

Research Letter

Rapid progression of synchronous ovarian and endometrial cancers with massive omental carcinomatosis

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Accepted 13 October 2011

We present a rare case of a 41-year-old woman with synchronous primary cancers of the endometrium and ovary, both in advanced stages. Palliative surgery with incomplete tumor debulking followed by the first trial of chemotherapy provided no treatment benefit to her prognosis and she died shortly thereafter.

A 41-year-old woman, para 1, was referred to our department for prolonged and profuse menstrual bleeding, poor appetite and marked abdominal distension. Abdominal ultrasound and computed tomography showed a large left adnexal tumor accompanied by massive ascites and carcinomatosis (Fig. 1). The levels of tumor markers, including cancer antigen (CA) 125, CA 19-9, and carcinoembryonic antigen (CEA), were 1588 U/mL, 21 U/mL, and 1.4 ng/mL, respectively. During her operation, we noted a huge omental cake of about 35 cm (Fig. 2), a left ovarian tumor with rectal serosa invasion, diffuse intraperitoneal (including bowels) tumor implantation, and massive ascites totaling about 6600 mL. The uterus, the contralateral ovary and tube, and the liver surface were not involved.

Suboptimal debulking surgery was done (residual tumor size > 1 cm), and the estimated blood loss was 2000 mL. The microscopic findings included two synchronous tumors of the left ovary and endometrium. The histological types were mixed clear cell (moderately differentiated), endometrioid (well-differentiated) carcinoma of the left ovary (90% clear and 10% endometrioid), and mucinous (moderately differentiated) carcinoma of the endometrium, respectively. The contralateral ovary revealed a microscopic tumor implant. The final histopathological findings were synchronous ovarian clear cell–endometrioid carcinoma and endometrial mucinous carcinoma, with massive omental carcinomatosis, without lymph nodes metastasis, FIGO IIIC (pT3cN1) (Figs. 3 and 4).

She received adjuvant chemotherapy with carboplatin and taxol immediately after the operation. The levels of tumor

markers CA 125 and CA 19-9 were 156 U/mL and 24 U/mL, respectively, after the operation and during chemotherapy. However, she suffered from poor appetite, abdominal distension, and a weight increase at the third month after the operation. The tumor markers CA 125 and CA 19-9 were elevated again (455 U/mL and 303 U/mL, respectively). Abdominal computed tomography showed peritoneal carcinomatosis with moderate ascites, along with irregular wall thickening of the transverse colon, about 9.7 cm in length, resulting in severe bowel obstruction. We proceeded with conservative treatment that included antibiotics and fluid supplements, but her condition rapidly worsened. She passed away on the 14th day after her second admission (3 months after her operation).

Synchronous primary cancers of the endometrium and ovary (SPCEOs) are uncommon, and the ovarian histology was endometrioid in 92% of these cases. Among the cases of coexistent ovarian involvement, 69% occurred in patients with grade 1 endometrial cancer, and 58% occurred with inner myometrial invasion. Careful preoperative and intraoperative assessment of the adnexa is mandatory in young women with endometrial cancer. Those who desire ovarian preservation should be counseled regarding the high rate of coexistent ovarian malignancy [1].

The cause of simultaneously arising neoplasms has yet to be elucidated. It has been suggested that embryologically similar tissues, such as those of the female genital tract, may be subject to the same carcinogenic or hormonal stimuli and thereby develop synchronous neoplasms. This phenomenon of synchronously arising malignancies of the female genital tract seems to be more commonly seen in premenopausal than postmenopausal women [2]. The occurrence of multiple malignancies decades earlier than expected raises the question of genetic susceptibility. Until now, we have not found any family histories that were clearly suggestive of an inherited genetic syndrome. However, the unusual characteristics of such patients, including the high incidence of concordant endometrioid histology [3,4] and the young age at the onset of malignancy, warrant further investigation. In the general population, endometrioid histology accounts for 16–24% of the epithelial ovarian carcinomas [4,5].

