[症例報告]Radiation-induced malignant lymphoma of the ileum : a case report

Radiation-induced malignant lymphoma of the ileum: a case report

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(Receiveed on August 2, 1996, accepted on November 18, 1996)

ABSTRACT

A case of intestinal malignant lymphoma which developed as a result of radiotherapy for uterine cervical cancer is herein reported. A 67-year-old female who underwent radiotherapy at a total dose of 74 Gy for uterine cervical cancer in 1988 was referred to our Obstetrics and Gynecology Department on October 6, 1995 with a chief complaint of lower abdominal distention. An abdominal CT scan showed pyometra and a large heterogeneous dense mass at the ileocecal region. After draining the pyometra, she developed an intestinal obstruction and was referred to our Department on the 4th hospital day. Despite conservative treatment, her general condition continued to deteriorate and an exploratory laparotomy was performed 2 weeks after admission. A laparotomy revealed a large inflammatory mass consisting of a folded ileum with radiation damage, and this mass was resected with the affected ileum. In the resected specimen, the tumor appeared as an inflammatory conglomerated mass forming a whitish, hard mass expanding to the mesentery and infiltrating into the adjacent ileum. Microscopically, the tumor was diagnosed as malignant lymphoma (diffuse, medium-sized cell and B-cell type) and the adjacent ileum showed a radiation enteritis. Since this neoplasm developed within the irradiated field 7 years after radiotherapy, and had a different histologic type, while the organ of origin was also differed from the initial cancer, the patient was thus diagnosed as having radiation-induced malignant lymphoma. *Ryukyu Med. J., 16(4)203~207, 1996*

Key words: malignant lymphoma, radiation-induced malignancy, ileum

INTRODUCTION

Radiotherapy is universally accepted as an effective measure for the treatment of various malignant neoplasms. In such patients, secondary malignancies induced by irradiation, are becoming increasingly apparent, along with a marked increase in the survival rate[1]. In the literature, radiation-induced rectal cancer, urinary bladder cancer, leukemia, and soft tissue sarcoma after radiotherapy have all been frequently reported[1~15]. The occurrence of non-Hodgkin's lymphoma following radiotherapy for Hodgkin's disease has also been occasionally reported[16]. However, malignant lymphoma following radiotherapy for uterine cervical cancer has been seldom described.

Primary gastrointestinal lymphoma constitutes about 4.5% of all lymphomas and 1% of all gastrointestinal neoplasms[17]. Furthermore, its clinical findings do not differ significantly from those of other gastrointestinal neoplasms[18]. Thus, it tends to be difficult to establish a diagnosis of gastrointestinal lymphoma prior to surgical exploration.

In this paper, we present a rare case of radiation-induced malignant lymphoma of the small intestine which could not be diagnosed preoperatively and also include a brief review of the literature.

CASE REPORT

A 67-year-old female had been irradiated with a dose of 74 Gy (external irradiation; whole pelvis 30Gy, center shield 20Gy and intracavitary therapy;RALS 24 Gy) for uterine cervical cancer (stage Ⅲ b, non-keratinizing large cell carcinoma) in 1988. She was clinically followed for 3 years after radiotherapy with no evidence of recurrence, but thereafter did not comply with the regular clinical follow-up. Seven years after irradiation, she was referred to the Ryukyu University Hospital with a chief complaint of abdominal pain and lower abdominal distention on October 6, 1995. An abdominal CT scan demonstrated a cystic mass measuring 12 cm in size in the lower abdomen (Fig. 1, top). She was diagnosed as having pyometra, and was thus admitted to the Obstetrics

