Metastatic rectal carcinoma from endometrial adenocarcinoma : a case report and review of the Japanese cases

Metastatic rectal carcinoma from endometrial adenocarcinoma : a case report and review of the Japanese cases

Tsuyoshi Teruya[1)], Atsushi Nakachi[1)], Shoko Doi[2)], Toshiyuki Maehama[2)] and Masaya Kiyuna[3)]

[1)]*Department of Surgery, Tomishiro Central Hospital, Okinawa, Japan.*
[2)]*Department of Obstetrics and Gynecology, Tomishiro Central Hospital, Okinawa, Japan.*
[3)]*Department of Pathology, Tomishiro Central Hospital, Okinawa, Japan.*

(Received on November 17, 2016, accepted on March 23, 2017)

ABSTRACT

We report a rare case of metastatic rectal carcinoma from endometrial adenocarcinoma , and review the Japanese cases. A 61-year-old woman underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy and pelvic lymphadenectomy for endometrial adenocarcinoma and metastatic ovarian tumors. Four years later, a follow-up examination using positron emission tomography-computed tomography revealed a rectal tumor with high ^{18}F-fluorodeoxyglucose accumulation. Colonoscopy subsequently revealed a submucosal tumor on the rectum, and the biopsy specimen revealed adenocarcinoma. As the distant metastasis was not recognized at the other examinations, we performed surgical resection of the rectal tumor. Pathological examination of the resected specimen revealed that the tumor was endometrioid adenocarcinoma with squamous differentiation with positive immunohistochemical staining for cytokeratin 7 and negative staining for cytokeratin 20 and CD10, positive for estrogen receptor and progesterone receptor. These findings suggest that the rectal tumor was metastasis from the endometrial adenocarcinoma. We should follow-up for gynecological lesions with that possibility in mind, and the resection of metastatic colorectal carcinoma can help to improve the prognosis which should be considered in similar cases. *Ryukyu Med. J., 36* (*1, 2*) *29~36, 2017*

Key words: endometrial adenocarcinoma, metastatic rectal carcinoma, surgical resection

INTRODUCTION

Colorectal carcinoma is the most common malignant disease worldwide, and its incidence has recently been increasing in Japan[1)]. Metastatic colorectal carcinoma from other organs is rare, with an incidence of only 0.1-1% among all colorectal carcinoma cases[2)]. We report a case of metastatic rectal carcinoma from endometrial adenocarcinoma which was reported several cases in Japan. Our case is the first case which is pointed out by positron emission tomography-computed tomography (PET/CT) among Japanese cases.

CASE REPORT

A 61-year-old woman (gravida 2 and para 0) concurrently underwent total abdominal hysterectomy and pelvic lymphadenectomy for endometrial adenocarcinoma, and bilateral salpingo-

Corresponding Author: Tsuyoshi Teruya, Department of Surgery, Tomishiro Central Hospital, 25 Ueda, Tomigusuku, Okinawa 901-0243, Japan. Tel: 098-850-3811 ; Fax: 098-850-3810, E-mail: tteruya@yuuai.or.jp

oophorectomy for bilateral ovarian tumors. Histological examination of the specimens revealed that the tumor was endometrioid adenocarcinoma with squamous differentiation without the metastases of lymph nodes, and immunohistochemical staining showed that tumor cells were positive for estrogen receptor (ER) and progesterone receptor(PgR) (Fig. 1a.b.c).The ovarian tumors were diagnosed as metastases of endometrial adenocarcinoma via postoperative histological examinations. The uterine carcinoma was stage IIIa, and the patient underwent treatment using paclitaxel (TAXOL®; 175 mg/m^2, 260 mg total dose) and carboplatin (PARAPLATIN ®; target area under the blood concentration-time curve = 6,660 mg total dose) every four weeks as postoperative adjuvant chemotherapy for 6 months. We performed the annual plain thoracoabdominal CT and PET/CT as part of her postoperative gynecological follow-up in this case because she suffered from bronchial asthma. Four years later, she underwent PET/CT and this test revealed high ^{18}F-fluorodeoxyglucose (FDG) accumulation in her rectum for the first time (maximum standardized uptake value: 6.5) (Fig. 2a). Her blood chemistry and tumor maker (carbohydrate antigen 19-9 and 125) findings were all within the normal limits, with the

