

CONCURRENT CHEMORADIATION-RELATED SUPERIOR MESENTERIC ARTERY OCCLUSION IN THE PATIENT WITH ADVANCED ENDOMETRIOID ENDOMETRIAL CANCER AFTER SURGERY

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The incidence of endometrial cancer (EC) has increased and it has approximately 16% of gynecologic cancers in Korea. For loco-regional or distant recurrence, adjuvant treatment after surgery is very important in patients with intermediate- or high-risk EC (IHR-EC). Recently clinical trials for treating patients with IHR-EC are focused on the efficacy of concurrent chemoradiation (CCR). However, increase in intestinal complications in the group of radiotherapy combined with chemotherapy was reported. In case of chemoradiation-related superior mesenteric artery (SMA) occlusion, it could be fatal nevertheless with intensive care. We present a case report of radiation-related arteritis leading to stenosis in SMA, which led the patient with EC to death in a year after CCR.

Keywords: Endometrial neoplasms; Radiotherapy, adjuvant; Chemotherapy, adjuvant; Mesenteric vascular occlusion

Endometrial cancer (EC) is the most common gynecologic malignancy in the USA, and its incidence has increased to approximately 16% of gynecologic cancers in Korea [1]. More than 80% of patients have International Federation of Gynecology and Obstetrics stages I or II of the disease [2]. Although most patients with low-risk EC may be cured after surgery, those with intermediate- or high-risk endometrial cancer (IHR-EC) often show loco-regional or distant recurrence [3]. Therefore, adjuvant treatment after surgery is very important in patients with IHR-EC.

Nowadays clinical trials for treating patients with IHR-EC are focused on the efficacy of concurrent chemoradiation (CCR) after a phase II study of the Radiation Therapy Oncology Group (RTOG 9708), which demonstrated that CCR may improve loco-regional control, and reduce extra-pelvic recurrence [4-6]. By the way, radiation-related arteritis (RRA) is a rare but well recognized complication of radiotherapy. A study reported increase in intestinal complications in the group of radiotherapy combined with chemotherapy [7].

We present a case report of RRA leading to stenosis in the superior mesenteric artery (SMA), which led the patient with EC to

death in a year after CCR.

Case Report

A 62-year-old woman visited her physician complaining of vaginal spotting which started 5 years ago. She was transferred to our in-

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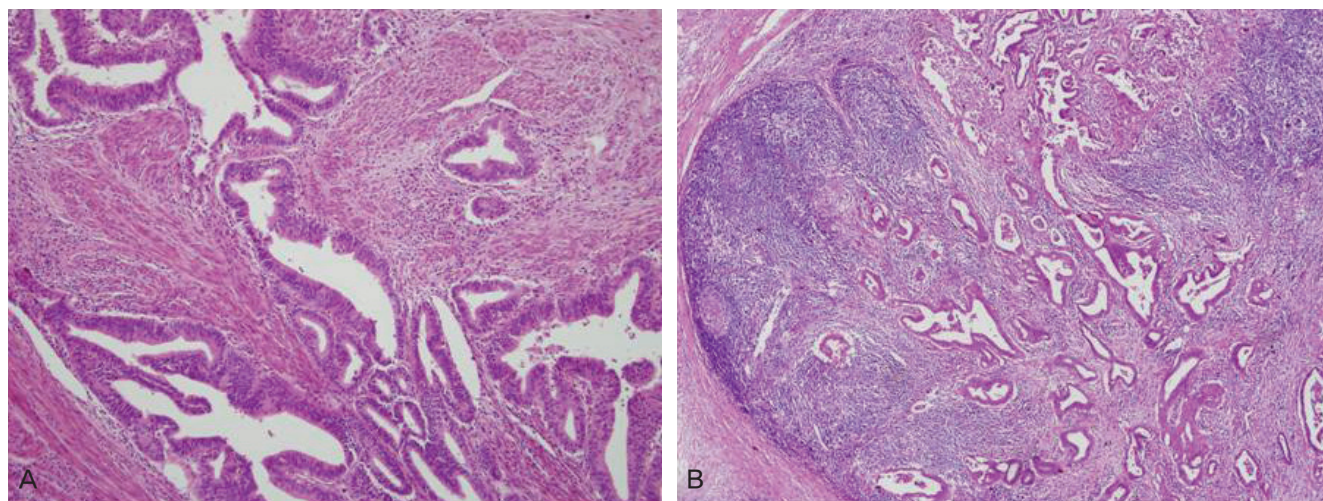


