

Two Cases of Synchronous Metastasis of Colon Cancer to the Ovary

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Introduction

Ovarian metastases from primary colorectal cancer are reported to be present in 6% (3-8%) of women who have undergone colorectal resection [1]. In Japan, among primary lesions that metastasize to the ovary, gastric cancer is the most frequent, followed by breast cancer and colon cancer [2]. In general, ovarian metastasis from colon cancer is more frequently simultaneous than meta-chronous. It is difficult to diagnose preoperatively, because there are no highly

specific radiological features that can differentiate between primary and metastatic ovarian masses [3]. However, differentiation between primary ovarian cancer and ovarian metastasis is important in order to prevent inappropriate management and suboptimal treatment. In most cases of ovarian metastasis, the primary tumor site is indicated by histopathological examination of the ovary. Herein, we report the cases of two women with synchronous ovarian metastasis from colon cancer, which was diagnosed by histopathological examination of the resected specimens.

Case 1

A 35-year-old Japanese woman who was 27 wk pregnant was referred to our gynecology department for investigation of increasing ascites and an elevated tumor marker after appendectomy for acute appendicitis. According to the patient's family history, she had an aunt with uterine cancer and a grandfather with stomach cancer. Although histology of the resected appendix revealed catarrhal appendicitis with no malignant findings, the ascites were yellow and gelatinous and cytology showed mucinous, well-differentiated adenocarcinoma clusters. Laboratory tests showed elevated serum CEA (228.5 ng/ml; normal range <5.0 ng/ml) and serum CA19-9 (6 U/ml; normal range <2.5 U/ml) values and normal serum CA125 values (33.6 U/ml; normal range <35 U/ml). Magnetic resonance imaging (MRI) revealed a 9 cm, well-circumscribed, cystic tumor that probably originated from the left ovary (Figure 1A). The right ovary was swollen. The mass had a high signal intensity on T2-weighted images. A contrast-enhanced Computed Tomography (CT) scan was not done because of the patient's pregnancy. At first, the tumor was diagnosed as ovarian cancer with malignant ascites found in pregnancy; thus, the patient planned to undergo cesarean section and bilateral oophorectomy after 34 wk of gestation. However, because of her elevated CA19-9 and CEA levels, a colonoscopy was performed. The colonoscopy identified a giant, protruding villous tumor in the transverse colon, which occupied almost the entire circumference of the lumen (Figure 1B). Biopsy revealed a tubulovillous adenoma of low grade only.

A definitive preoperative diagnosis was impossible. The patient was presumed to have bilateral ovarian metastasis from colon cancer or ovarian cancer concomitant with colon cancer. The patient underwent a laparotomy at 34 wk of gestation. The operative findings revealed that massive, yellow gelatinous ascites filled the pelvic cavity, including the

