SPANDIDOS PUBLICATIONS

ONCOLOGY LETTERS 11: 668-672, 2016

Sigmoid colonic metastasis by lymphatic spread occurring with unilateral Krukenberg tumor considered to be caused by stage IA early gastric cancer: A case report

DAISUKE FUJIMOTO, YASUO HIRONO, TAKANAORI GOI and AKIO YAMAGUCHI

First Department of Surgery, Faculty of Medicine, University of Fukui, Fukui 910-1193, Japan

Received November 11, 2014; Accepted September 21, 2015

DOI: 10.3892/ol.2015.3919

Abstract. Gastric cancer is one of the most common malignancies in Asia, and the second most common cause of cancer-associated mortality in Japan. Colorectal metastases originating from gastric adenocarcinoma are extremely rare. The present study reports an unusual case of lymphogenous sigmoid metastasis of gastric adenocarcinoma occurring in a 58-year-old female patient. Endoscopic and radiological findings were indicative of 0-IIc+IIa early gastric cancer, and radical distal gastrectomy with D2 lymph node dissection was performed. The pathological diagnosis was stage IA gastric adenocarcinoma (T1bN0M0), according to the Japanese classification of gastric cancer. A follow-up examination at 18 months post surgery revealed a recurrence of paraaortic lymph node metastasis, detected by abdominal computed tomography (CT) and positron emission tomography (PET)/CT. The patient received chemotherapy with S-1 and cisplatin. Subsequently, radiotherapy was administered to the paraaortic lymph nodes at levels Th11-L3. Follow-up abdominal CT and PET/CT revealed an enlarged left ovary, and abnormal uptake in the left ovary and sigmoid colon. An oophorectomy and sigmoidectomy with D3 lymph node dissection were performed. The pathological diagnosis was metastatic adenocarcinoma; this was identical to the gastric pathology in the previous pathological report. The patient continued treatment with chemotherapy. Although sigmoid colonic metastasis from gastric cancer is extremely rare, metastasis from gastric cancer must be considered during the differential diagnosis of cases involving a colorectal mass and a previous history of gastric cancer.

Introduction

Gastric cancer is one of the most common malignancies in Asia, and the second most common cause of cancer-associated mortality in Japan, accounting for 49,830 mortalities and 13.9% of all Japanese cancer mortalities in 2011 (1). Gastric cancer typically disseminates via hematogenous routes, lymphatic metastasis, local invasion of adjacent tissues, or transcoelomic or peritoneal spread (2). Common sites of metastasis include the regional lymph nodes, liver, peritoneum, lungs and bones (3). Metastases to the colon are more rare, and typically originate from kidney, skin, breast, prostate or ovarian carcinomas (4). From gastric cancer, colonic metastasis is extremely rare; this typically presents as linitis plastica or an annular stricture resembling advanced primary colon cancer (5). There have been reports of cases of colonic metastases assuming a polypoid or non-polypoid form that mimics early colon cancer; however, all of these previous cases were multiple metastases (5-7).

The present study reports a case of a patient with early gastric cancer who developed a heterochronous, single, non-polypoid colonic metastasis in the sigmoid colon and unilateral Krukenberg tumor, composed of poorly differentiated adenocarcinoma and signet ring cell carcinoma.

Case report

In September 2010, a 58-year-old female presented to the University of Fukui Hospital (Fukui, Japan) with anemia and was scheduled for an upper-GI endoscopy. A gastroscopy revealed a typical type 0-IIc+IIa-like tumor on the lesser curvature of the gastric body (8). Endoscopic biopsy specimens revealed a well-differentiated tubular adenocarcinoma. The patient underwent a distal gastrectomy with D2 lymphadenectomy and Billroth I reconstruction in October 2010 (Fig. 1A). The histopathological examination of the gastric tumor revealed a well-differentiated adenocarcinoma, with submucosal invasion and no lymph node metastasis (Fig. 1B). However, poorly differentiated adenocarcinoma and signet ring cell carcinoma were detected in the deepest part of the lesion in the submucosal layer (Fig. 1B). The tumor was staged as T1bN0M0 according to the Japanese classification of gastric cancer (8).

