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Two cases of severe esophageal ulcer caused by chemotherapy for breast cancer after particle beam therapy for esophageal cancer

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Abstract

Background: Particle beam treatment for esophageal cancer can produce a better local therapeutic effect than can conventional radiotherapy. However, events that occur in the esophagus during or after the treatment of other cancers after that are unknown.

Case summary: The first patient, a 64-year-old woman, had undergone heavy ion radiotherapy for esophageal cancer. Endoscopic submucosal dissection was performed for local residual tumor. Five years later, cancer was found in the right breast, and the patient underwent partial mastectomy and adjuvant chemotherapy. Six years after heavy ion radiotherapy, oral intake became difficult. A benign esophageal ulcer with circumferential stenosis was observed at the site of heavy particle irradiation.

The second patient, a 63-year-old woman, had undergone proton therapy for esophageal cancer and photodynamic therapy for local residual tumor. Four years later, cancer was found in the left breast, and the patient underwent preoperative adjuvant chemotherapy, which reduced the size of the breast cancer. Oral intake became difficult 5 years after proton therapy. Endoscopy showed a benign esophageal ulcer with severe stenosis at the site of proton irradiation.

Conclusion: After particle beam therapy for esophageal cancer, patients who undergo chemotherapy for other cancers may develop an esophageal ulcer.

Keywords: Particle beam therapy; esophageal cancer; esophageal ulcer; breast cancer; chemotherapy.

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Introduction

Particle beam therapy for esophageal cancer, such as heavy ion radiotherapy or proton therapy, can produce better local therapeutic effects than can conventional radiotherapy [1-3]. The ability of the esophageal mucosa to regenerate is significantly impaired after particle beam therapy. However, in association with this impairment, the treatment of other cancers has an unknown effect on the site of irradiation. We encountered two patients with severe esophageal ulcer that was triggered by chemotherapy for breast cancer after particle beam therapy for esophageal cancer.

Case 1 presentation

Chief complaints

A 64-year-old woman had dysphagia and diarrhea.

History of present illness

Right breast cancer (cT1cN0M0, clinical stage I) was diagnosed; she underwent partial mastectomy and axillary lymph node dissection, because of three sentinel lymph nodes metastasis. She had four courses of fluorouracil, epirubicin, and cyclophosphamide (FEC) therapy as postoperative adjuvant chemotherapy, followed by two courses docetaxel (DTX) therapy. During DTX therapy, dysphagia and watery diarrhea developed.

History of past illness

She had undergone heavy ion radiotherapy (48 Gray equivalents in 12 fractions) for esophageal cancer (cT1bN0M0, clinical stage I). Subsequently, endoscopic submucosal dissection was performed for local residual tumor. The cancer did not recur for 5 years (Figure 1A).

Physical examination

Her temperature was 38.2°C; pulse, 78 bpm; respiratory rate, 15/min; blood pressure, 127/78 mm Hg; and oxygen, saturation 99%. On general physical examination, she appeared mildly dehydrated.

Laboratory examinations

Blood analysis revealed severe leukopenia (300/μL), with neutropenia (12.0%), low hematocrit (22.3%), and low platelet count (108 × 10^3/μL). Her serum C-reactive protein level was remarkably high: 11.01 mg/dL (normal, <0.30 mg/dL).

Imaging examinations

Endoscopy revealed a benign but severe esophageal ulcer with circumferential stenosis at the site of the earlier heavy particle irradiation (Figure 1B). No necrosis of the esophageal wall was seen.

Final diagnosis

The final diagnoses were esophageal ulcer and febrile neutropenia caused by chemotherapy.

Treatment

She was admitted to our hospital and was given antibiotics, granulocyte colony-stimulating factor, and antacids.

Outcome and follow-up

Her temperature returned to normal after 2 days, and blood sampling data and diarrhea improved in 1 week. However, oral intake continued to be difficult, and a gastrostomy was performed 3 weeks after her admission. She resumed partial oral intake 2 months later and was discharged. Six months later, she was able to eat almost normally by chewing well (Figure 1C).

