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Abstract

The records of 159 patients who underwent surgical resection of colorectal cancer were reviewed to assess the incidence of ovarian metastasis and to define the role of oophorectomy. Four of these patients presented with metachronous metastases, and one patient had synchronous ovarian involvement. The incidence of ovarian involvement was higher in younger patients. While most patients with ovarian involvement had the primary tumor located at the rectosigmoid region, a similar distribution of the primary tumor was observed in patients without ovarian metastasis. The histological type and degree of differentiation was similar regardless of whether or not ovarian metastasis was present. Of the patient without ovarian metastasis, 57% presented with nodal metastases and 3.2% with peritoneal dissemination, while all patients with ovarian metastasis had nodal and peritoneal involvement. Our results suggest that histological type and degree of differentiation of the primary tumor do not influence likelihood of ovarian metastasis. However, the exposure of the tumor to the serosal surface and the subsequent peritoneal dissemination may be an important route by which malignant tumor cells reach the ovaries. However, due to the wide lymphatic involvement in patients with ovarian metastasis, the lymphatic route may be important as well. Thus, we consider that oophorectomy should be performed in all postmenopausal women, when the ovaries are macroscopically affected, and in premenopausal patients with Astler-Coller B2 tumors or over.

KEYWORDS: colorectal carcinoma, metastasis, ovarian cancer, surgical treatment

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The records of 159 patients who underwent surgical resection of colorectal cancer were reviewed to assess the incidence of ovarian metastasis and to define the role of oophorectomy. Four of these patients presented with metachronous metastases, and one patient had synchronous ovarian involvement. The incidence of ovarian involvement was higher in younger patients. While most patients with ovarian involvement had the primary tumor located at the rectosigmoid region, a similar distribution of the primary tumor was observed in patients without ovarian metastasis. The histological type and degree of differentiation was similar regardless of whether or not ovarian metastasis was present. Of the patient without ovarian metastasis, 57% presented with nodal metastases and 3.2% with peritoneal dissemination, while all patients with ovarian metastasis had nodal and peritoneal involvement. Our results suggest that histological type and degree of differentiation of the primary tumor do not influence likelihood of ovarian metastasis. However, the exposure of the tumor to the serosal surface and the subsequent peritoneal dissemination may be an important route by which malignant tumor cells reach the ovaries. However, due to the wide lymphatic involvement in patients with ovarian metastasis, the lymphatic route may be important as well. Thus, we consider that oophorectomy should be performed in all postmenopausal women, when the ovaries are macroscopically affected, and in premenopausal patients with Astler-Coller B2 tumors or over.

Key words: colorectal carcinoma, metastasis, ovarian cancer, surgical treatment.

Oophorectomy for women with colorectal cancer has been the subject of much discussion, and the indications and contraindications for prophylactic oophorectomy in these patients are far from clear.

Undoubtedly, if the ovaries are found to be grossly involved, they have to be removed *en bloc* with the tumor. Such a procedure provides long-term local control and eventually improves patient survival (1). The oophorectomy also seems to be the clear choice in postmenopausal patients, in whom a 1% increased risk to develop primary carcinoma of the ovary has been reported (2, 3). Additionally, Graffner *et al.* (4) and MacKeigan and Ferguson (5) reported microscopic metastases in ovaries that appeared macroscopically normal, supporting the use of prophylactic oophorectomy in this group of patients. These authors also reported a high incidence of ovarian metastases in premenopausal patients (5). Blamey *et al.* (6), however, did not recommend this procedure for all patients due to the low incidence of clinical ovarian recurrence requiring operation. Instead, they advised careful intraoperative assessment of the ovaries.

Therefore, the aim of this study was to determine the outcome with regard to ovarian metastasis of all female patients with colorectal cancer treated in this department, and further, to determine which factors may be useful indicators of the need for oophorectomy.

Patients and Methods

The records of 163 consecutive female patients with colorectal cancer were reviewed who had been surgically treated with curative resection from January 1978 to December 1992, in the First Department of Surgery, at Okayama University Medical School.

