary

The authors report a case of carcinosarcoma (CS) of the fimbria of the fallopian tube in which carcinoma cells disappeared with neoadjuvant chemotherapy (NAC). A 74-year-old woman visited the present hospital with a large pelvic mass and pleural effusion. A magnetic resonance image of the tumor was highly suggestive of ovarian carcinoma. Due to the presence of both serous adenocarcinoma cells in pleural effusion and pulmonary thrombosis, the patient was given NAC consisting of carboplatin plus paclitaxel (TC) and anti-coagulant therapy with warfarin potassium. With six courses of NAC, the pleural effusion and pulmonary thrombosis disappeared, and the tumor decreased 36.2% in greatest diameter. Maximum debulking surgery was then performed. The tumor was found to be located in the fimbria of the right fallopian tube. Hysterectomy and bilateral salpingo-oophorectomy were performed, and histologic examination revealed chondrosarcoma with the presence of necrotic epithelial cells. The necrotic areas were interspersed with papillary structures, and immunohistochemical study showed positivity for CK7 and negativity for CK20, p53, and estrogen receptor (ER), indicating serous adenocarcinoma. Thus, heterologous CS with disappearance of viable carcinoma cells by NAC was diagnosed. The patient was given adjuvant chemotherapy consisting of three courses of TC, and there has been no evidence of disease for 20 months. The authors' experience in this case of gynecologic CS indicates that a serous adenocarcinomatous component of tubal CS can be well cured by TC-based NAC.

Key words: Carcinosarcoma; Fallopian tube; Neoadjuvant chemotherapy.

Introduction

Carcinosarcoma (CS) of the female genital tract, though uncommon, occurs most often in the uterus, followed by the ovary and fallopian tube [1]. Although several kinds of chemotherapy and operative procedures have been performed in patients with gynecological CS, survival rates are poor. Herein, the authors report a case of CS of the fallopian tube in which the carcinoma cells disappeared with neoadjuvant chemotherapy (NAC).

Case Report

Clinical course

A 74-year-old multiparous woman visited the present hospital complaining of lower abdominal pain. Thirty years prior, she had undergone gastrectomy with omentectomy for gastric cancer, and there had been no recurrence. Upon admission to this hospital, a large solid pelvic mass was detected by abdominal ultrasonography. Magnetic resonance imaging revealed a 17.1 cm solid tumor of variable signal intensity on T2-weighted images (Figure 1). On contrast-enhanced images, the tumor was of heterogenous signal intensity, with the polypoid portion of the tumor showing intense enhancement. Computed tomography showed massive pleural effusion and revealed filling defects in both pulmonary arteries indicative of pulmonary thrombosis. Blood tests revealed serum CA125 elevation (3,470 U/ml), whereas CA19-9 and CEA levels were within normal ranges. Cytologic examination of the pleural effusion revealed the presence of serous adenocarcinoma cells. Accordingly, the tumor was diagnosed as an FIGO Stage IV ovarian serous adenocarcinoma.

Due to the pulmonary thrombosis, the patient was first given anti-coagulant therapy with heparin and warfarin. She then underwent NAC consisting of paclitaxel (175 mg/m2 on day 1) and carboplatin (area under curve = 5 on day 1) at three-week intervals. Her serum CA125 level decreased to 340 U/ml after four courses of chemotherapy and to 183 U/ml after six courses. The pleural effusion disappeared, the tumor shrank from 17.1 cm to 10.9 cm (36.2%), and the result was classified as a partial response according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria.

Maximum debulking surgery was performed after NAC. During surgery, the tumor was found to be located in the fimbria of the right fallopian tube, with no extension into the pelvic and upper abdominal cavities. Hysterectomy and bilateral salpingo-oophorectomy were performed, and the patient was given three courses of postoperative adjuvant chemotherapy consisting of TC. Now, 20 months after the initial chemotherapy, the patient remains well with no recurrence.