Fig. 1. This slide shows (A) endometrial cancer grade 1 (H&E, $\times 100$), and (B) positive lymph node metastases (H&E, $\times 20$).

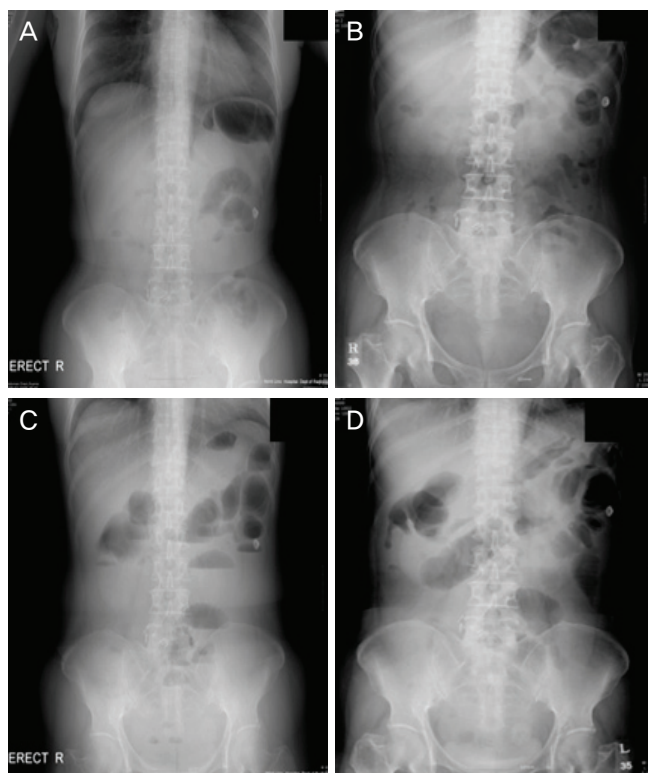


Fig. 2. Simple X-ray films before operation. (A, B) Simple abdomen erect and supine showed normal finding but multiple surgical clips in mid abdomen. (C, D) Just before operation, simple X-ray hinted at ileus with diffuse edematous bowel wall thickening.

stitution under the impression of EC. Endometrial biopsy revealed endometrioid EC (EEC), grade 1. Preoperative computed tomography (CT) implied EC without parametrial invasion or cervical invasion, and showed neither distant metastasis nor lymphadenopathy.

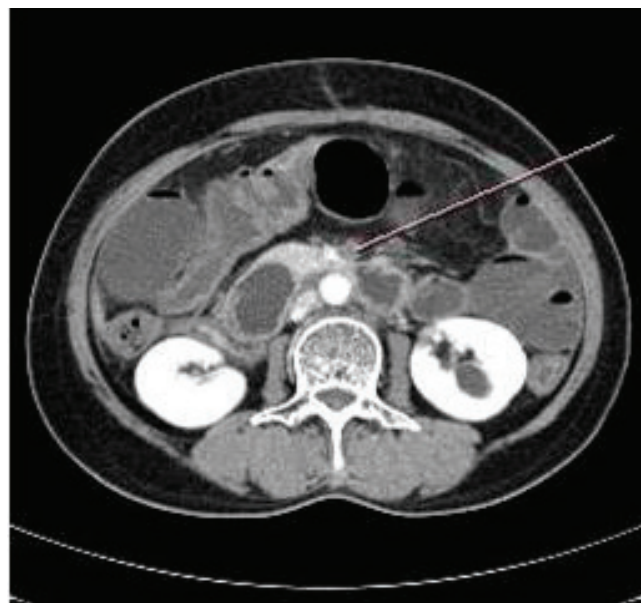


Fig. 3. CT showed small bowel ischemia with superior mesenteric artery thrombosis.