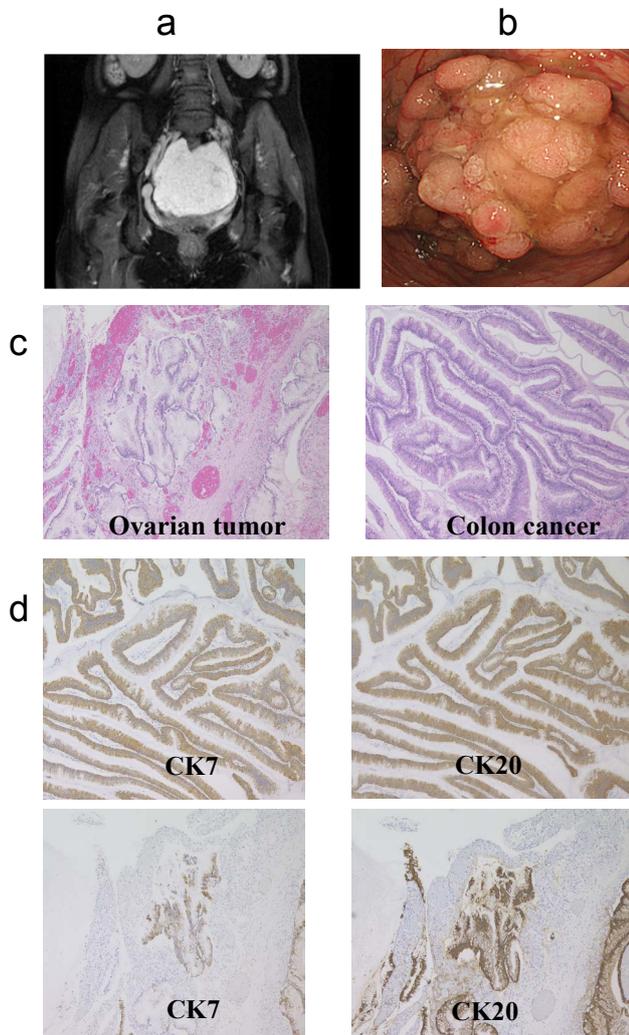


Figure 1: (A) MRI (T2 weight) revealed an approximately 9 cm well-circumscribed cystic tumor with a cord-like structure in the recto uterine pouch (arrow). Based on the MRI, the tumor appeared to originate in the left ovary. (B) Colonoscopy revealed a giant protruding villous tumor in the transverse colon that occupied almost the entire circumference of the lumen. (C) Histology of the ovarian tumor (left) was microscopically similar to that of the colon cancer (right). (D) Immuno-histochemical staining revealed that both the colon cancer and the ovarian tumor were positive for CK7 and CK20.

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recto uterine pouch and around the ovaries, and that the advanced transverse colon cancer had invaded the serosa. There were several nodules in the omentum and the whole abdominal cavity. Cytology revealed malignant ascites. We next performed cesarean section, colectomy, bilateral oophorectomy, and resection of the nodules in the omentum. The operation was incomplete, because of diffuse peritoneal dissemination.

Microscopically, the histology of the bilateral ovarian tumors and nodules in the omentum was similar to that of the colon cancer (Figure 1C). The transverse colon cancer consisted of mucinous adenocarcinoma cells that had invaded the serosa, with lymph node metastasis. Although there was continuity in the normal and atypical epithelium components in the transverse colon, the normal ovarian parenchyma was intact.

Histology and immune histochemistry showed that both the colon cancer and the ovarian tumor were positive for CK7 and CK20 (Figure 1D). Based on these similarities, the patient was diagnosed with transverse colon cancer that had metastasized to the ovaries. After the operation, the patient underwent multidisciplinary treatment and survived for 4 y after the operation.

Case 2

A 46-year-old Japanese female was referred to our gynecology department for treatment of an ovarian tumor. Laboratory tests revealed elevated serum CEA (29.0 ng/ml) and CA19-9 (88 U/ml) values and normal serum CA125 values (236 U/ml). An enhanced CT scan revealed a giant polycystic tumor of the left ovary with a solid component (Figure 2A). A barium enema revealed a protruding tumor measuring 2.2 cm in diameter in the descending colon, which occupied half of the circumference of the lumen, with wall deformation. The right ovary was swollen, but no tumor was identified. There were several 1-2 cm nodules in the recto uterine pouch.

A Positron Emission Tomography (PET)/CT scan showed a 10 cm polycystic tumor with solid parts in the abdomopelvic cavity. The cystic walls of this tumor were thick. There were ascites in the pelvis and numerous small nodules diffusely located in the subphrenic peritoneal space and around the liver and right kidney. Although the cystic component of the tumor was negative for fludeoxyglucose (FDG) uptake, the solid part showed strong FDG uptake, followed by delayed enhancement. The peritoneal nodules exhibited FDG uptake similar to that of the tumor. The primary descending colon cancer also could be visible at PET scan (Figure 2B).

Based on a diagnosis of disseminated descending colon cancer, the patient underwent a laparotomy. Surgery included left-sided hemicolectomy; appendectomy; bilateral oophorectomy; total hysterectomy; right nephrectomy; and resection of the omentum and peritoneal nodules located on the S6 segment of the liver, in the mesocolon, and in the subphrenic peritoneal space.