Pathological findings

Cytologic examination of pleural effusion specimens revealed atypical epithelioid cells with a high nuclear/cytoplasmic ratio. Cells in the papillary structures were clear with vacuolated cytoplasm (Figure 2a). Immunohistochemical study of effusion cell blocks showed atypical cells that were positive for CK7 (Figure 2b) and negative for CK20 (Fig. 2c), p53, estrogen receptor (ER), and TTF-1. Thus, the atypical cells were identified as serous adenocarcinoma cells, and the ovary was thought to be the origin of the carcinoma.

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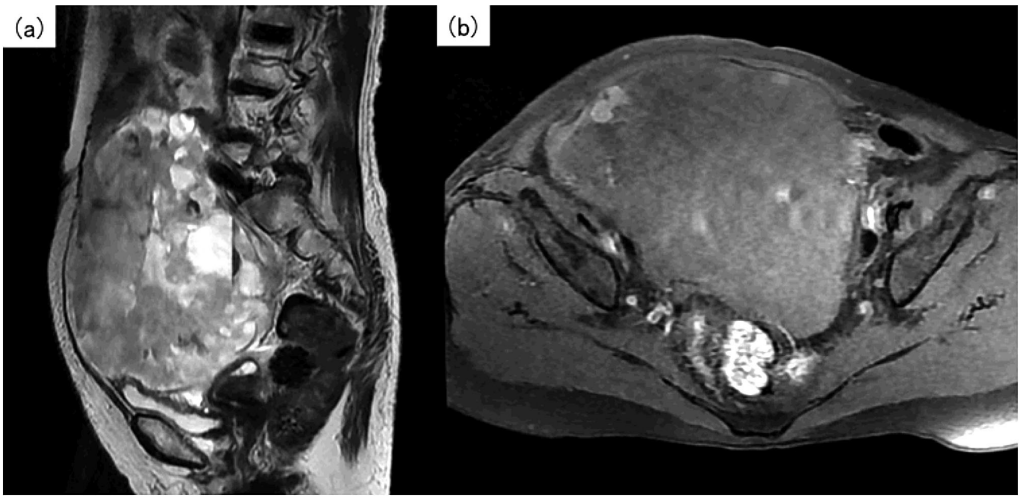

Figure 1. — Magnetic resonance image of the tumor. (a) The tumor appears as a solid mass with variable signal intensity on T2-weighted image. (b) Intense enhancement of the tumor is seen on T1-weighted contrast-enhanced image.