CA-125 level was elevated to 364.95 U/mL. A total hysterectomy, both salpingo-oophorectomies (TH+BSO), pelvic and para-aortic lymphadenectomy was done as cancer cells were found at para-aortic lymph nodes excised during operation. Permanent biopsy reported EEC grade 1, and the size of the tumor was 4.5×3.5 cm, and the cancer had metastasized to 13 out of 42 regional lymph nodes (LN) including paraaortic LN (Fig. 1). CCR was applied using doxorubicin and cisplatin for 2 times, and pelvis radiation using 10MV energy with total dose 3,240 cGy, daily tumor dose 180 cGy, 18 fractions for 5 weeks simultaneously. One day she came to

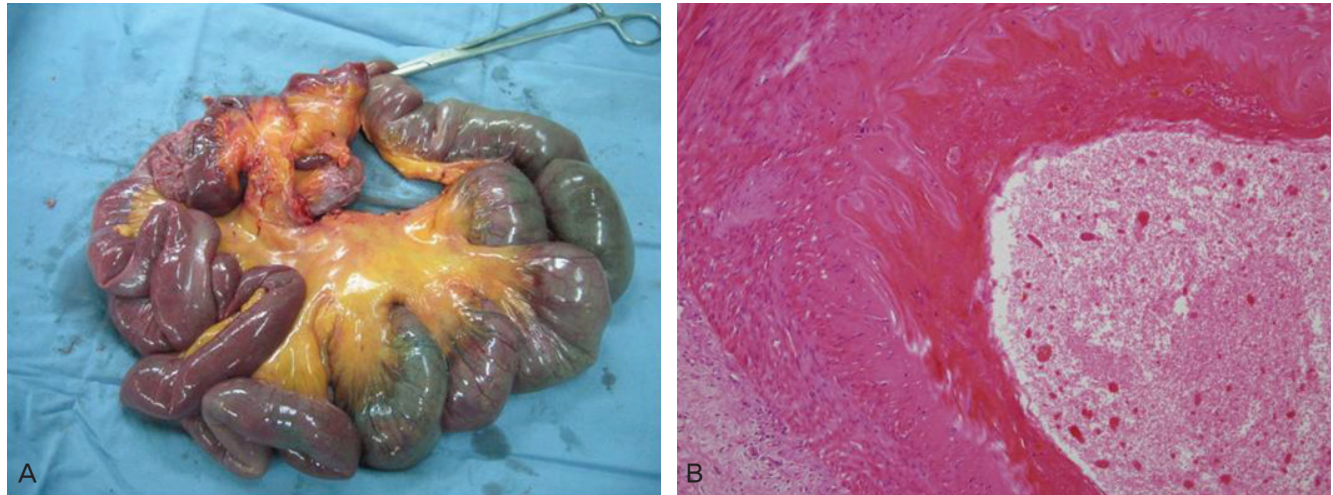


Fig. 4. (A) The nearly totally resected intestine at emergency operation. There were foul odor and the intestine had shown ischemic and necrotic appearance. (B) This slide shows thrombus with intimal fibrinous necrosis and fibrosis (H&E, $\times 100$).

emergency room for acute and severe abdominal pain. X-ray films showed normal abdominal finding with multiple surgical clips (Fig. 2A, 2B). The next day, pain did not subside. Abdominal CT showed small bowel ischemia with SMA thrombosis (Fig. 3). Just before operation, simple X-ray hinted at ileus with diffuse edematous bowel wall thickening (Fig. 2C, 2D). Emergent operation of nearly total small bowel resection was done. The pathologic report revealed thrombus with intimal fibrinous necrosis and fibrosis (Fig. 4). After operation, general care has been given. Complications related to central and peripheral nutrition, stress ulcer as well as recurrent infection for a long time had induced her emaciated. Even though intensive care had been given, she died after 1 year.