Following surgery, the patient was examined on outpatient basis. In February 2013, the patient's serum carcinoembryonic antigen (CEA) level had increased from the normal range (<5.0 ng/ml) to 42.1 ng/ml. An abdominal computed tomography (CT) scan and fludeoxyglucose-positron emission tomography (FDG-PET)/CT revealed recurrent paraaortic lateral lymph node metastasis (Fig. 2A and B). The patient received 7 cycles of

Correspondence to: Dr Daisuke Fujimoto, First Department of Surgery, Faculty of Medicine, University of Fukui, 23-3 Matsuoka Shimoaizuki, Eiheiji, Yoshida, Fukui 910-1193, Japan
E-mail: fujimoto@u-fukui.ac.jp

Key words: early gastric cancer, colonic metastasis, lymphatic spread

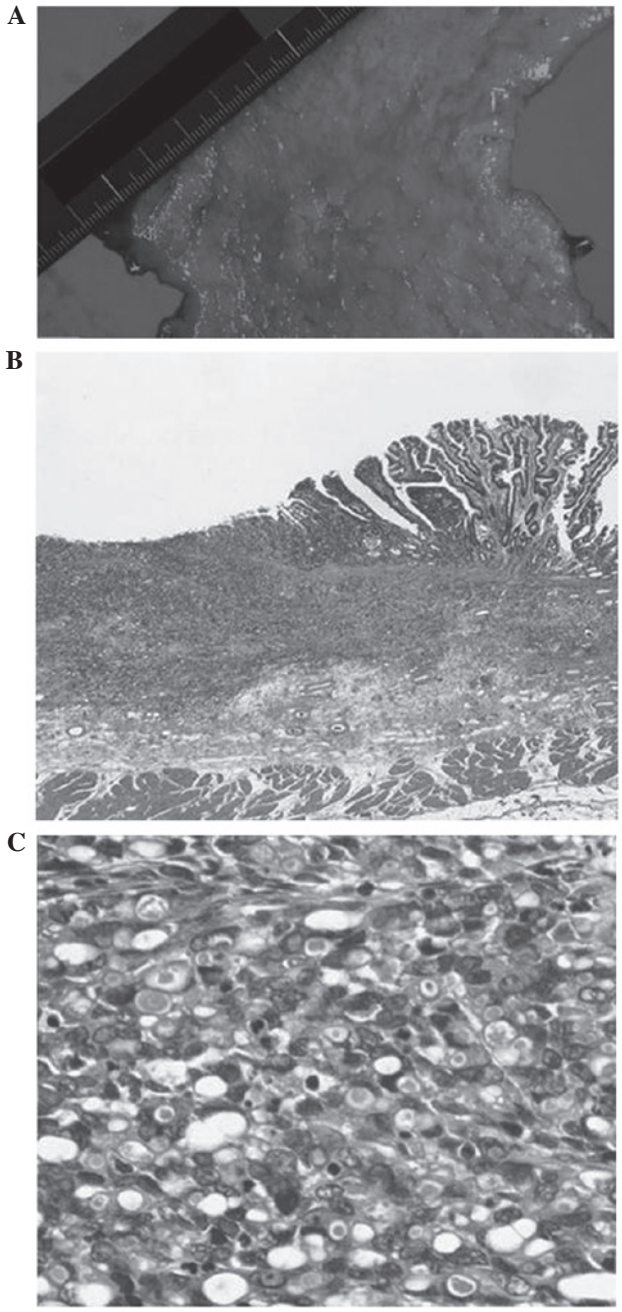

Figure 1. (A) Macroscopic view of the lesion. A well demarcated 3x2-cm shallow depressed (0-IIc) lesion (Japanese classification of gastric cancer) (7) in the lower body of the stomach. (B) On histological examination, the resected gastric tumor was composed of well-differentiated adenocarcinoma, with submucosal invasion. (C) In the deepest lesion of the submucosal layer, poorly differentiated adenocarcinoma and signet ring cell carcinoma were confirmed.