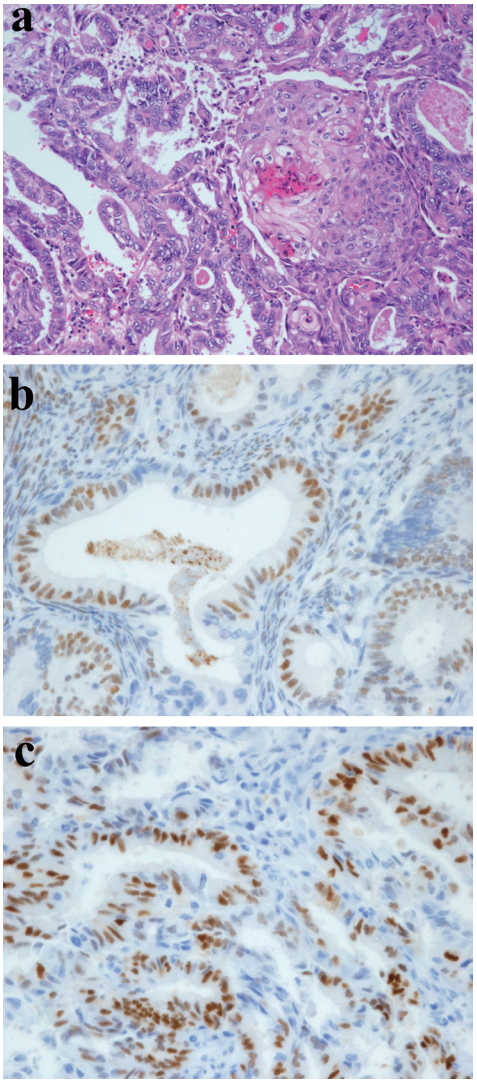

Fig. 1 **Histological findings from endometrial adenocarcinoma.**
(a) Microscopic findings reveal that the tumor is well-differentiated endometrial adenocarcinoma with squamous differentiation(hematoxylin and eosin). Immunohistochemical staining reveals positive expression of estrogen receptor (b) and progesterone receptor (c).