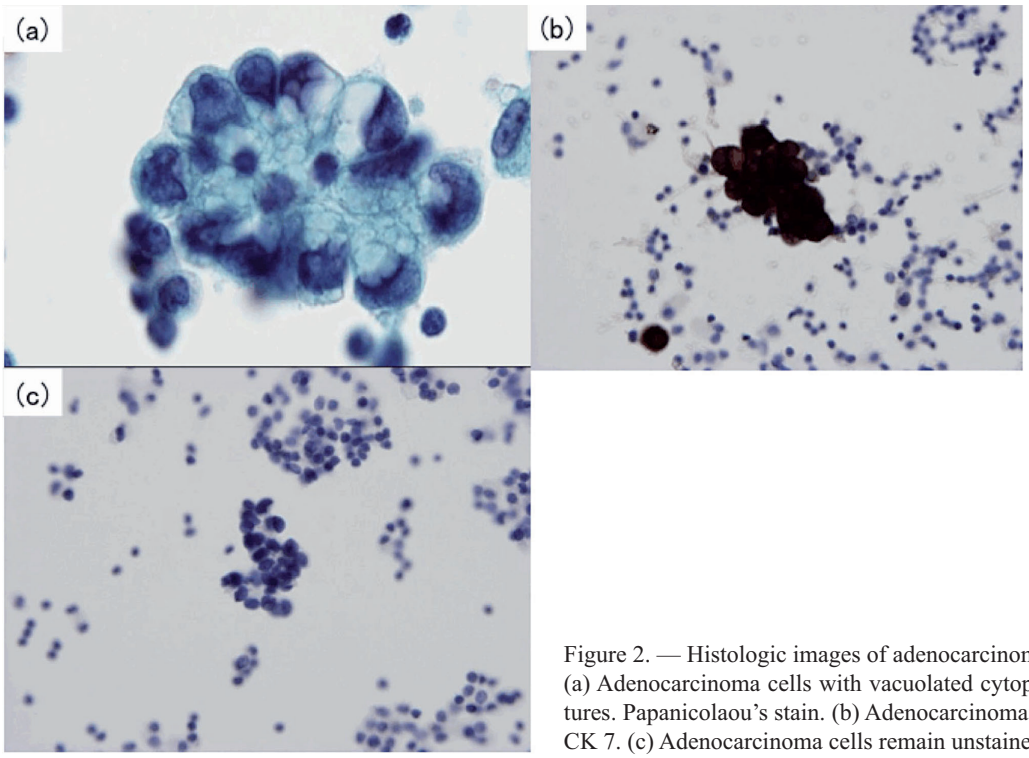

Figure 2. — Histologic images of adenocarcinoma cells in pleural effusion. (a) Adenocarcinoma cells with vacuolated cytoplasm form papillary structures. Papanicolaou's stain. (b) Adenocarcinoma cells stained positively for CK 7. (c) Adenocarcinoma cells remain unstained for CK20.

Examination of the surgical specimens, including the uterus and bilateral adnexa, showed the tumor to be 15 x 10 x 10 cm in size and located in the fimbria of the right fallopian tube (Figure 3a). The tumor was a solid mass, markedly hemonecrotic, with fibrous and myxoid areas (Figure 3b). Histologically, chondromatous islands with atypical chondrocytes having bizarre or multiple nuclei were noted at many sites (Figures 4a and b), and this element was diagnosed as chondrosarcoma on the basis of the marked cellular atypia. Massive necrosis was observed in many areas of the tumor, and no viable carcinoma cells were found in the tumor tissue, even by examination of many histologic sections. However, in some areas, necrotic epithelioid cells and papillary structures were noted (Figures 5a and b). Immunohistochemically, the necrotic cells were positive for CK7 (Figure 5c) and negative for CK20 (Figure 5d), p53, and ER. Cells in the pleural effusion and the necrotic cells had the same immunoprofile, positivity for CK7 and negativity for CK20 in particular. Thus, the necrotic cells were thought to have derived from the serous adenocarcinoma, with necrosis resulting from the NAC. In addition, in many areas, fibrosis and inflammatory cell infiltration were noted.

Discussion

CS of the fallopian tube is rare, with fewer than 100 cases reported in the literature. The present authors previously

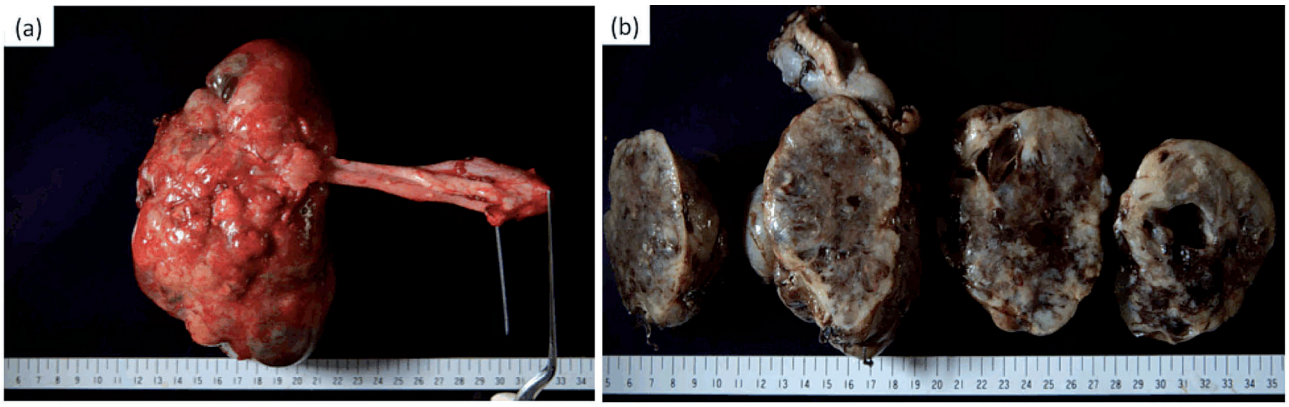

Figure 3. — Gross photograph of the carcinosarcoma in the right fallopian tube. (a) The bulky solid tumor originates from the fimbria of right fallopian tube. (b) Marked hemonecrosis with fibrous and myxoid areas is seen in cut sections of the tumor.