The cytology of the ascites was positive. Because of diffuse peritoneal dissemination, the operation was a macroscopically incomplete resection. Microscopically, the descending colon cancer consisted of mucinous adenocarcinoma cells invading the serosa, with multiple lymph node metastases. Histological examination revealed similarities between the descending colon and ovarian tumors (Figure 2C). Immunohistochemistry revealed that the ovarian tumor was negative for CK7 and positive for CK20 (Figure 2D). These findings indicated that the tumor was an ovarian metastasis from descending colon cancer. The patient was followed up, but she died 12 months after the operation.

Discussion

The ovaries are the site of metastasis for many cancers, and colorectal cancer is the most common primary cancer [4,5]. Colorectal cancer accounts for 65% of the malignancies that were found to have ovarian metastases at the time of primary surgery [6]. The incidence of ovarian metastases from gastrointestinal tumors seems to be higher in young menstruating women [7]. A previous report suggested that metastasis to the ovaries could be due to steroid hormone affinity between the primary colon cancer, which possesses hormone receptors, and hormone secretion organs, such as the ovaries [8].

Ovarian metastasis is generally found synchronously rather than meta-chronously thus, ovarian masses discovered at initial treatment

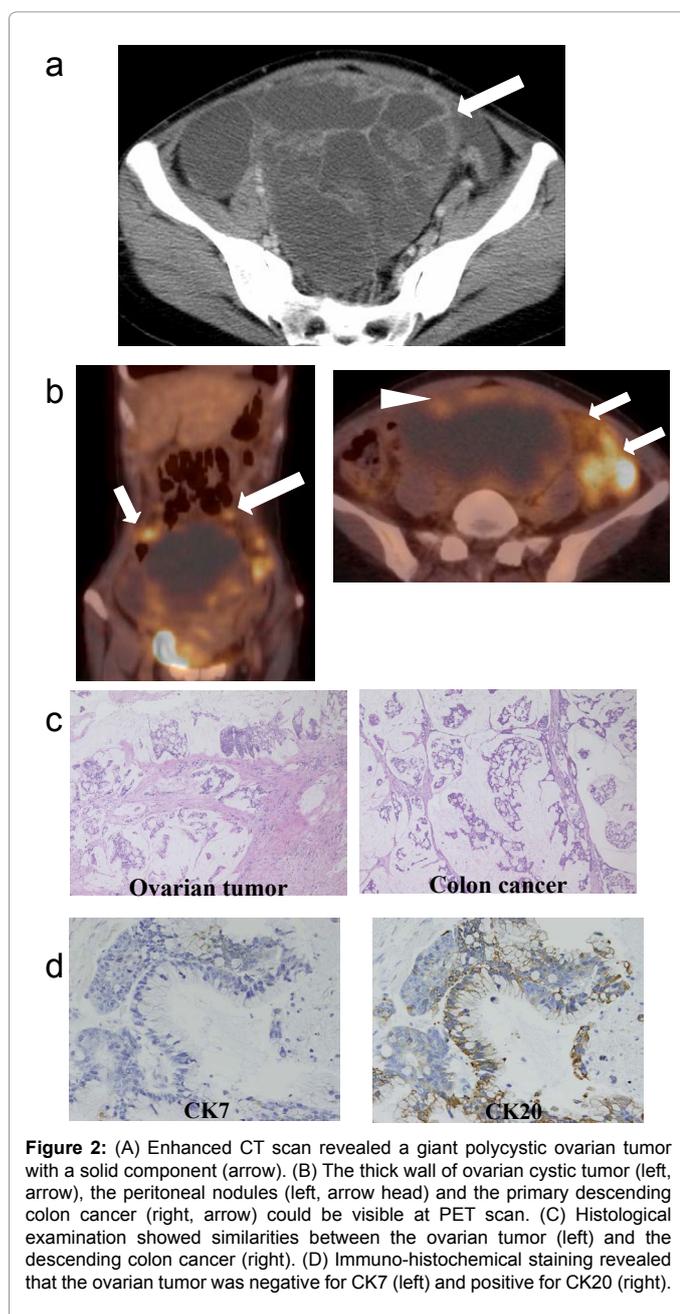


Figure 2: (A) Enhanced CT scan revealed a giant polycystic ovarian tumor with a solid component (arrow). (B) The thick wall of ovarian cystic tumor (left, arrow), the peritoneal nodules (left, arrow head) and the primary descending colon cancer (right, arrow) could be visible at PET scan. (C) Histological examination showed similarities between the ovarian tumor (left) and the descending colon cancer (right). (D) Immuno-histochemical staining revealed that the ovarian tumor was negative for CK7 (left) and positive for CK20 (right).