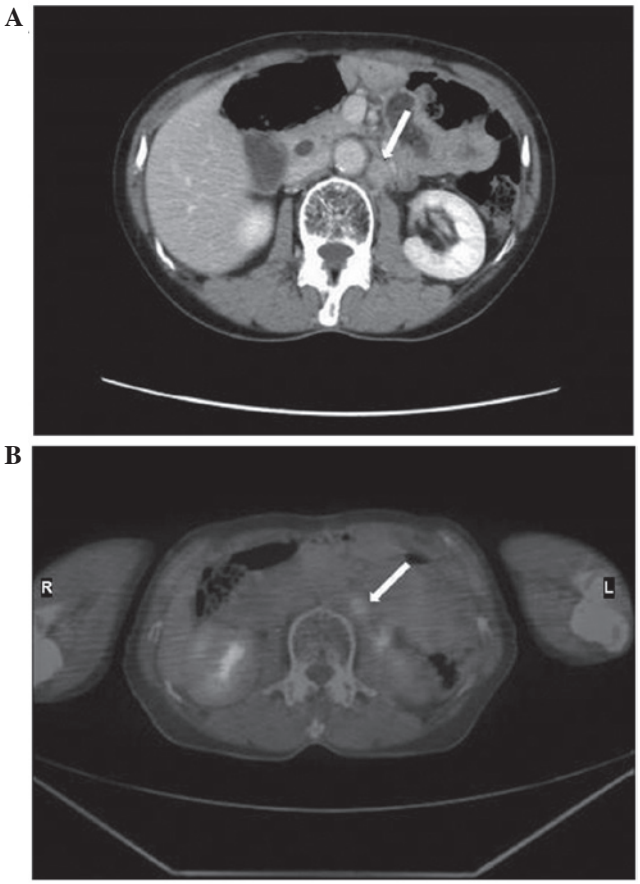

Figure 2. (A) CT scan revealed swollen lateral paraaortic lymph nodes (white arrow). (B) FDG-PET/CT showed hypermetabolism in the lateral paraaortic lymph nodes (white arrow); the maximum standardized uptake value of the tumor was 6.8. CT, computed tomography; FDG-PET, fludeoxyglucose-positron emission tomography.

chemotherapy with S-1 (80 mg/m^2/day; days 1-21) and cisplatin (60 mg/m^2/day; day 8). Following chemotherapy, radiotherapy was administered to the paraaortic lymph nodes of levels Th11-L3, to a total dose 54 Gy (2 Gy/fraction).

Subsequent to chemotherapy and radiation therapy, abdominal CT and FDG-PET scans were performed for evaluation of the therapy. The abdominal CT scan revealed an enlarged left ovary, and FDG-PET/CT indicated abnormal uptake unilaterally in the left ovary and sigmoid colon (Fig. 3A and B). In addition, a barium enema examination revealed an elevated lesion with central depression in the sigmoid colon, located at the site exhibiting abnormal accumulation on FDG-PET/CT (Fig. 3C). However, no abnormal uptake was observed in the paraaortic lymph nodes. On the basis of these findings, a diagnosis of unilateral Krukenberg tumor from gastric cancer and early colon cancer was determined. The patient underwent an oophorectomy and sigmoidectomy with D3 lymph node dissection (Fig. 4A-C).

Intraoperative findings indicated no peritoneal dissemination from gastric cancer, and intraoperative peritoneal washing cytology of the rectouterine pouch was negative for malignancy. On pathological examination, the left ovarian tumor was revealed to be a poorly-differentiated adenocarcinoma and signet ring cell carcinoma (Fig. 5A); the right ovary was unremarkable (Fig. 5B). The sigmoid colon tumor was also revealed to be a poorly-differentiated adenocarcinoma with scattered signet ring cell carcinoma (Fig. 5C), which had spread into the submucosal layer and partly permeated the serosal layer. Metastasis was detected in the sigmoid mesocolon lymph nodes, including the inferior mesenteric artery lymph nodes. Immunohistological staining revealed that the primary gastric cancer cells, ovarian tumor cells and sigmoid colon tumor cells were positive for cytokeratin (CK) 7 and negative for CK20 (Fig. 5D-I). Thus, the diagnosis was determined to be a unilateral Krukenberg tumor and sigmoid colonic metastasis from gastric cancer.