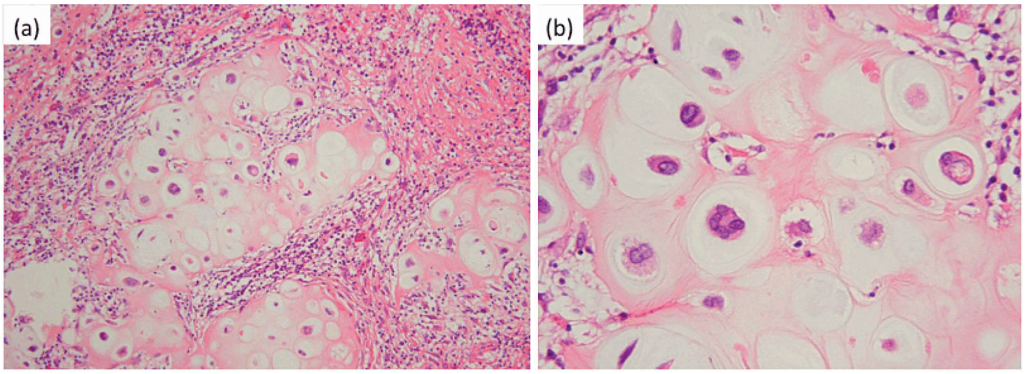

Figure 4. — Histologic images of the chondrosarcomatous element in the carcinosarcoma. (a) Chondromatous islands surround and intermingle with fibrous elements and necrotic areas. (b) High-power view of a chondromatous island. Atypical chondrocytes with multinucleated and bizarre nuclei are seen.