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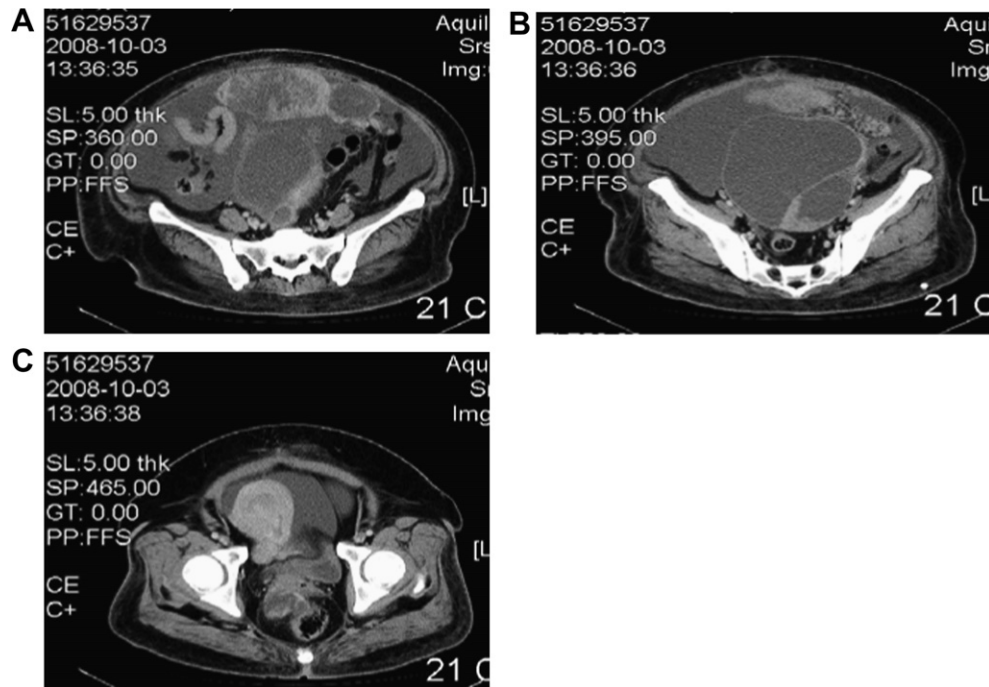


Fig. 1. Diffuse peritoneal carcinomatosis and massive ascites (A). A large locular cystic mass, 14.7 cm \times 14 cm, with a solid component in the left adnexa, favored of left ovarian origin (B). Enlarged uterus with some debris in the cavity (C).

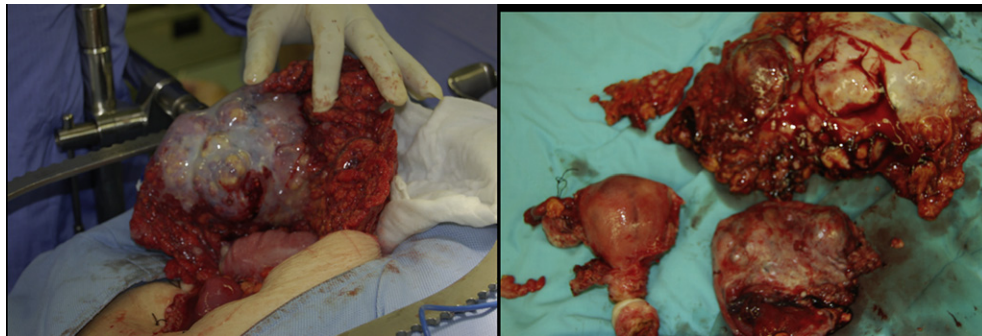


Fig. 2. Huge omental cake of about 35 cm and the main tumor about 20 cm from the left ovary.

Zaino et al reported that 96% of the ovarian tumors found concurrently with type 1 endometrial cancers were endometrioid or adenosquamous, and some showed as high as 88%

endometrioid ovarian histology [4]. Although no stimulating factor has been described to account for the effect, estrogens [6], androgens [2] and endometriosis [7,8] have been hypothesized as possible contributing factors.