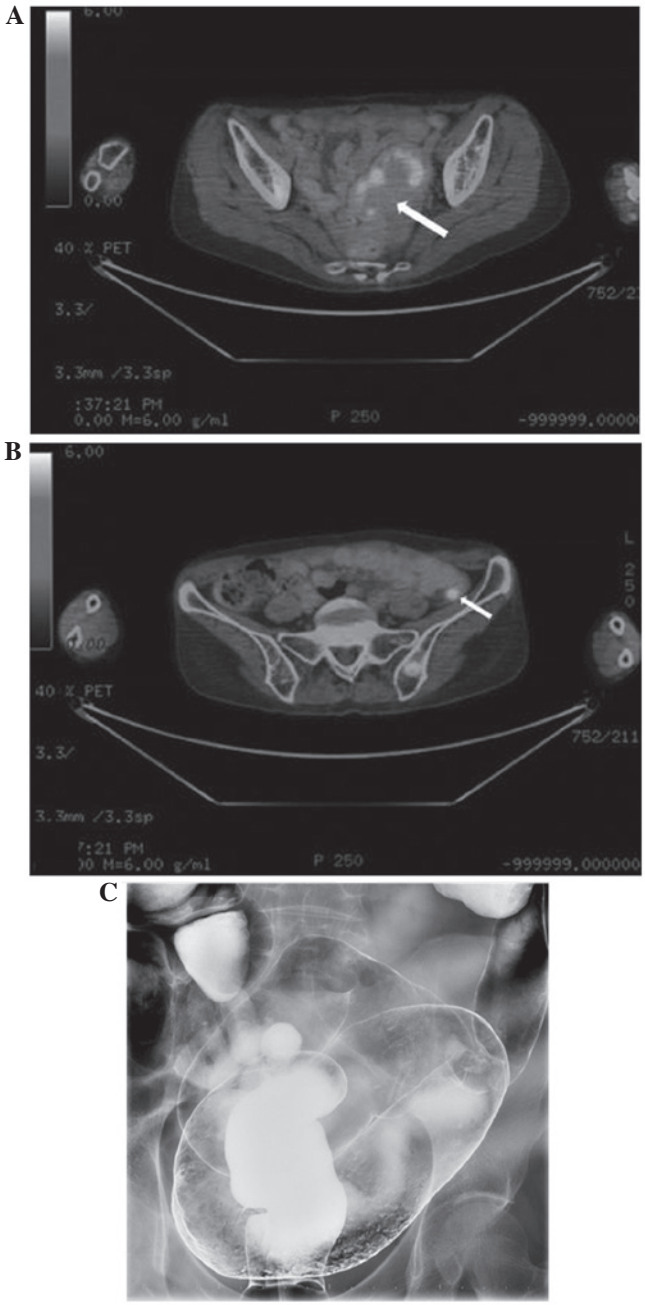

Figure 3. Fludeoxyglucose-positron emission tomography/computed tomography revealed a focal hypermetabolic lesion in the (A) left ovary and (B) sigmoid colon (white arrows). (C) Barium enema examination revealed an elevated lesion with central depression located in the sigmoid colon.