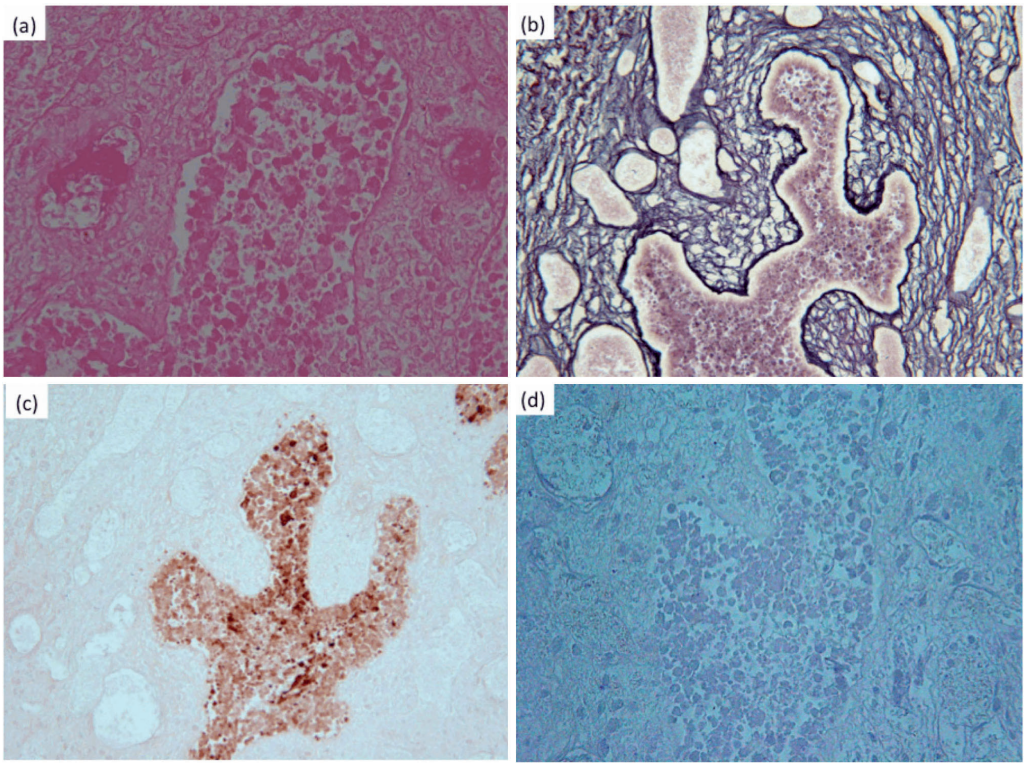

Figure 5. — Histological images of the necrotic carcinomatous element in the carcinosarcoma. (a) Necrotic atypical cells with epithelioid structure. HE stain. (b) Confirmation of the papillary formation of necrotic atypical cells by reticulum staining. (c) Necrotic atypical cells are positive for CK7. (d) Necrotic atypical cells are negative for CK20.

encountered two cases of CS of the fallopian tube [1], and, based on their previous experience, they diagnosed the mass described herein as that of a heterologous CS with disappearance of viable carcinoma cells by NAC. Moreover, in the present case, positivity for CK7 and negativity for CK20, which are key findings for a diagnosis of serous adenocarcinoma, were detected in the necrotic atypical cells. Immunohistochemical detection of necrotic tumor cells in cases of malignant diffuse large B-cell type lymphoma is similar. Carcinomas of the fallopian tube have the same immunoprofile as ovarian carcinomas because the two carcinomas are of the same origin. The characteristic findings of serous adenocarcinoma in both organs are positivity for CK7 and negativity for CK20 and ER. Therefore, in the present case, the authors considered the disappearing carcinomatous element as serous adenocarcinoma.

In general, the treatment strategy for tubal carcinoma follows that of ovarian carcinoma. Primary debulking surgery is the cornerstone of treatment in patients with ovarian carcinoma. It is performed to establish the diagnosis, and the tumor reduction improves the response to chemotherapy. Recently, however, NAC followed by interval surgical debulking has been proposed for patients with established bulky disease [2]. Possible advantages of NAC include resolution of the pleural effusion and ascites, an increased rate of optimal residual disease, a need for less extensive surgery, reduced blood loss, decreased morbidity, shortened hospital stay, and improved quality of life [2]. Kuhn *et al.*, in their nonrandomized phase II study of FIGO Stage III patients, compared three cycles of NAC followed by debulking surgery and three cycles of additional chemotherapy to conventional tumor debulking surgery followed by six cycles of adjuvant chemotherapy, and the resulting tumor resection rate (84%) and median survival (42 months) were significantly superior to those (63% and 23 months, respectively) in the conventionally treated group [3]. Vergote *et al.* compared primary debulking surgery performed for patients with advanced ovarian carcinoma during the period 1980-1988 *vs.* the period 1989-1997 (285 total patients). Patients treated during the latter period were surgically evaluated to receive primary NAC or primary debulking surgery. The resulting three-year crude survival rate was significantly higher in the latter period (26% vs. 42%) [4]. These results suggest that NAC is a good alternative to primary debulking surgery especially for patients with advanced-stage ovarian carcinoma and/or poor performance status. In the present case, the patient was given NAC because of the pulmonary thrombosis, and the neoadjuvant therapy resulted in a cure for the serous adenocarcinoma component of the CS.

To the present authors' knowledge, there is no report regarding the optimal chemotherapy regimen for tubal CS, and most reports detailing therapy and outcomes in cases of ovarian CS describe small numbers of patients treated with various regimens over extended periods of time [5]. The recently published Gynecologic Oncology Group phase II study of single-agent cisplatin as initial chemotherapy for ovarian CS had 136 eligible patients enrolled between 1977 and 1996, underscoring the rarity of these tumors and the difficulty of adequate enrollment in prospective clinical trials [6]. The study showed an overall response rate of 20% with single-agent cisplatin, providing the first prospective evidence that platinum is active as an initial therapy for patients with ovarian CS [6]. Because of the high response rates in this series, agreement exists regarding cisplatin as the main component of first-line therapy, but the optimal combination regimen remains undetermined [6, 7]. Duska *et al.* reported that 16 of 26 patients who were treated with paclitaxel and platinum as first-line therapy achieved a high complete clinical response of 55% with a total response rate of 72% [8]. Leiser *et al.* reported 40% complete and 23% partial response in patients treated with platinum-paclitaxel combinations, which included particularly carboplatin-paclitaxel [9]. In view of the established role of the doublet carboplatin-paclitaxel chemotherapy in patients with epithelial ovarian carcinoma and of the lack of data regarding the best agent for use in combination with a platinum compound in patients with ovarian CS, the platinum-taxane combination is considered a reasonable and certainly better tolerated option [10]. In the case described herein, the authors selected paclitaxel-carboplatin combination chemotherapy because they initially suspected a serous adenocarcinoma of the ovary. With the tumor being a serous adenocarcinoma, albeit of the fallopian tube, the carcinomatous element disappeared.