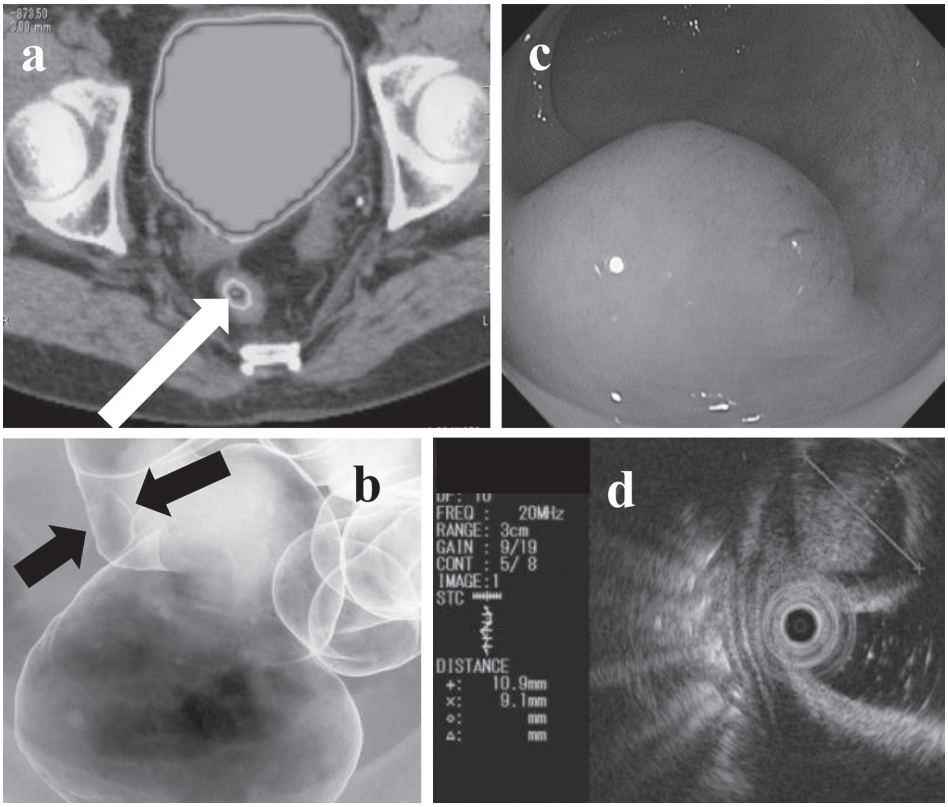

Fig. 2 **A metastatic rectal tumor is discovered via positron emission tomography-computed tomography (PET/CT), barium enema, colonoscopy, and endoscopic ultrasonography.**
(a) PET/CT reveals high 18F-fluorodeoxyglucose accumulation in the rectum (arrow). (b) Barium enema and (c) colonoscopy reveal a submucosal tumor with a smooth mucosal surface on the upper rectum (arrows). (d) Endoscopic ultrasonography reveals an isoechoic mass beyond the muscular layer of the rectum (dotted line).

exception of her carcinoembryonic antigen levels (6.0 ng/mL; normal: $<$ 5.0 ng/mL).

Barium enema and colonoscopy subsequently revealed a submucosal tumor (SMT) with the smooth mucosal surface, which was approximately 12 cm from the anal verge of the upper rectum (Fig. 2b,c). Endoscopic ultrasonography also revealed an isoechoic mass that measured 11 $\times$ 9 mm and was located beyond the muscular layer of the rectum (Fig. 2d). Although the histological analysis of the colonoscopy biopsies revealed no malignant cells, we further performed boring biopsies to reach a definitive diagnosis because SMT was showed the abnormality by PET/CT. Cytological examination of the biopsy specimens revealed adenocarcinoma cells in the obtained specimens, which suspected endometrioid adenocarcinoma with the positive for ER and PgR (Fig. 3a.b.c),and led us to suspect that the rectal tumor was metastasis from the former endometrial adenocarcinoma.

Because the distant metastasis was not recognized at the other examinations, we also intended to perform the resection of the rectal tumor. The intraoperative findings indicated that there were no ascites or peritoneal dissemination, and that the solid tumor was located on the anterior rectal wall at the peritoneal reflection. We performed low anterior resection of the rectal tumor for safety surgical margin by intraoperative findings. Macroscopic examination of the specimen revealed that the rectal mucosa was normal, and that the resected tumor was 11 $\times$ 7 mm (Fig. 4a,b). Histological examination of the specimen revealed that the tumor was endometrioid adenocarcinoma with squamous differentiation (Fig. 5a) without lymphovascular invasion and regional lymph node metastases. Additional immunohistochemical staining was performed to determine the tumor's origin, and

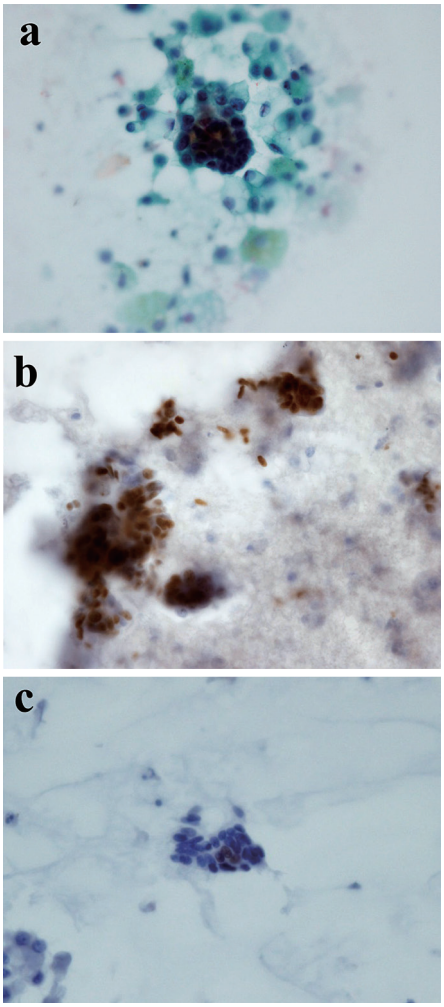

Fig. 3 **Histological findings from boring biopsy.**
(a) Microscopic findings revealed adenocarcinoma cells which suspected endometrioid adenocarcinoma. Immunohistochemical staining reveals positive expression of estrogen receptor (b) and progesterone receptor (c).