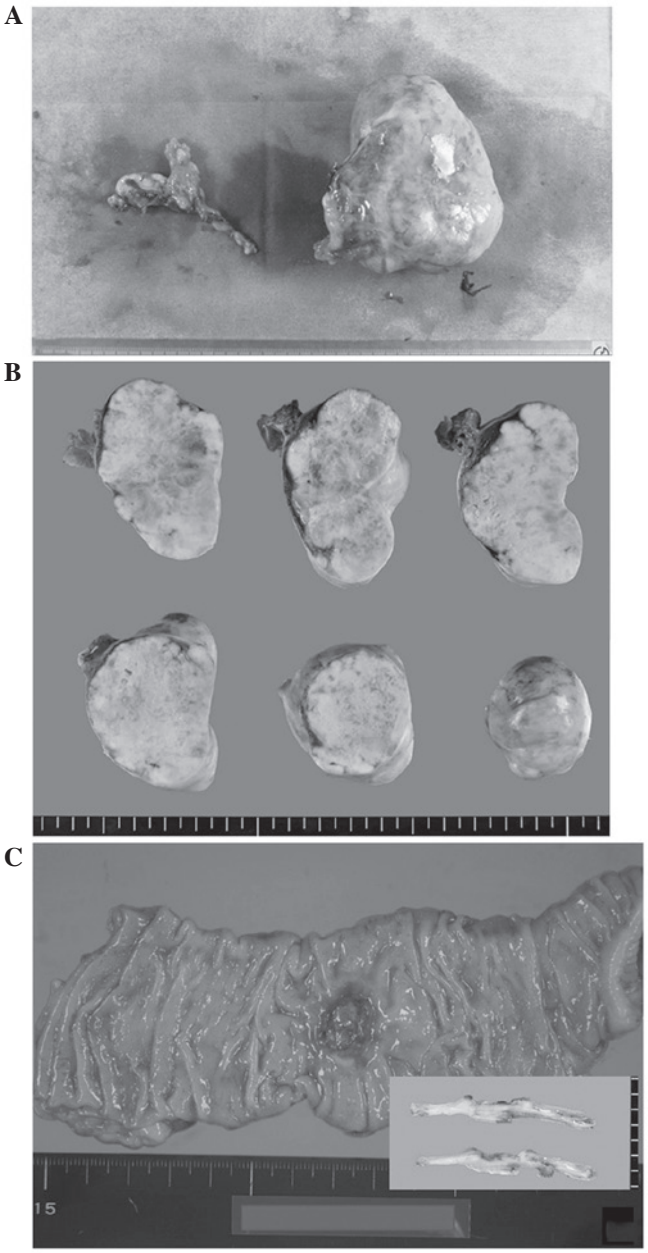

Figure 4. (A) Macroscopic appearance of resected both ovaries; the right ovary was normal in size, whilst the left ovary measured 10x7 cm. (B) Cross section of the ovary shows a predominantly yellow, solid tumor mass, almost replacing the ovary. (C) Gross appearance of the sigmoid tumor; the tumor mass exhibited central ulceration (inset: cut surface of the tumor).

Following the second surgery, the patient was administered with further chemotherapy consisting of S-1 (80 mg/m^2/day; days 1-14) and docetaxel (40 mg/m^2/day; day 1). The patient's clinical course is close observation; the patient has exhibited stable disease during this chemotherapy regimen, and is still disease-free with ongoing S-1 and docetaxel combined chemotherapy as of August 2015.

Discussion

Gastric cancer is one of the most fatal types of cancer, particularly in East Asian countries, including Japan. In clinical practice, the major routes of recurrence of gastric cancer following radical resection include hematogenous spread, peritoneal seeding, lymph node metastasis and local recurrence. Distant metastasis most frequently arises via the hematogenous route.