should always be assumed to be secondary lesions [3,9]. However, there are no highly specific radiological features that can be used to differentiate between primary and metastatic ovarian tumors. Therefore, precise preoperative diagnosis is difficult [10,11] Although bilateral ovarian masses are generally found far more often in cases of ovarian metastasis than with primary ovarian cancers they are also regularly seen in primary ovarian tumors [11-14]. Most metastases to the ovaries from the GI tract are of a cystic nature but primary ovarian neoplasms are also often cystic in nature [11,15]. Laboratory tests can be a useful reference during the diagnostic process. CA125 is thought to be a prognostic and predictive tumor marker for primary ovarian cancer [16]. On the other hand, elevated levels of the tumor markers CA-19-9 and CEA suggest a metastasis from GI tract cancer. Previous reports have shown that these tumor markers can help to discriminate between primary ovarian tumors and metastasis to the ovaries [11]. In the present cases, when we suspected ovarian metastasis based on laboratory data, including highly elevated CA19-9 and CEA levels, we were able to detect the concomitant colon cancer by searching for the primary site of cancer. Histopathological tests and observations were necessary to distinguish ovarian metastasis from a primary ovarian lesion. A previous report found that all ovarian metastases from GI tract cancer were adenocarcinoma, and 29% were mucinous-type adenocarcinoma [17].

CK7 and CK20 expression patterns are reported to be helpful in differentiating between primary and metastatic lesions. The CK7-/CK20+ expression pattern is found in high proportions of colorectal carcinomas (68%); the proportion is dependent on the tumor's histologic grade (75% of low-grade versus 52% of high-grade tumors). Moreover, almost all ovarian metastases from colon cancer are CK7-/CK20+ [18].

In the present cases, based on the histology of the tumors and on the immune histochemical results for CK7 and CK20, we were able to diagnose the tumors accurately as ovarian metastases from colon cancer. There is no consensus on how ovarian metastases arise from primary colorectal cancers. Hematogeneous metastasis is a likely possibility, as ovarian metastasis often occurs without peritoneal dissemination or lymph node metastasis [19]. On the other hand, previous reports have shown that ovarian metastasis results from direct implantation or lymphatic spread [20]. According to the 2010 guidelines of the Japanese Society for Cancer of the Colon and Rectum (JSCCR), ovarian metastasis from colon cancer is classified as peritoneal dissemination. The frequency of primary colorectal cancer with concomitant peritoneal dissemination is reported to be 4.3-7.3%. In such cases, the average survival is 6.9-8.5 months [21,22]. Unlike other primary gastrointestinal cancers, in cases of primary colorectal cancer with peritoneal dissemination, if an R0 resection can be obtained, long-term survival can be expected in selected patients. A previous report showed that prophylactic oophorectomy during primary resection for colorectal cancer was not beneficial in terms of survival [23]. Thus, in cases in which synchronous ovarian metastasis from colon cancer is identified, cyto-reduction surgery in addition to removal of the primary colon cancer during the initial operation is an option [17,24,25] In the present two cases, although the second patient died 12 months after surgery, the first patient survived 4 y after cyto-reduction surgery in addition to colectomy with subsequent multidisciplinary treatment, even though the initial resection was incomplete.

In summary, ovarian metastasis from colon cancer is not uncommon and should be considered when investigating ovarian tumors, especially those of a cystic nature found in conjunction with

elevated serum CA19-9 and CEA levels. Microscopic patterns and characteristic immune histochemical phenotypes, including CK7 and CK20, may facilitate an accurate diagnosis. Although the prognosis for ovarian metastasis from colon cancer is generally not good, radical surgical resection may be an option for long-term survival in selected patients.

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