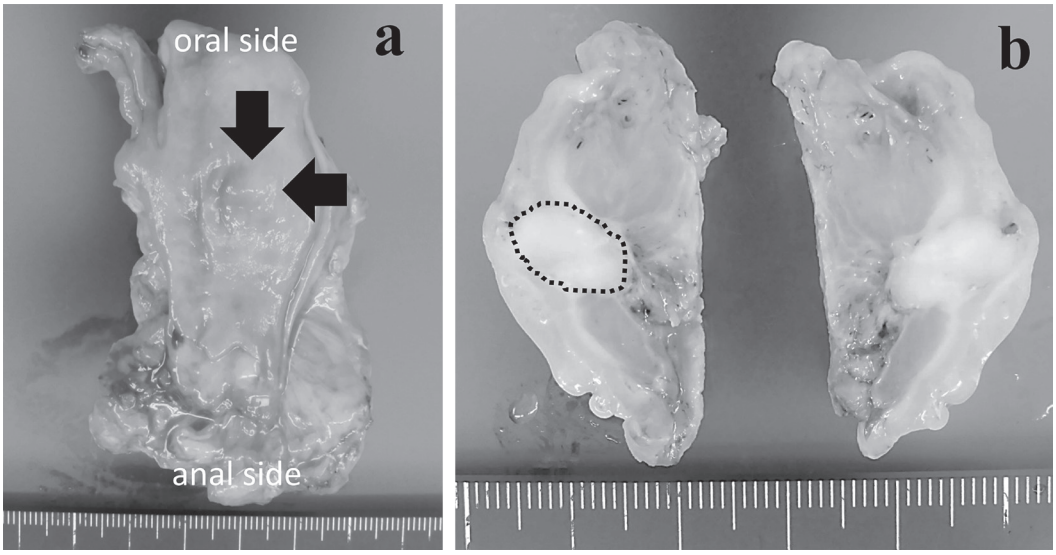

Fig. 4 **Macroscopic findings from the excised specimen.**
(a) The rectal submucosal tumor with normal mucosa (arrow). (b) The resected submucosal tumor in the cross section (dotted ellipse).