Colonic metastases are uncommon, typically originating from stomach, breast, skin (melanomas), renal, prostatic or ovarian carcinomas (4). In cases where colonic metastases arise from gastric adenocarcinoma, the hematogenous route is the most common mode of metastasis; metastatic deposits invade the submucosal lymphatic system, extending to form a linitis plastica appearance or an annular stricture (9). However, in the present case, lymphatic spread was considered to be the route of colonic metastasis from gastric cancer cells, which were determined to consist of poorly differentiated adenocarcinoma

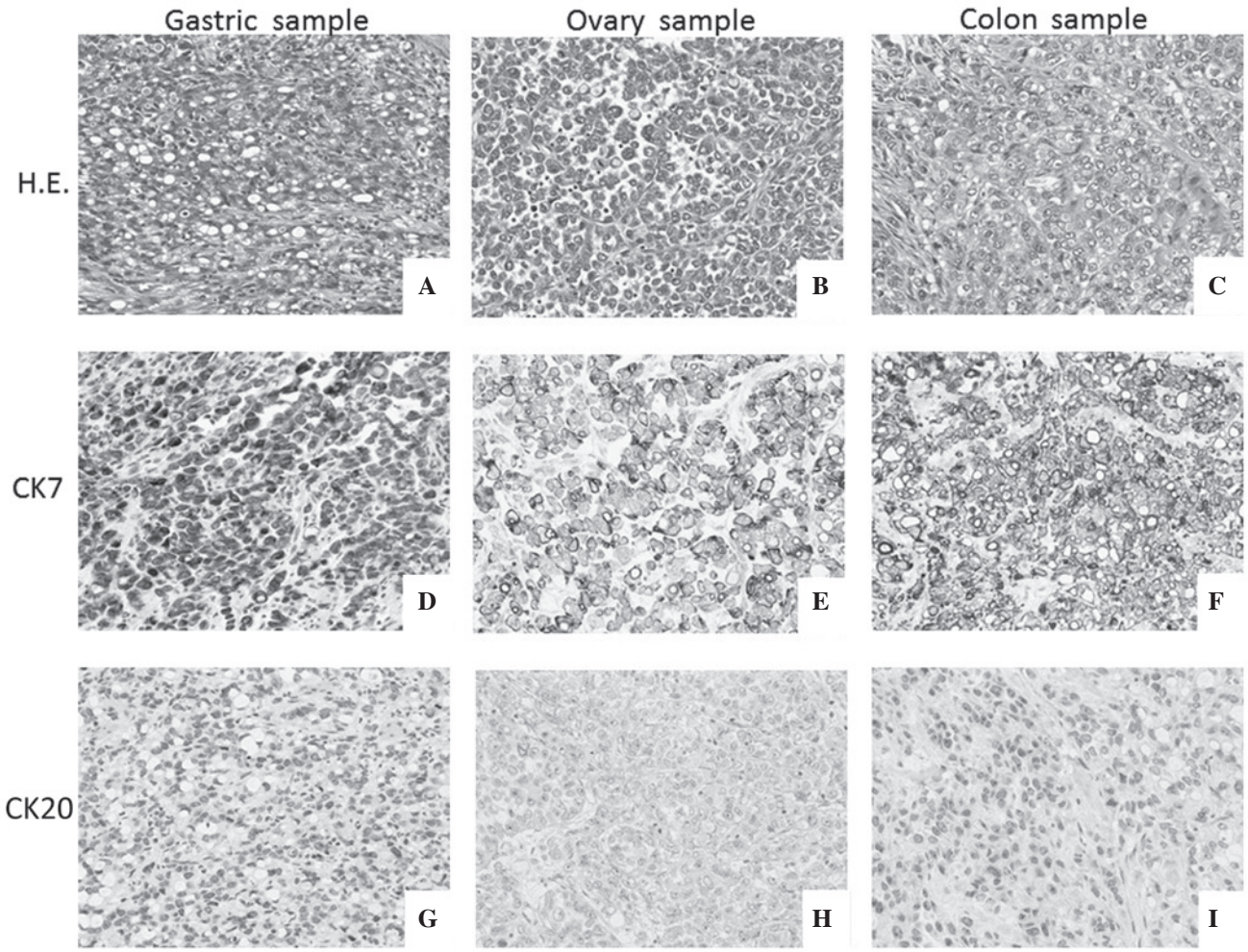

Figure 5. Histopathological analyses of gastric, colonic and ovarian tissues. (A, D and G) Gastric samples; (B, E and H) left ovary samples; (C, F and I) colon samples. (B and C) The left ovarian tumor and sigmoid tumor revealed a poorly-differentiated adenocarcinoma and signet ring cell carcinoma. (D-F) Immunostaining for CK7 was positive. (G-I) Immunostaining for CK20 was negative. CK, cytokeratin; H.E., hematoxylin and eosin.

