Metastatic colon cancer of an ovarian cancer origin mimicking primary colon cancer: A case report

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Metastatic colorectal cancer is rare and its origins are difficult to define if the gross features of colorectal cancer mimic primary colorectal cancer. However, accurate diagnosis is essential because the treatment and prognosis may vary depending on the origin of the cancer. This report is about a 74-year-old female patient with metastatic sigmoid colon cancer of ovarian origin that mimicked primary sigmoid colon cancer. She spent a 3-year period disease-free from ovarian cancer after surgery and adjuvant chemotherapy. At the time of initial diagnosis, the cancer was diagnosed as a primary sigmoid colon cancer, because the cancer appeared to be a solitary intra-luminal fungating mass. However, the final pathologic result showed that the cancer was metastatic sigmoid colon cancer of ovarian origin and it was confirmed by immunohistochemical staining of cytokeratins-7, -20, and Wilms tumor-1. Therefore, even if colorectal cancer is a single intra-luminal lesion, patients should be suspected of having metastatic colorectal cancer if they have other cancer histories. At this time, immunohistochemical staining using various cancer markers may be a useful tool to distinguish the origin of cancer.

Keywords: Neoplasm metastasis, Ovarian neoplasms, Immunohistochemistry

INTRODUCTION

Epithelial ovarian carcinoma usually metastasizes to adjacent organs through direct invasion and intraperitoneal dissemination. The most common route of dissemination is through transcoelomic metastasis; conversely, hematogenous spreading is rare. Distant metastasis often occurs in the liver, lung, or brain [1,2]. Considering these facts, it is expected that metastatic colorectal cancer originating from ovarian cancer will initiate from serosal seeding and invade inward. Therefore, if metastatic colon cancer is isolated only in the colon and grows from the colonic mucosa to the serosa, it is difficult to distinguish it from primary colorectal cancer.

We report a case in which a patient who underwent surgery and adjuvant chemotherapy for ovarian cancer and had a disease-free period was diagnosed with metastatic colon cancer mimicking primary colon cancer 3 years later.

CASE REPORT

A 74-year-old woman diagnosed with sigmoid colon cancer was hospitalized for surgery in December 2017. Her past medical problems were hypertension, hypothyroidism, and ovarian cancer. Her medical examination in 2014 revealed that her serum cancer antigen 125 (CA-125) level was elevated at 285.4 IU/mL and that her other tumor marker levels (α-fetoprotein and carcinoembryonic antigen [CEA]) were within the normal ranges. A 5-cm left ovarian mass was observed on gynecology sonography and computed tomography (CT). She underwent exploratory laparotomy and left salpingo-oophorectomy at a local hospital. Because the malignant tumor cells were observed in frozen biopsy of the left ovary, total abdominal hysterectomy combined with both adnexectomy and total omentectomy were additionally performed. In the final pathologic examination, carcinoma (probably serous adenocarcinoma) was only limited to the left ovary (pT1a). However, because the histologic grade was poorly differentiated, she underwent adjuvant chemotherapy with paclitaxel and carboplatin. After six cycles of chemotherapy, she spent a 3-year disease-free period from ovarian cancer.
After the 3-year disease-free period, an abnormal finding in the sigmoid colon was observed in her follow-up CT (Fig. 1). Further evaluation was performed for a more accurate diagnosis. A 3-cm bleeding polypoid mass lesion was found 40 cm from the anal verge on colonoscopy. The tumor arose from the bowel mucosa and appeared as primary colon cancer. An endoscopic biopsy was performed. The pathologic examination revealed poorly differentiated tubular adenocarcinoma. The laboratory examination showed that although the serum CA-125 level was slightly elevated at 48.70 IU/mL, the CA 19-9 and CEA levels were normal. Taken together, the tumor was initially regarded as primary sigmoid colon cancer, not metastatic colon cancer.