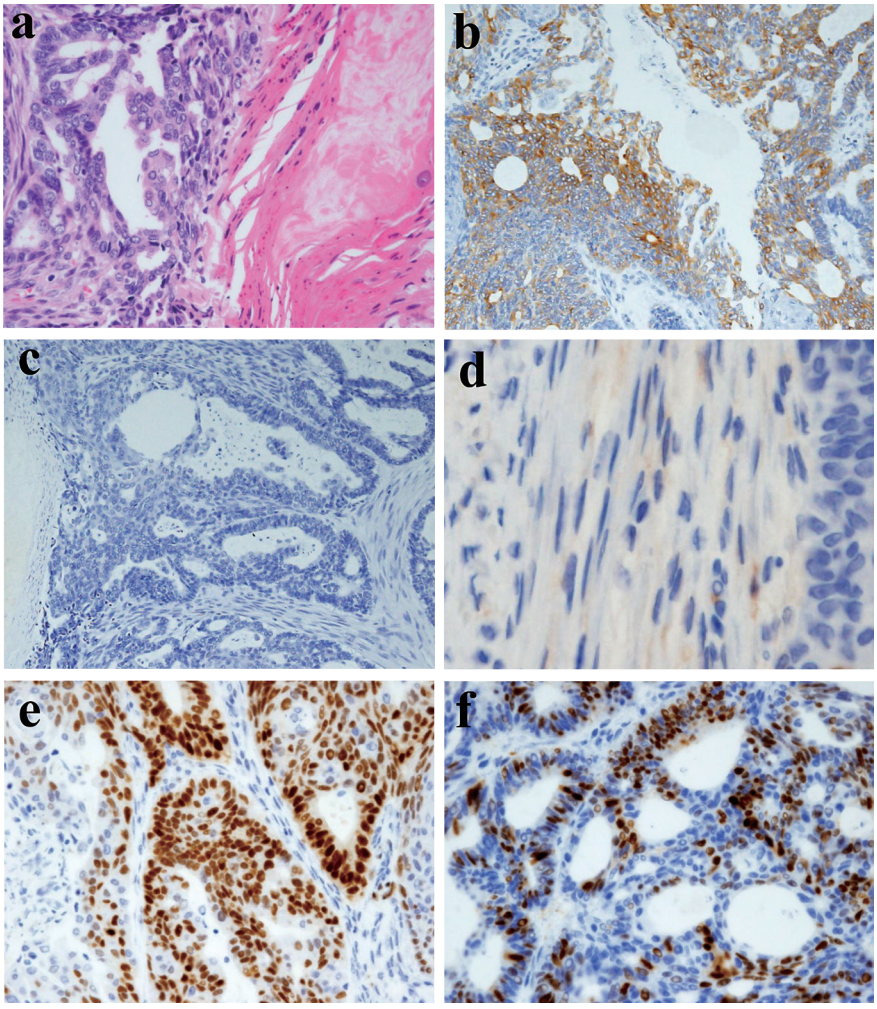

Fig. 5 **Histological findings from the excised specimen of the rectum.**
(a) Microscopic findings reveal that the tumor is well-differentiated endometrial adenocarcinoma with squamous differentiation(hematoxylin and eosin). Immunohistochemical staining reveals positive expression (b) of cytokeratin(CK) 7 and negative expression (c) of cytokeratin 20 and CD10(Fig. d), positive expression for estrogen receptor (e) and progesterone receptor (f).

revealed that tumor cells were positive for cytokeratin 7 (CK7) (Fig. 5b) and negative for CK20(Fig. 5c) and cluster of differentiation (CD10) (Fig. 5d), were positive for ER(Fig. 5e) and PgR(Fig. 5f). Therefore, we finally diagnosed the resected rectal tumor as being derived from endometrial adenocarcinoma of uterus with the judgement of unnecessity for caudal-type homeobox transcription factor2 (CDX2) staining.

The patient's postoperative course was uneventful, and she was discharged at 12 days after the surgical procedure. The patient was treated using postoperative chemotherapy (similar to the paclitaxel and carboplatin regimen) for an additional 6 months, and no tumor recurrence has been observed for 11 months after the end of her chemotherapy. .

DISCUSSION

The incidence of colorectal carcinoma has been increasing in Japan[1]. However, metastatic colorectal carcinoma from other organs accounts for only 0.1-1% of all colorectal carcinoma cases[2], and the primary lesion of metastasis indicate that the stomach is the most common site of metastasis, is secondly followed by gynecological disease[3]. The incidence of endometrial adenocarcinoma has also

recently been increasing in Japan[1, 4]. The reported sites of recurrence for endometrial carcinoma are the distant organs, pelvic cavity[5], while the metastatic regions from endometrial carcinoma are the peritoneum, ovaries, lung, liver, and bowels[6].

We searched the Japan Centra Revus Medicina database for publications from 1990 to 2015, using the terms "endometrial adenocarcinoma" and "colorectal metastasis" or "Japanese" (although we excluded conference proceedings). This search returned 10 case reports[7-16] of metastatic colorectal carcinoma from uterine adenocarcinoma, which including one case of carcinosarcoma (Table 1). The characteristics of these cases revealed that the clinical staging of endometrial adenocarcinoma is variable (3 cases of stage I, 2 cases of stage II, 3 cases of stage III, and 1 case of stage IV; staging was not reported in 2 cases). The mean duration for recurrence of endometrial adenocarcinoma was approximately 76.6 months, and the frequent symptoms that were caused by the recurrent lesion were pain and bleeding. The most common location of the colorectal metastasis was the rectum (6 cases) as pelvic organ was estimated to affect to be close to the rectum, and the common macroscopic type of the recurrent tumor was a submucosal tumor (as in the present case).