and signet ring cells in the deepest submucosal layer of the primary gastric cancer. The following features indicated a lymphatic route of metastasis: i) Metastatic paraaortic lateral lymph nodes were detected prior to the second surgery; ii) pathologically metastatic lymph nodes were detected in the sigmoid mesocolon, considered to originate from paraaortic lymph node metastasis via lymphatic vessels; iii) no intraoperative indications of peritoneal metastasis were observed, and free cancer cells were not detected by cytological examination of the peritoneal washings; and iv) a Krukenberg tumor was diagnosed; although Krukenberg tumors may also be induced by complex mechanisms, lymph node metastasis is considered to be the most potent risk factor for their recurrence (10-12).

Secondary gastric carcinomatous deposits (metastatic tumors) in the colorectum invariably appear as single or multiple strictures; this stricture appearance is similar to that of primary colorectal cancer or inflammatory bowel disease. In rare cases, flat or depressed lesions or polyps arising from colonic metastasis of poorly differentiated gastric cancer and signet ring cell carcinoma have been reported; however, all previously reported cases presented as multiple synchronous lesions, which further serves to accent the novelty of the current presentation of single colonic depressed metastasis (4,13-15).

It is thought that the confirmed diagnosis of metastatic colon cancer has the most useful pathological finding. Immunohistochemical analyses may be performed to differentiate between gastric and colonic primary tumors, with CK7 and CK20 commonly used as tumor markers (16). CK7 expression has been observed in the majority of types of carcinoma, in carcinoid tumors originating from lungs and gastrointestinal tract (17), and in Merkel cell tumors of the skin (18). $CK20^+$ staining is observed in the vast majority of cases of colorectal carcinoma (17) and Merkel cell tumors (19), in addition to a high proportion of cases of gastric carcinoma, cholangiocarcinoma, pancreatic carcinoma and transitional cell carcinoma (16). In a previous study, all colorectal cancer samples metastatic to the ovary were $CK7^-/CK20^+$, while the majority of gastric carcinomas metastatic to the ovary exhibied a $CK7^+/CK20^-$ staining pattern (20). In the present case, the following features were observed: i) Sigmoid colon tumor cells with similar appearance to the pathology of the previous gastric cancer; ii) no tumor cells in the colonic mucosa, and proliferating tumor cells in the colonic submucosal layer; and iii) positive CK7 expression and negative CK20 expression on immunohistochemical analysis of the primary gastric cancer cells, metastatic ovarian tumor cells and sigmoid colon tumor

cells. Due to the aforementioned findings, a diagnosis of unilateral Krukenberg tumor and sigmoid colonic metastasis from gastric cancer was confirmed.

In conclusion, the present study reports the case of a patient with a unilateral Krukenberg tumor and sigmoid colonic metastasis derived from early gastric cancer. Although this is an extremely rare presentation, doctors must be aware of the possible occurrence of colonic metastasis from gastric cancer, particularly poorly-differentiated adenocarcinoma and signet ring cell carcinoma. It is necessary to postoperatively examine patients diagnosed with gastric cancer considering all possibilities, including colonic metastasis.