On January 2018, she underwent laparoscopic anterior resection and end-to-end colon anastomosis. During the surgery, several enlarged mesentery lymph nodes and a hard para-aortic lymph node were observed and excised. However, there was no adjacent organ invasion or peritoneal dissemination. Macroscopically, a polypoid mass developed from the mucosa without involvement of the colonic wall (Fig. 2). However, the pathology results were different from the previous endoscopic biopsy results. Microscopically, poorly differentiated metastatic adenocarcinoma invaded the

![Fig. 1. Computed tomography demonstrated an irregular mass in the sigmoid colon.](image)

![Fig. 2. Photograph of the gross specimen. A polypoid mass was limited in the bowel lumen; no involvement of the bowel serosa was observed.](image)

![Fig. 3. Sigmoid colon tumor. (A) Lower magnification with routine hematoxylin and eosin (H&E) staining. The sigmoid colon tumor invaded the mucosa (×10). (B) Higher magnification with routine H&E staining. The sigmoid colon tumor showed histologic features of high-grade serous adenocarcinoma (×200).](image)
subserosa or pericolic adipose tissue (pT3) (Fig. 3). There were lymphovascular invasion and metastasis in 22 regional lymph nodes and one para-aortic lymph node of the 29 lymph nodes harvested in total. Immunohistochemical staining of the tumor showed positivity for cytokeratin-7 (CK-7) and Wilms tumor-1 (WT-1) protein but negativity for CK-20 and CEA (Fig. 4).

On the basis of the findings of immunohistochemical staining, we considered the possibility that the tumor was a metastatic serous adenocarcinoma of the ovary. The paraffin block of the previous left ovarian cancer was reviewed again in Gil Medical Center and pathologically diagnosed as high-grade adenocarcinoma, consistent with serous adenocarcinoma (Fig. 5). This consistent histologic result between the previous left ovarian cancer and sigmoid colon cancer demonstrated that the mimicked primary colon cancer was metastatic colon cancer originating from the previous ovarian cancer. The final diagnosis was recurrent ovarian cancer with colon metastasis (stage IV). Even though systemic chemotherapy with bevacizumab and paclitaxel was planned through multidisciplinary discussion, the patient refused the chemotherapy. The postoperative serum CA-125 level had normalized to 27.40 IU/mL. At 3 months follow-up examination after the surgery, serum CA-125 level was still normal and there was no evidence of recurrence on CT scan.

**DISCUSSION**

Colorectal cancer is the third most common cancer in Korea [3]. Of the types of colorectal cancer, metastatic colorectal cancer accounts for only 1% [4]. Metastatic colorectal cancer of an ovarian origin is very rare. Therefore, as shown in our case, metastatic colorectal cancer is easily misdiagnosed as primary colorectal cancer.

According to a Japanese autopsy study, only 5.97% of metastatic colorectal cancers were of an ovarian origin [5]. Only a few cases have been reported in which ovarian cancer recurs as an intraluminal bowel tumor without serosal invasion after a disease-free period. Zighelboim et al. [6] reported a case of a patient who underwent only left salpingo-oophorectomy without any further evaluation owing to a low malignancy potential. However, the patient was diagnosed with metastatic colorectal cancer 6 months after the ovarian cancer surgery. Kohyama et al. [7] reported a case of colon metastasis from ovarian cancer, which presented with intussusception 6 years after ovarian cancer surgery and adjuvant chemotherapy. Shibahara et al. [8] reported a case of a patient who underwent surgery and adjuvant chemotherapy for bilateral ovarian cancer but had colon metastasis after a disease-free period of 20 years. Kim et al. [9] reported a case of colonic metastasis presenting as an intraluminal fungating mass 8 years after surgery for ovarian cancer. Our case is similar to the presented case reports. Our patient who had no evidence of ovarian cancer recurrence after surgery and adjuvant chemotherapy for 3 years showed recurrence of metastatic sigmoid colon cancer mimicking primary colorectal cancer.