The histological findings for these cases were described that 1) endometrioid adenocarcinoma (3 cases), 2) endometrioid adenocarcinoma with squamous differentiation (5 cases ;as in the present case), 3) serous adenocarcinoma (2 cases), and 4) carcinosarcoma (one case). Although the rectal tumor in the present case was asymptomatic, we discovered the tumor during PET/CT while the surveillance of endometrial adenocarcinoma, which revealed high FDG accumulation in the original and recurrent lesions. Thus, PET/CT is a useful imaging modality for detecting endometrial adenocarcinoma and metastasis during the postoperative follow-up[17]. We preoperatively recommended to her an additional examination of magnetic resonance imaging (MRI), but she did not desire to receive MRI.

There are various metastatic routes for endometrial adenocarcinoma[15]. The first pathway is the hematogenous pathway, through which the adenocarcinoma cells move to the liver, lungs, and bone. The second pathway is the lymphogenous pathway, through which the adenocarcinoma cells move via the lymphatic vessels and lymph nodes. The third pathway is the peritoneal dissemination pathway, through which the adenocarcinoma cells spread to the peritoneum. So called implantation through which adenocarcinoma cells are dispersed and subsequently implant during the operation, is one of the mechanism to explain dissemination to the abdominal cavity.

Immunohistochemical staining is also useful for identifying the primary lesion for metastatic colorectal carcinoma, as colorectal cancer is CK7-negative and CK20-positive, while endometrial adenocarcinoma is CK7-positive and, CK20 and CDX2-negative[16, 18]. In the present case, the lymph nodes were dissected at the hysterectomy (4 years before), and were found to not contain endometrial adenocarcinoma cells. Furthermore, we did not detect intraoperative peritoneal dissemination during the resection of the rectal tumor, and the tumor was pathologically localized in the rectal wall between the mucosa and serosa. Moreover, the resected tumor exhibited immunohistochemical characteristics of endometrioid adenocarcinoma (CK7-positive, CK20-negative, positive for ER and PgR), and we added CD10 immunohistochemical staining, which was the marker for endometrial stromal cells, to discriminate between metastasis from endometrial adenocarcinoma of uterus and adenocarcinoma arising in rectal endometriosis [15], thereupon CD10 staining was negative. Based on these findings, we finally diagnosed the rectal tumor as metastasis from endometrial adenocarcinoma of uterus, which would rather have developed via the hematogenous and/or lymphogenous pathways than the peritoneal dissemination pathway.

If the metastatic colorectal carcinoma can be radically removed, some cases may experience long survival[7]. In addition, surgical resection of a solitary metastasis from endometrial adenocarcinoma is associated with a good prognosis[19]. Furthermore, the Japanese cases have reported relatively good outcomes for all but one case, as we guessed that adjuvant chemotherapy was performed in seven of eleven cases and the short follow-up term in Japanese cases (Table 1). Chemotherapy with carboplatin and paclitaxel had been reported an effective regimen for endometrial adenocarcinoma[20]. Therefore, in cases with a metastatic solitary lesion from gynecological disease, the resection and adjuvant chemotherapy may provide a good prognosis as well as our case.

Table 1 **Japanese reports of metastatic colorectal carcinoma from endometrial adenocarcinoma**