The most common presenting symptom has been abnormal vaginal bleeding, as in both of the tumors presented here. During the past two decades, maximum cytoreductive surgery (also called debulking surgery; residual tumor is ≤ 1 cm) has been the recommended surgical approach for advanced stages of ovarian carcinoma. The residual tumor volume after surgery is one of the strongest prognostic factors, and only patients who undergo complete or optimal surgery are likely to survive long term (i.e., 50% after 5 years). A well-trained surgeon in the field of gynecological oncology can achieve an optimal tumor reduction in up to 75% of patients with advanced stage ovarian cancer. During the procedure, bowel resection, especially rectosigmoid, must be undertaken in 30–40% of cases, and para-aortic and pelvic lymphadenectomy should be

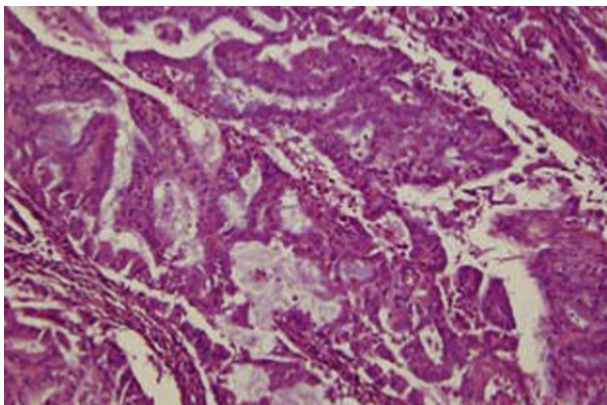


Fig. 3. Mucinous carcinoma of the endometrium.

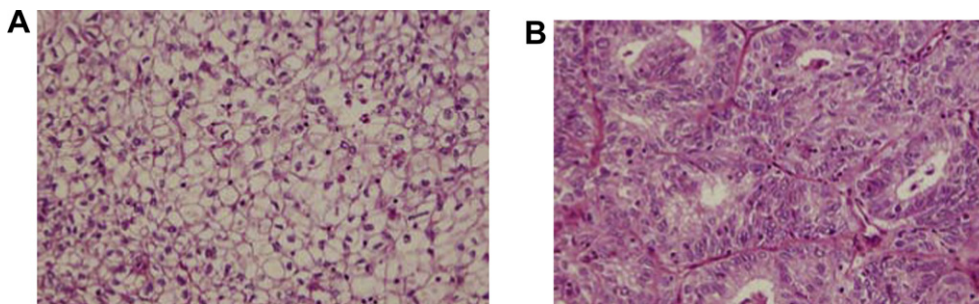


Fig. 4. (A) Clear cell carcinoma of the ovary (90%). (B) Endometrioid carcinoma of the ovary (10%).

performed after there has been adequate tumor reduction in the abdominal cavity. In advanced ovarian cancer patients, many studies have demonstrated that cytoreduction to 1–2 cm residual volume does not offer a significant survival advantage as compared to those with > 2 cm residual volume. The current Gynecologic Oncology Group definition of optimal residual volume is ≤ 1 cm [9–12].

Very advanced cancer with massive peritoneal carcinomatosis and/or stage IV disease requires an aggressive surgical procedure but yields a poor prognosis and a higher risk of unacceptable complications. For these worst cases, the concept of cytoreductive surgery is moving toward the alternative strategy of chemosurgical cytoreduction, in which interval cytoreductive surgery is undertaken after three cycles of front-line chemotherapy. The goal of this experimental strategy is to achieve a complete tumor response after front-line chemosurgical therapy, and a better quality of life [13]. The Scottish Randomized Trial in Ovarian Cancer (SCOTROC) was an excellent trial, adding important information to our knowledge regarding chemotherapy for ovarian cancer. However, its attempt to analyze the benefit of aggressive surgery, which was not an endpoint of the trial, by retrospectively using unclear and faulty definitions and a nonvalidated, preoperative prognostic model, is significantly flawed. The notion that performing bowel resection and/or pelvic/para-aortic node dissection to achieve optimal (≤ 1 cm residual) cytoreduction is too aggressive is not supported by the data in this study or any other. It is the concept itself – that the need to perform such procedures is an indication of poor tumor biology – which should be abandoned, not the cytoreductive procedures themselves.

Patients diagnosed with a single primary tumor with metastasis (SPM) have a significantly worse survival rate than patients with dual primary tumors (SPCEOs). Patients in whom both tumors are of endometrioid histology survive longer than patients with other histological subtypes, and patients diagnosed with SPM have a worse survival rate if the mode of spread is from the ovary to the endometrium rather than vice versa. Genetic analysis may represent a powerful tool for use in clinical practice to distinguish between SPM and SPCEO in patients with synchronous ovarian/endometrial cancer and to predict disease outcome [14].

For the case we presented here, no obvious family history could be determined. Genetic analysis is strongly suggested for her family in the future.

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