Colorectal cancer is usually treated with 5-fluorouracil and platinum agents, whereas ovarian cancer is treated with paclitaxel and platinum agents [10,11]. Therefore, defining the cancer origin is critical. A malignant medical history may be a helpful clue for the diagnosis of a metastatic colorectal tumor. However, as presented in this case, if a colorectal tumor is revealed after complete remission of ovarian cancer, defining its origin becomes more complicated.
The features of the tumor may be helpful to distinguish its origin. Ovarian cancer usually metastasizes through the transcoelomic route rather than the hematogenous route. Therefore, the colonic serosa is initially invaded, and the tumor infiltrates in an inward direction in most cases [1,2]. However, if the macroscopic features of metastatic colorectal cancer mimic those of primary colorectal cancer, it may be difficult to distinguish between metastatic colorectal cancer and primary colorectal cancer. In some cases, preoperative screening of serum tumor markers, such as CA-125 and CEA, may be a useful tool for an accurate diagnosis. However, up to 15% of ovarian cancer does not present with elevated serum CA-125 levels [12].

When the origin of the colorectal tumor is still unclear because of all of the problems presented above, immunohistochemical analysis can be used to demonstrate that the tumor is of an ovarian origin. Several tumor markers, such as CK-7, CK-20, CDX2 (homeobox protein CDX-2), MUC2 (mucin 2), MUC5AC (mucin 5AC), and AMACR (alpha-methylacyl-CoA racemase), have been studied to distinguish between colonic-origin and ovarian-origin tumors on immunohistochemical staining [13]. CK-7/CK-20 has been regarded as the standard panel for differentiation. CK-7 is expressed in the breast, lung, ovary, and urothelium, but usually not in the gastrointestinal or stratified squamous epithelium. CK-20 is commonly found in colorectal and gastric cancers, transitional cell carcinomas, and Merkel cell carcinomas, but is absent in lung, prostate, and non-mucinous ovarian cancers. In a study by Loy et al. [14], CK-7 positivity/CK-20 negativity in immunohistochemical staining is nearly 100% specific for an ovarian-origin tumor, and the specificity for CK-7 negativity/CK-20 positivity was up to 90% in a colonic-origin tumor. Other tumor markers, such as CEA and CA-125, can also be used although their specificity is slightly low.

Unlike metastatic colorectal cancer, metastatic ovarian cancer is common. Many studies have searched for an immunohistochemical marker to aid in the differential diagnosis of primary and metastatic ovarian carcinomas. WT-1 plays an essential role in the normal development of the organs of the genitourinary tract and mesothelium as well as Wilms tumors when it mutates. Although its biologic role is still unclear, most serous carcinomas of the ovary and peritoneum, mesothelium, and Wilms tumors have been shown to express WT-1 [15]. In our case, immunohistochemical staining of the sigmoid colon cancer revealed a positive finding for CK-7 and a negative finding for CK-20. Immunohistochemical staining of WT-1 protein and CEA was also performed to confirm that the cancer was of an ovarian origin. The cancer revealed positive findings for WT-1 and negative findings for CEA.

We misdiagnosed the solitary intraluminal sigmoid tumor as primary sigmoid colon cancer at first. Although the patient had an ovarian cancer history, she spent 3 years disease-free after surgery and adjuvant chemotherapy. In the preoperative evaluation, the gross features of the tumor mimicked primary colorectal cancer, and the biopsy results from the colonoscopy revealed poorly differentiated tubular adenocarcinoma. Even the CA-125 level was almost normal. However, the treatment and prognosis of primary colorectal cancer and metastatic colorectal cancer of an ovarian origin may be different. Although similar cases are rarely reported, accurate diagnosis is mandatory. Immunohistochemistry with final pathologic examination is a useful tool for distinguishing between primary colorectal cancer and metastatic colorectal cancer as proven by many studies. Therefore, if a patient with colorectal cancer has a history of cancer, metastatic colorectal cancer should be considered as one possibility, and differential examination should be performed for correct diagnosis, even though all factors suggest that the tumor is primary colorectal cancer.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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