The histopathological data in all cases were reviewed by two pathologists. Four cases were excluded because of incomplete data. Age and menstrual status were also

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recorded. Pre- and postoperative assessment included computed tomography or magnetic resonance imaging, colonoscopy, barium enema, and measurement of the serum level of carcinoembryonic antigen. Tumor grade, depth of invasion, lymph node involvement, and venous and lymphatic vessel invasion were also examined.

The depth of invasion was classified according to the criteria of the Japanese Research Society for Studies of Cancer of the Colon, Rectum and Anus (7): s_0 or a_1 , invasion extends beyond the proper muscle, but has not reached the serosal surface and has not penetrated deeper into the adventitia; s_1 or a_2 , the tumor is exposed to the serosal surface or infiltrates deeper into the adventitia, but without infiltration to surrounding organs; and s_2 or a_3 , infiltration into other organs was noted.

The location of positive lymph nodes was also studied and classified based on the same classification (7). Venous and lymphatic vessel invasion was classified as V_0 or Lym_0 if absent, V_1 or Lym_1 if a few vessels were involved (mild invasion), V_2 or Lym_2 if there were a considerable number of involved vessels (moderate invasion), and V_3 or Lym_3 if diffuse involvement (marked invasion) was noted.

Liver metastasis was classified as H_0 if absent, H_1 if a single lobe was involved, H_2 for few scattered metastases in both lobes, and H_3 if numerous metastases in both lobes were noted. Peritoneal seeding was also classified in a similar manner. P_0 for the absence of peritoneal dissemination, P_1 if dissemination reached the adjacent peritoneum, and P_2 or P_3 for moderate or marked dissemination in the remote peritoneum, respectively.

Results

Of the 159 patients with colorectal carcinoma, 5 (3.1

%) had synchronous ($n = 1$) or metachronous ($n = 4$) metastases to the ovaries. In the patient with synchronous involvement, both ovaries were observed to be macroscopically affected. The pathological findings were compatible with metastatic colorectal adenocarcinoma. In the other 4 patients, bilateral metastases were associated with peritoneal seedings. Also, the histological samples showed adenocarcinoma from the colon.

Table 1 shows the most important clinical and histopathological findings of these 5 patients. By July 1992, 2 of the 5 patients were still alive, 12 and 15 months after surgery.

Age distribution. The age distribution of all patients with colorectal cancer ranged from 27 to 69 years, with a mean of 62 years. However, 3 of the 5 patients with ovarian metastases were under 50 years, with a

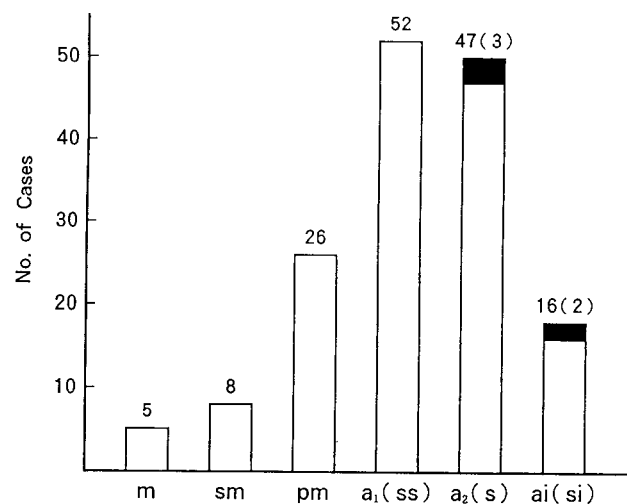


Fig 1 Depth of invasion of the colorectal carcinoma.

m, mucosa; sm, submucosa; pm, proper muscle; a, adventitia; ss, submucosa and s, serosa. (□) without ovarian metastasis; (■) with ovarian metastasis.