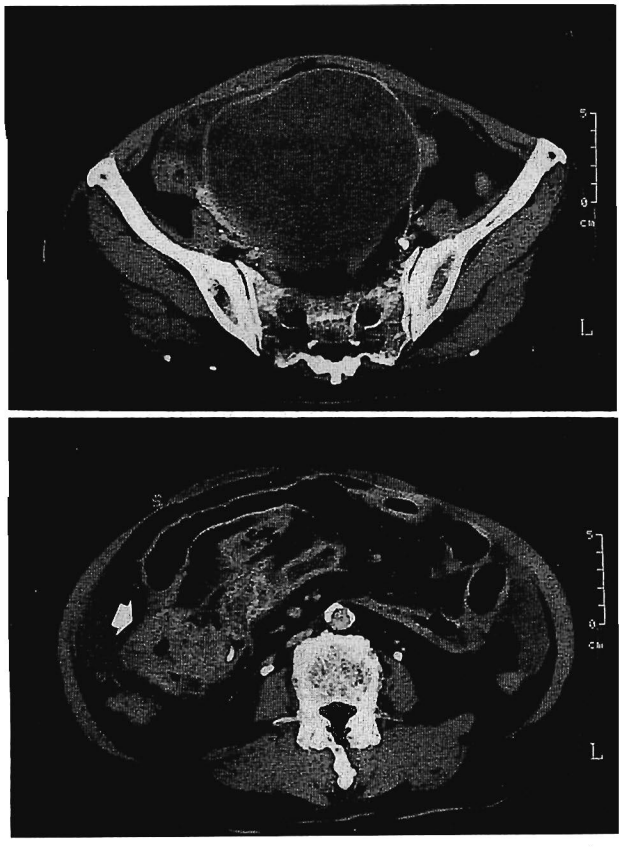

Fig. 1 Abdominal CT showing a huge cystic mass (pyometra) in the pelvic cavity (top) and a heterogeneous dense mass with a dotted calcification (arrow) in the ileocecal region (bottom).

and Gynecology Department in our hospital. Pyometra was treated with drainage (1000ml of dark brown fluid from the uterus). No local recurrence of uterine cervical cancer was detected either on palpation or by ultrasonography, while the cytology findings of the uterine discharge showed no malignancy. She developed an indolent intestinal obstruction after the drainage of pyometra. Plain abdominal X-rays showed gas accumulation in the small intestine in the right flank region. An abdominal CT scan revealed a heterogeneous dense mass in the ileocecal region (Fig. 1, bottom). She was thus transferred to our department on the 4th hospital day. The physical examination revealed late radiation changes in the suprapubic skin, mild paraumbilical tenderness and a distended abdomen. The laboratory findings showed hemoglobin level of10.9 g/dl, a leukocyte count of 9,200/μl, CRP of 20 mg/dl, LDH of 671 IU/l and serum albumin of 1.9 g/dl. A long intestinal tube was introduced into her small intestine for gastrointestinal decompression, and the following massive fluid and electrolyte loss was replaced by intravenous infusion. In spite of these conservative treatments, her general condition continued to deteriorate.

On October 20, 1995, an exploratory laparotomy was performed with a diagnosis of intestinal obstruction. The abdominal cavity contained a large amount of clear, serous ascites. The ileum showed chronic radiation enteritis, forming a large inflammatory mass (Fig. 2). An ileocecal resection of the mass was performed using an ileostomy and ascending colostomy because of a presence of radiation enteritis and an insufficiency of preoperative bowel preparation. In the resected specimen, a

Fig. 2 An exploratory laparotomy showing a whitish, hen-egg sized tumor of the ileum 10 proximal from the terminal ileum demonstrating radiation enteritis.