Discussion

Radiation therapy (RT) is the most effective adjuvant treatment in patients with IHR-EC, and many gynecologic oncologists prefer RT for treating patients after surgery [8]. Patients with stage II and III disease are also offered postoperative radiotherapy. There have been three randomised trials that have addressed the effect of postoperative radiotherapy in high-risk patients [8,9]. No overall survival (OS) advantage has ever been shown for postoperative radiotherapy, but an improved progression-free survival (PFS) of around 10% has been seen.

Doxorubicin is one of the most effective agents in the treatment of EC, and doxorubicin/cisplatin (AP) is in most countries commonly accepted as the standard regimen for EC [10]. Currently, chemoradiation is not regarded as standard management for EC. The clinical

trial data in this area are sparse [11]. The Gynecologic Oncology Group study (GOG-122) randomised 422 patients with stage III or IV EC after TH+BSO and maximal debulking with no residual tumour less than 2 cm into radiotherapy consisting of whole abdominal radiotherapy delivering 30 Gy in 20 fractions followed by an additional 15 Gy pelvic boost and chemotherapy in which AP were given every 3 weeks for seven cycles followed by one cycle of cisplatin. Both OS and PFS were significantly better for patients receiving chemotherapy, despite an increased incidence of grade 3 and 4 toxicity, such that less than two-thirds of patients completed all eight cycles of chemotherapy [12]. A study randomised 156 patients with high-grade disease or stage IC-IIIA disease to receive radiotherapy alone or radiotherapy combined with three courses of chemotherapy. No difference in OS or PFS was seen in this study either and there was an increase in intestinal complications in the chemotherapy group [7]. However, there is increasing interest in the role of chemotherapy in high-risk EC and this is the basis of the current PORTEC-3 study. This study randomized patients with stage I or IIA grade 3 disease and stages IIB and above after hysterectomy to receive either radiotherapy alone or chemoradiation with two courses of cisplatin week 1 and week 4 followed by adjuvant chemotherapy with carboplatin and docetaxel.

RRA has since been described in numerous large vessels [13]. These lesions include fibrosis of the internal elastic membrane, injury to the vasa vasorum, and ischemic necrosis of the vessel wall, periarterial fibrosis, and hyalinization and thickening of the vessel wall with fibrin deposition [14]. The dose of radiation associated with this unique clinical entity is 20 to 80 Gy [14], and 39.5 to 80 Gy is specifically mentioned for the iliac and femoral arteries [13].

The dose used to the patient was much higher than these.

Treatment of RRA has not been extensively studied, likely because of the scarcity of cases. The basic treatment options described in the literature include medical therapy, anatomic revascularization, extraanatomic bypass, percutaneous transluminal angioplasty, and stenting (balloon-expandable and self-expanding stents) [15].

Although RRA in the large vessels is a rare complication of radiotherapy, it may become more common as a result of the increasing use of radiotherapy and increasing duration of survival in patients with cancer. We tried to review the risk factors for SMA embolisation after CCR, but we could not find these. We present a case report of RRA leading to stenosis in SMA, which led the patient with EC to death in a year after CCR.

Acknowledgments

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진행된 자궁내막암 환자에서 수술 후 동시항암화학방사선요법 후 생긴 상부장간막동맥폐쇄증

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자궁내막암은 점차 발생빈도가 높아져서 현재 한국에서 부인암의 16%를 차지하고 있다. 중증도 또는 고위험군에서는 국소적 재발 또는 전이가 때문에 수술 후 보조적 요법이 매우 중요하다. 최근에서 동시항암화학방사선요법이 주목 받고 있다. 그러나 이 치료에 의한 장의 합병증이 증가하고 있다. 방사선치료에 동반된 장간막동맥폐쇄증 폐색이 생기면, 집중치료에도 불구하고 치명적일 수 있다. 동시항암화학 방사선요법 후 생긴 상부 장간막동맥폐쇄증으로 치료 후 1년 만에 사망한 증례를 간단한 문헌 고찰과 함께 보고하고자 한다.

중심단어: 자궁내막암, 보조적 방사선요법, 보조적 항암화학요법, 장간막동맥폐쇄