Table 1 Characteristics of patients with colorectal cancer and ovarian metastasis

Case No.	Age	Location	Histological grade	Depth of ^a Invasion	Hepatic metastasis	Peritoneal dissemination	Node status	Lymphovascular invasion ^b	Survival (Months)
1	53	Rectum	Mucinous	s	0	3	1	Lym ₂ -V ₀	14 (dead)
2	27	Ascending colon	M.D.A.	s	0	3	2	Lym ₂ -V ₂	16 (dead)
3	61	Rectum	W.D.A.	s	1	1	1	Lym ₀ -V ₀	20 (dead)
4	35	Sigmoid colon	W.D.A.	si	2	1	4	Lym ₂ -V ₂	15 (alive)
5	49	Rectum	M.D.A.	si	0	2	1	Lym ₂ -V ₂	12 (alive)

W.D.A: Well-differentiated adenocarcinoma, M.D.A: Moderately differentiated adenocarcinoma

^a: According to the criteria of the Japanese Research Society for Studies of Cancer of the Colon, Rectum, and Anus. See Text.

^b: See text.

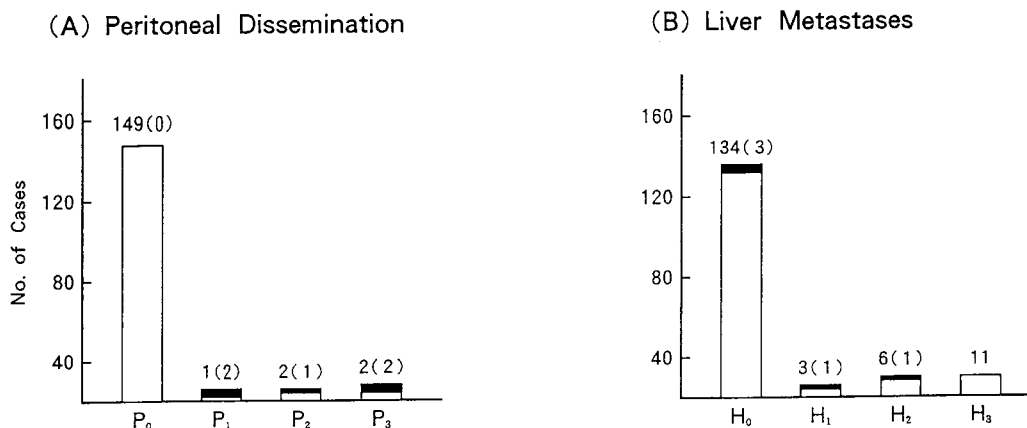


Fig 2 Peritoneal Dissemination (A) and Liver Metastases (B) in patients with Colorectal Carcinoma.

Figures in parentheses are numbers of cases with ovarian metastases. (□) without ovarian metastasis; (■) with ovarian metastasis. P₀-P₃, H₀-H₃: See text.

mean age of 45 years.

Site of colorectal carcinoma. In the 5 patients with ovarian metastasis, the primary tumor was located in the rectum and sigmoid colon in 4 (80%) and in the ascending colon in 1 (20%). Of the patients without ovarian metastasis, 119 (77%) had the tumor at the rectosigmoid region, 8 (5%) in the descending colon, 8 (5%) in the transverse colon and 15 (10%) and 4 (2.5%) in the ascending colon and cecum, respectively.

Histological findings. Histologically, in the cases without ovarian involvement, there were 135 (87.6%) well- or moderately differentiated adenocarcinoma, 11 (7.1%) poorly differentiated adenocarcinoma, 7 (4.6%) mucinous carcinoma, and 1 (0.7%) squamous cell carcinoma. In the ovarian metastatic group, 80% were well- or moderately differentiated, and the remaining 20% were poorly differentiated adenocarcinoma. With regard to the depth of invasion, in all 5 cases of ovarian metastases, the carcinoma was exposed to the serosal surface and infiltration to adjacent organs was found in 2 cases. In contrast, none of the patients whose carcinoma was confined to the bowel wall presented with ovarian involvement (Fig 1).

Regarding lymph node status, all patients with ovarian metastases presented with at least proximal lymph node involvement. Eighty-six patients (57%) without ovarian metastasis also presented with positive lymph nodes.