No.	Author (year)	Age (years)	Symptom	Clinical stage	Months from operation to recurrence	Metastatic pathway	Colorectal location of the metastasis	Macroscopic type	Surgical procedure	Outcome (months)	Histological type	Adjuvant Chemotherapy
1	Ohtsuka [7] (1990)	45	Melena	Ⅱ	44	NR	Rectum	1	Low anterior resection	No recurrence (72)	Serous adenocarcinoma	Unknown
2	Okabe [8] (1993)	54	Lower abdominal pain	NR	60	hematogenous and/or lymphogenous	Sigmoid-colon	3	Sigmoidectomy	No recurrence (7)	Endometrioid adenocarcinoma with squamous differentiation	5-FU+CDDP +Leucovorin
3	Ishii [9] (1998)	63	Left lower abdominal pain	Ⅳb	0 (synchronous)	Peritoneal dissemination	Transverse-colon	SMT likely	Transverse colectomy	No recurrence (6)	Serous adenocarcinoma	CAP
4	Tsugawa [10] (2000)	58	Right flank pain	Ia	42	hematogenous	Ascending-colon	2 (SMT likely)	Right hemicolectomy	No recurrence (19)	Endometrioid adenocarcinoma with squamous differentiation	5-FU+CDDP
5	Kawase [11] (2004)	77	Lower abdominal pain/fecal occult blood test positive	Ic	31	hematogenous and/or lymphogenous	Rectum	2	Abdominoperineal resection	Dead (11)	Endometrioid adenocarcinoma with squamous differentiation	MPA
6	Isogai [12] (2004)	75	Lower abdominal pain	Ⅲb	30	hematogenous and/or lymphogenous	Rectum	2 (SMT likely)	Abdominoperineal resection	No recurrence (6)	Endometrial adenocarcinoma with squamous differentiation	Not prefered
7	Murakami [13] (2005)	67	Melena	Ⅲb	154	Peritoneal dissemination, hematogenous and/or lymphogenous	Descending-colon	2	Left hemicolectomy	No recurrence (18)	Carcinosarcoma	Unknown
8	Ookawa [14] (2011)	74	Pain on defecation	Ⅱ	93	NR	Rectum	NR	Low anterior resection	No recurrence (6)	Endometrioid adenocarcinoma	CBDCA+PTX
9	Sakata [15] (2013)	65	Computed tomography abnormality	Ia	84	Perioperative implantation	Rectum	SMT	Low anterior resection	No recurrence (12)	Endometrioid adenocarcinoma	Unknown
10	Shimada [16] (2014)	58	Left flank pain	NR	180	Peritoneal dissemination	Descending-colon	NR	Left hemicolectomy	No recurrence (10)	Endometrioid adenocarcinoma	AP
11	**Our case (2015)**	**61**	**PET abnormality**	**Ⅲa**	**48**	**hematogenous and/or lymphogenous**	**Rectum**	**SMT**	**Low anterior resection**	**No recurrence (11)**	**Endometrioid adenocarcinoma with squamous differentiation**	**CBDCA+PTX**

PET: positron emission tomography; SMT: submucosal tumor; NR: not reported
CDDP: cis-diammine dischloroplatinum; CAP:cyclophosphamide adriamycin CDDP; MPA: medroxyprogesterone acetate; CBDCA:carboplatin; PTX: paclitaxel; AP: adriamycin+CDDP

CONCLUSION

Metastatic colorectal carcinoma from endometrial adenocarcinoma is a rare condition, although we should perform examinations and treatments for gynecological lesions with this possibility in mind. Furthermore, given that resection of the metastatic colorectal carcinoma can help improve the prognosis, resection should be considered in similar cases.

REFERENCES

1) Center for Cancer Control and Information Services, National Cancer Center, Japan. Available: http://www.ncc.go.jp/en/cis/index.html. Accessed: September 26, 2015.
2) Balthazar EJ, Rosenberg HD, Davidian MM. Primary and metastatic scirrrhous carcinoma of the rectum. Am J Roentgenol. 1979;132:711-5.
3) Ohta H, Azekura K, Seki M, Takagi K, Nishi M, Maruyama M, Yanagisawa A, Katoh H. Clinicopathological study on metastatic colorectal cancer. I to Cho (Stomach and Intestine). 1988;23:633-43. [Japanese with English abstract]
4) Matsumoto K, Ochi H, Onuki M, Yagi H, Nakao S, Sakurai M, Kawasaki A, Nakamura Y, Okazaki Y, Satoh T. Short-term outcomes of laparoscopic surgery for early stage endometrial cancer. Nihon Gekakei Rengou Gakkai Zasshi (JJCS). 2014;39:651-6. [Japanese with English