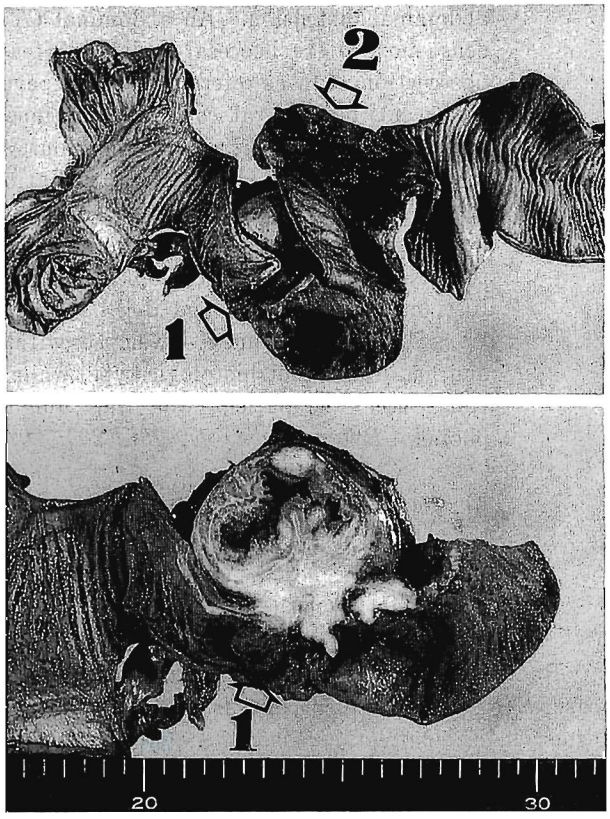

Fig. 3 Macrophotographs of the resected ileum showing the ileum to fold around a mass in several ways with infiltration to the adjacent ileum (1, 2) in the opened intestine (top) and a mass forming a diverticulum-like folded ileum with a tumor infiltrating to the ileum on a cut section (bottom).

Table 1 The diagnostic reliability of radiation-induced cancers following radiotherapy for malignant neoplasms

Reliability		Criteria			
		Histological type	Organ of origin	Latent period	Site of origin
A	1	different	different	more than	Within the
(High)	2	different	Same	5 years	irradiated field
B	1	Same	different (non-continuous)	more than	Within the
(Medium)	2	Same	different (continuous)	5 years	irradiated field
C	1	Same	same (non-continuous)	more than	Within the
(Low)	2	Same	same (continuous)	5 years	irradiated field

Sakai *et al.*, 1981[1]

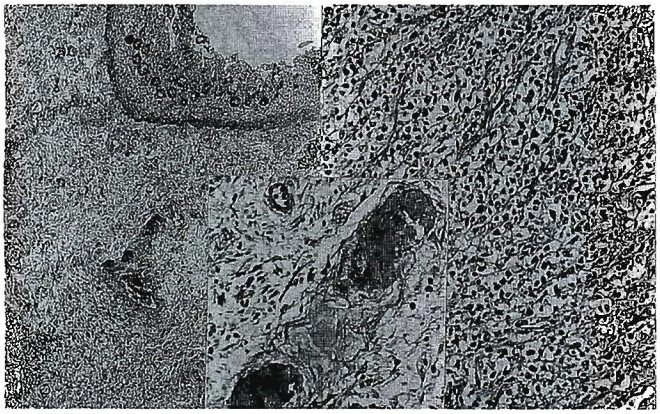

Fig. 4 Microphotographs of the tumor revealing malignant lymphoma of diffuse, medium-sized cell type, infiltrating through the intestinal wall of the ileum (right) (HE, × 10). The wall of the bowel adjacent to the tumor showing ul ceration and fibrosis (left) (HE,×25) and hyalinization of the small vessel walls (inset) bue to irradiation (HE, ×50).

tumor was found in the center of an inflammatory folded intestine. The tumor was whitish in color and measured 5 cm in size, located 10 cm proximal from the terminal ileum, with infiltration to the adjacent ileum forming circular ulcers (Fig. 3, top). On a cut section, the tumor resembled a diverticulum-like folded ileum expanding to the mesentery and infiltrated into the adjacent ileum (Fig. 3, bottom). Microscopically, the tumor was diagnosed to be malignant lymphoma (diffuse, medium-sized cell and B-cell type). Medium-sized atypical lymphocytes infiltrated diffusely throughout the intestinal wall of the ileum with necrosis and mitosis (Fig. 4, right). Immunohistochemical staining was positive for leukocyte common antigen (LCA), B cells(CD20), and *negative for T cells*(CD45RO). The adjacent ileum showed histological features of radiation enteritis (ulceration, fibrosis and hyalinization of the small vessel walls) (Fig. 4, left and inset).

On the 5th postoperative day (October 25), she developed massive bleeding from a duodenal ulcer and hemostasis by endoscopic ethanol injection was failed. Subsequently, an emergency laparotomy was performed and hemostasis was thus successfully achieved. However, the patient later developed postoperative pulmonary edema, pneumonia and liver failure, and expired on November 13, 1995. An autopsy was not allowed.