Venous and lymphatic vessel invasion. Three (60%) and 4 (80%) patients with ovarian metastases had venous and lymphatic vessel invasion, respectively. Among the patients without ovarian metastasis,

40 (26%) and 107 (69%) presented with venous and lymphatic vessel invasion, respectively.

Peritoneal dissemination and liver metastases. Only 10 of 159 patients with colorectal cancer presented with peritoneal dissemination at least to the surrounding peritoneum. All 5 of the patients with ovarian involvement showed peritoneal dissemination (Fig 2-A). Liver metastases were found in 20 patients without and in 2 patients with ovarian involvement (Fig 2-B).

Discussion

The poor prognosis of patients with colorectal cancer and ovarian metastasis (3, 5, 8, 9) has led to attempts to determine the parameters related to ovarian metastasis to better identify patients at risk, decrease morbidity, and improve prognosis.

Macroscopic evaluation of the ovaries has been suggested (6), but this alone is not enough to determine whether or not an oophorectomy is indicated since some patients may have microscopic involvement, and may develop metachronous lesions at a later time. This is observed with relative frequency, and may be the possible explanation for 4 of our patients.

Our findings of ovarian metastasis are in agreement with previous reports which describe an increased probability for the occurrence of ovarian metastasis in premenopausal women (5, 10, 11). This could be considered a risk factor, but many patients would not agree with resection of both ovaries due to its implications regarding fertility.

On the other hand, in postmenopausal women, we believe there are no contraindications to removing the ovaries since they are no longer functioning. In addition, it would serve as a protective measure to prevent the possible development of a primary ovarian tumor (12).

Since the question of how to treat premenopausal women is more complex, we attempted to identify which clinical or pathological factors may have prognostic value in the development of ovarian metastasis. Some investigators have already attempted to establish the pathway to the ovaries from a colorectal cancer. Herrera *et al.* (10) and Graffner *et al.* (4) suggested that hematogeneous spread could be the main route. The latter investigators, in one clinico-pathological study of a series of 58 patients found 4 cases of microscopic metastases to the ovaries, and all 4 exhibited deep stromal metastases rather than superficial. Unfortunately, there are no other works to support those findings. In contrast, there are some reports considering other possible pathways such as the peritoneal and lymphatic routes.

In our 5 patients with ovarian involvement, the tumor extended to or through the serosal surface of the colon, and none of the patients had ovarian metastasis when the tumor was confined into the bowel wall. This finding could be a consequence of the protective action of the colonic serosa which prevents the passage of cancer cells to the peritoneal cavity. Moreover, of the 10 patients with peritoneal dissemination, 5 (50%) presented with ovarian involvement, and none of the 149 patients without peritoneal-dissemination.

Like Mason and Kovalcik (13), these findings suggest that the peritoneal route is an important pathway in the spread to the ovaries, although the preference for these organs is still not clearly understood (12).

However, after noting that all 5 patients with ovarian metastasis had tumor spread to proximal lymph nodes, and 4 of whom also had lymphatic vessel invasion, the lymphatic route must be considered as a route for tumor dissemination.

Based on our data, we believe that oophorectomy should be performed in patients in whom the tumor has already extended to the colonic serosa, with or without peritoneal involvement, and with or without lymphatic spread (7, 14).

In our opinion, by ovarian resection one can prevent an important source of morbidity and mortality by removing a potential site of metastasis or even metachronous primary cancer, and in this way may improve the progn-

sis.

We believe that in more advanced stages, as previously suggested by Morrow and Enker (15), oophorectomy is indicated as a palliative maneuver, since ovarian involvement is simply regarded as part of the disseminated disease.

Therefore, we suggest that oophorectomy should be done in the following instances: (a) in all postmenopausal patients regardless of tumor stage; (b) when the ovaries are included in *en bloc* resection, once they are macroscopically affected; and (c) in premenopausal patients with Astler-Coller's (14) B2 tumors or over, regardless the macroscopic appearance.

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