abstract]
5) Sartori E, Laface B, Gadducci A, Maggino T, Zola P, Landoni F, Zanagnolo V. Factors influencing survival in endometrial cancer relapsing patients: a Cooperating Task Force (CTF) study. Int J Gynecol Cancer. 2003;13:458-65.
6) Henricksen E. The lymphatic dissemination in endometrial carcinoma. A study of 188 necropsies. Am J Obstet Gynecol. 1975;123:570-6.
7) Ohtsuka M, Ohta H, Yanagisawa A, Kato Y. A clinicopathological study on 18 cases with metastatic colon cancer. Nihon Daicho Koumonbyo Gakkai Zasshi (J Jpn Soc Coloproctol). 1990;43:354-60. [Japanese with English abstract]
8) Okabe S, Kure T, Kanenobu M, Matsumoto A, Yabata E, Tsubaki M, Endo M, Koike M. A case of endometrial carcinoma metastatic to the sigmoid colon. Shoukakigeka. 1993;16:1471-7. [Japanese]
9) Ishii K, Shimizu K, Yamazaki T, Oono T. A case of uterine serous papillary carcinoma. Nihon Sanfujinka Gakkai Saitama Chihoubukai Zasshi. 1998;28:12-6. [Japanese]
10) Tsugawa T, Kameyama M, Murata K, Ohigashi H, Hiratsuka M, Sasaki Y, Kabuto T, Ishikawa O, Imaoka S, Kasugai T. A case of the metastatic colonic carcinoma from an endometrial carcinoma with malignant lymphoma. Nihon Shoukakigeka Gakkai Zasshi (Jpn J Gastroenterol Surg). 2000;33:1539-43. [Japanese with English abstract]
11) Kawase H, Kawamura T, Nakakubo Y, Okushiba T, Naoe K, Kondo S. A case of metastatic rectal carcinoma from endometrial carcinoma. Nihon Rinsho Geka Gakkai Zasshi (J Jpn Surg Assoc). 2005;66:3015-8. [Japanese with English abstract]
12) Isogai K, Kato N, Moriuchi R, Tarasawa I, Yabana T, Nakahara S, Murakami R, Senota A, Ban T. A case report of the metastatic rectal carcinoma from endometrial. Nihon Shoukaki Naishikyo Gakkai Zasshi (Gastroenterological Endoscopy). 2004;46:943-8. [Japanese with English abstract]
13) Murakami K, Matsui Y, Kaninuma O, Ohira G, Taniguchi T, Urano M, Ochiai T. A case of metastatic colon cancer from carcinosarcoma of the uterus. Nihon Shoukakigeka Gakkai Zasshi (Jpn J Gastroenterol Surg). 2005;38:560-5. [Japanese with English abstract]
14) Ookawa M, Kojima N, Asami Y, Kobayashi S, Nakayama Y, Takami M, Matsumoto H, Kikuchi T, Kimizuka K, Miyake H, Takimoto T. A case of recurrent rectal carcinoma from endometrial carcinoma 7 years after surgery. Saitamaken Igakkai Zasshi. 2011;45:336-9. [Japanese]
15) Sakata M, Umemoto T, Goto T, Kigawa G, Nemoto H, Hibi K. Metastatic rectal tumor derived from the endometrial adenocarcinoma of uterus: Report of a case. Nihon Gekakei Rengou Gakkai Zasshi (JJCS). 2013;38:174-7.
16) Shimada T, Morohashi H, Watanabe N, Murata A, Hakamada K, Hirai H. A case of uterine cancer recurred together with infiltration into the descending colon 15 years after surgery. Nihon Rinsho Geka Gakkai Zasshi (J Jpn Surg Assoc). 2014;75:1707-11. [Japanese with English abstract]
17) Park JY, Kim EN, Kim DY, Kim JH, Kim YM, Kim YT, Nam JH. Clinical impact of positron emission tomography or positron emission tomography/computed tomography in the posttherapy surveillance of endometrial carcinoma: evaluation of 88 patients. Int J Gynecol Cancer. 2008;18:1332-8.
18) Chu P, Wu E, Weiss LM. Cytokeratin 7 and cytokeratin 20 expression in epithelial neoplasms: A survey of 435 cases. Mod Pathol. 2000;13:962-72.
19) Campagnutta E, Giorda G, De Piero G, Sopracordevole F, Visentin MC, Martella L, Scarabelli C. Surgical treatment of recurrent endometrial carcinoma. Cancer. 2004;100:89-96.
20) Pectasides D, Xiros N, Papaxoinis G, Pectasides E, Sykiotis C, Koumarianou A, Psyrri A, Gaglia A, Kassanos D, Gouveris P, Panayiotidis J, Fountzilas G, Economopoulos T. Carboplatin and paclitaxel in advanced or metastatic endometrial cancer. Gynecol Oncol. 2008;109:250-4.