The main carcinomatous elements of tubal and ovarian CSs are serous and endometrioid adenocarcinomas. The authors' limited experience indicates that a serous adenocarcinomatous component of tubal CS can be cured by NAC with TC. The authors believe that further studies of NAC for gynecologic CS will lead to fully effective treatment strategies.

References

[1] Fujii H., Yoshida M., Gong Z.X., Matsumoto T., Hamano Y., Fukunaga M., et al.: "Frequent genetic heterogeneity in the clonal evolution of gynecological carcinosarcinoma and its influence on phenotypic diversity". *Cancer Res.,* 2000, *60*, 114.

[2] Le T., Shahriari P., Hopkins L., Faught W., Fung K., Fung M., *et al.*: "Prognostic significance of tumor necrosis in ovarian cancer patients treated with neoadjuvant chemotherapy and interval debulking surgery". *Int. J. Gynecol. Cancer,* 2006, *16*, 986.

[3] Kuhn W., Rutke S., Späthe K., Schmalfeldt B., Florack G., von Hundelshausen B., *et al.*: "Neoadjuvant chemotherapy followed by tumor debulking prolongs survival for patients with poor prognosis in International Federation of Gynecology and Obstetrics Stage IIIC ovarian carcinoma". *Cancer,* 2001, *92*, 2585.

[4] Vergote I., De Wever I., Tjalma W., Van Gramberen M., Decloedt J., van Dam P., et al.: "Neoadjuvant chemotherapy or primary debulking surgery in advanced ovarian carcinoma: a retrospective analysis of 285 patients". *Gynecol. Oncol.,* 1998, *71*, 431.

[5] Rauh-Hain J.A., Growdon W.B., Rodriguez N., Goodman A.K., Boruta D.M. 2nd, Schorge J.O., *et al.*: "Carcinosarcoma of the ovary: a case-control study". *Gynecol. Oncol.,* 2011, *121*, 477.
[6] Tate Thigpen J., Blessing J.A., DeGeest K., Look K.Y., Homesley H.D.; Gynecologic Oncology Group: "Cisplatin as initial chemotherapy in ovarian carcinosarcomas: a Gynecologic Oncology Group study". *Gynecol. Oncol.,* 2004, *93*, 336.
[7] Cicin I., Saip P., Eralp Y., Selam M., Topuz S., Ozluk Y., et al.: "Ovarian carcinosarcomas: clinicopathological prognostic factors and evaluation of chemotherapy regimens containing platinum". *Gynecol. Oncol.,* 2008, *108*, 136.
[8] Duska L.R., Garret A., Eltabbakh G.H., Oliva E., Penson R., Fuller A.F., *et al.*: "Paclitaxel and platinum chemotherapy for malignant mixed mullerian tumors of the ovary". *Gynecol. Oncol.,* 2002, *85*, 459.
[9] Leiser A.L., Chi D.S., Ishill N.M., Tew W.P.: "Carcinosarcoma of the ovary treated with platinum and taxane: The Memorial Sloan-Kettering Cancer experience". *Gynecol. Oncol.,* 2007, *105*, 657.
[10] Harris M.A., Delap L.M., Sengupta P.S., Wilkinson P.M., Welch R.S., Swindell R., *et al.*: "Carcinosarcoma of the ovary". *Br. J. Cancer,* 2003, *88*, 654.

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