References

1. Hamashima C, Ogoshi K, Okamoto M, Shabana M, Kishimoto T and Fukao A: A community-based, case-control study evaluating mortality reduction from gastric cancer bϑy endoscopic screening in Japan. PLoS One 8: e79088, 2013.
2. Baston OV: The function of the vertebral veins and their role in the spread of metastases. Ann Surg 112: 138-149, 1940.
3. Rodriguez Salas N, González PC, Rivera T, López AA, Martín Marino A and Lara Alvarez MA: Colonic anastomosis and colonic polyp mucosal metastasis of signet ring cell gastric adenocarcinoma. Clin Transl Oncol 12: 238-239, 2010.
4. Ogiwara H, Konno H, Kitayama Y, Kino I and Baba S: Metastases from gastric adenocarcinoma presenting as multiple colonic polyps: Report of case. Surg Today 24: 473-475, 1994.
5. Katon RM, Brendler SJ and Ireland K: Gastric linitis plastica with metastases to the colon: A mimic of Crohn's disease. J Clin Gastroenterol 11: 555-560, 1989.
6. Metayer P, Antonietti M, Oumrani M, Hemet J, Lemoine F and Basuyau J: Metastases of gastric adenocarcinoma presenting as colonic polyposis. Report of a case. Dis Colon Rectum 34: 622-623, 1991.
7. Iwabuchi M, Hiwatashi N, Suzuki T, Teshima S, Saito T, Suzuki H, Mori Y, Ishibashi J, Chida N and Tadokoro K: Multiple depressed-type colonic cancer (IIc)-like configurations: metastases from gastric cancer. Dig Endosc 14: 73-77, 2002.
8. Japanese Gastric Cancer Association: Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer 14: 101-112, 2011.
9. Feczko PJ, Collins DD and Mezwa DG: Metastatic disease involving the gastrointestinal tract. Radiol Clin North Am 31: 1359-1373, 1993.
10. D'Angelica M, Gonen M, Brennan MF, Turnbull AD, Bains M and Karpeh MS: Patterns of initial recurrence in completely resected gastric adenocarcinoma. Ann Surg 240: 808-816, 2004.
11. Yoo CH, Noh SH, Shin DW, Choi SH and Min JS: Recurrence following curative resection for gastric carcinoma. Br J Surg 87: 236-242, 2000.
12. Berek JS and Natarajan S: Ovarian and fallopian tube cacner. J Korean Gastric Cancer Assoc 1: 106-112, 2001.
13. Lee HC, Yang MT, Lin KY, Tu HY, Zhang TA and Chen PH: Metastases from gastric carcinoma to colon in the form of multiple flat-elevated lesions: A case report. Kaohsiung J Med Sci 20: 552-557, 2004.
14. Hiraga Y, Yasui W, Kumamomto T, Watanabe M, Kobayakawa M, Eguchi N, Nakamura T, Kawamura H, Nakai S and Kamei F: Colonic metastases of signet-ring cell carcinoma presenting as multiple small depressed lesions like erosions: Report of a case. Nippon Shokakibyo Gakkai Zasshi 99: 615-621, 2002 (In Japanese).
15. Metayer P, Antonietti M, Oumrani M, Hemet J, Lemoine F and Basuyau J: Metastases of a gastric adenocarcinoma presenting as colonic polyposis. Report of a case. Dis Colon Rectum 34: 622-623, 1991.
16. Gao B, Xue X, Tai W, Zhang J, Chang H, Ma X, Qi Y, Cui L, Yan F and Pan L: Polypoid colonic metastases from gastric stump carcinoma: A case report Oncol Lett 8: 1119-1122, 2014.
17. Kummar S, Fogarasi M, Canova A, Mota A and Ciesielski T: Cytokeratin 7 and 20 staining for the diagnosis of lung and colorectal adenocarcinoma. Br J Cancer 86: 1884-1887, 2002.
18. Jaeger T, Ring J and Andres C: Histological, immunohistological, and clinical features of merkel cell carcinoma in correlation to merkel cell polyomavirus status. J Skin Cancer 2012: 983421, 2012.
19. Chu P, Wu E and Weiss LM: Cytokeratin 7 and cytokeratin 20 Expression in Epithelial Neoplasms: A Survey of 435 cases. Pathol 13: 962-972, 2000.
20. Park SY, Kim HS, Hong EK and Kim WH: Expression of cytokeratins 7 and 20 in primary carcinomas of the stomach and colorectum and their value in the differential diagnosis of metastatic carcinomas to the ovary. Hum Pathol 33: 1078-1085, 2002.