DISCUSSION

Although radiotherapy is recognized as an effective treatment for uterine cervical cancer, it sometimes results in severe complications, such as radiation cystitis and enterocolitis[19]. Furthermore, the occurrence of secondary malignancies following radiotherapy for the primary cancers have also increased with the improvement of the survival rate after radiotherapy.

Although it is difficult to assess the precise role of radiotherapy in developing the second malignant neoplasms, the induction of neoplasms in the small intestine and colon by localized irradiation in animal experiments have been previously described[20,21]. In these reports, the rate of tumor induction was directry related to the dose of radiation with an unknown mechanism[20].

Many reports have also clinically shown possible second cancers after radiotherapy for uterine cervical cancer[1~15] and thus proposed a definitions of "radiation-induced cancer"[1~5] . Regarding such definitions, Sakai et al. reported the survey on second cancer following radiotherapy in Japan and also suggested the criteria of diagnostic reliability of radiation-induced cancers[1,2]. Their criteria require that the second cancers develop within the irradiated field and with a latent period of more than 5 years after radiotherapy. In addition, the diagnostic reliability is classified into 3 grades, A, B and C based on the difference of histological type and the organs of origin from the primary cancer (Table 1). Grade A-1, which differs both in histological type and the organs of origin from the initial cancer, was classified as a highly probable instance of radiation-induced cancer. According to this criteria, the second neoplasm in our case also fulfilled the A-1 grade criteria. In addition, the malignant lymphoma in our case originated from the

intestine which also demonstrated findings that were compatible with the features of radiation enterocolitis. We thus diagnosed the present tumor as radiation-induced malignant lymphoma with high reliability.

The incidence of radiation-induced cancer was 0.11% of all irradiated patients and 0.3% of the 5-year survivors after radiotherapy. In cases of radiotherapy for uterine cancer, radiation-induced cancer has been reported to originate in 0.22% of all patients[1,2].

Statistically, a radiation-induced second malignancy occurs more frequently in females than in males, with an approximately 5 : 1 ratio[2]. The women who have been irradiated for gynecologic cancer under 30 or over 50 year of age are at greatest absolute risk of developing second cancers[6,10]. In the present case, the patient had a high risk of inducing a second malignancy because she has also received a relatively high dose of radiotherapy at the age of 60.

The development of radiation-induced cancers after treatment for uterine cancer, colorectal cancer, urinary bladder cancer and leukemia have all been reported by many investigators[3~15]. In these reports, the occurrence of malignant lymphoma was seldom included, and no other such report could be found in the literature from 1986 to 1996 besed on our extensive search.

The relationship between the radiation dosage or the degree of radiation damage and the developement of a second malignancy remains controversial[3,14,15]. Arai *et al.* reported that high dose irradiation of more than 50 Gy was suggested to more likely induce a second cancer than low dose irradiation[3]. Our patient had a long disease free interval of 7 years after the relatively high dose radiation, and did not demonstrate any severe radiation damage. From these findings, we thus suppose that the dose of irradiation or the degree of radiation damage is not correlated with the development of a second malignancy.

Most malignant lymphomas of the small intestine occur in the ileocecal region[17], and histologically, are typically B cell, diffuse and large cell type[22,23]. In the present case, on the other hand, the histopathological finding showed lymphomas of diffuse, B cell type and medium-sized cell type, which is rare type in intestinal lymphoma. These features may thus suggest that our second malignancy was thus a radiation-induced type of malignant lymhoma.

In cases of intestinal malignant lymphoma without any distant metastasis, a surgical resection of the primary lesion should be the treatment of choice[22]. Further improvements in the survival rate can be expected with adjuvant chemotherapy[22]. However, the prognosis of gastrointestinal malignant lymphoma is still poor, with a 10-year survival of only 46.5% in patients with curative resection and 20.8% with noncurative resection[22]. The combined findings of both the literature and our case thus suggest the importance of the diagnosis and a surgical resection of the malignant lymphoma at an early stage. However, the radiation enteritis observed in our case, which formed an inflammatory mass surrounding the malignant lymphoma, made the diagnosis of this tumor very difficult and thus delayed early curative resection.

In conclusion, our case therefore indicates the necessity of a long term follow-up after radiotherapy to identify the possible induction of second neoplasms, including malignant lymphoma.

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