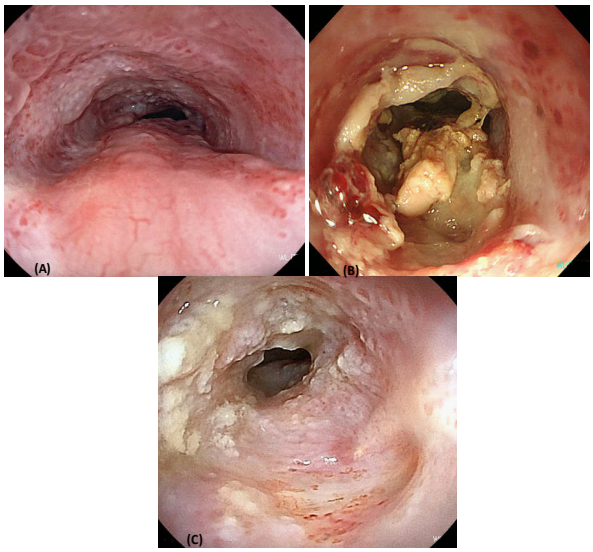

Figure 1: Case 1 endoscopic views
(A) After heavy ion radiotherapy and endoscopic submucosal dissection for esophageal cancer, the esophagus showed chronic esophagitis with edema.
(B) During docetaxel therapy for breast cancer, the esophagus showed severe ulceration with stenosis at the site of the earlier heavy ion radiotherapy.
(C) The esophageal ulcer improved, but mild stenosis remained.

Case 2 presentation

Chief complaints

A 63-year-old woman had dysphagia.

History of present illness

Cancer (cT3N0M0, clinical stage IIB) of intrinsic subtype with triple negative was diagnosed in the left breast. Preoperative adjuvant chemotherapy comprised four courses of FEC and DTX. The breast cancer was reduced, but during the fourth DTX treatment, dysphagia developed.

History of past illness

She had undergone proton therapy (60 Gray equivalents in 30 fractions) for esophageal cancer (cT1bN0M0, clinical stage I). Subsequently, photodynamic therapy was performed for local residual tumor. The cancer did not recur for 4 years (Figure 2A).

Physical examination

Almost all her vital signs were normal. On general physical examination, no abnormalities were found.

Laboratory examinations

Blood analysis revealed a normal level of leukocytes (6400/μL), low hematocrit (29.2%), and normal platelet count

(342 × 10^3/μL). Serum C-reactive protein levels were mildly increased: 0.45 mg/dL (normal, <0.30 mg/dL).

Imaging examinations

Endoscopy revealed a benign esophageal ulcer with severe stenosis at the site of the earlier proton irradiation (Figure 2B).

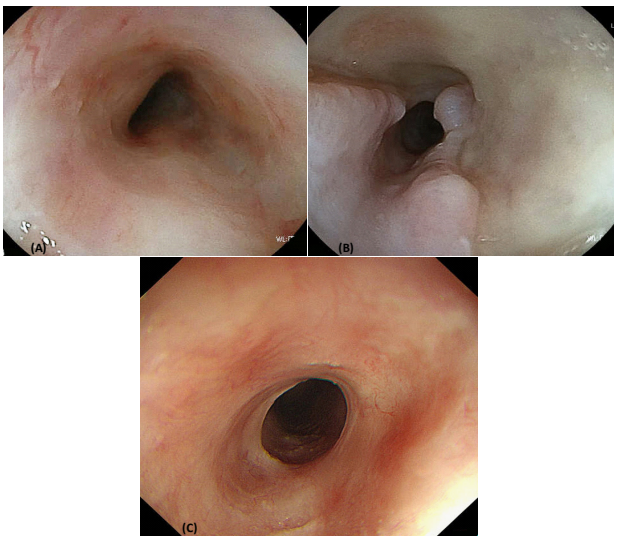

Figure 2: Case 2 endoscopic views
(A) After proton therapy and photodynamic therapy for esophageal cancer, the esophagus showed chronic esophagitis with edema.
(B) During docetaxel therapy for breast cancer, the esophagus showed severe ulceration with stenosis at the site of the earlier proton therapy.
(C) The esophageal ulcer improved, but mild stenosis remained.

Final diagnosis

The final diagnosis was esophageal ulcer caused by chemotherapy.

Treatment: H_2-blocker treatment was administered for 2 months.

Outcome and follow-up: After 2 months of H_2-blocker management, she no longer suffered from dysphagia (Figure 2C).

Discussion

Chemotherapy is well known to cause mucosal damage in the digestive tract. Our two patients had not only mucosal damage but also severe ulceration in the area where particle beam therapy had been focused and where regeneration capacity was subsequently impaired. When patients who have undergone particle beam therapy for esophageal cancer then undergo chemotherapy for other cancers, this severe adverse event can occur. The development of multidisciplinary treatment for esophageal cancer enables long-term survival of patients [4,5]. Thus, physicians should account for the events associated with treatment for esophageal cancer in long-term survivors of esophageal cancer who then receive treatment for other cancers.

Particle beam treatment with heavy ions or protons for esophageal cancer can produce better local therapeutic effects than can conventional radiotherapy [1-3]. Our two patients unfortunately did not achieve complete response with the particle beam treatment alone for esophageal cancer. Additional local treatments-the endoscopic submucosal dissection and the photodynamic therapy performed for each small residual tumor-were necessary for a complete response. Particle beam therapy has a unique physical advantage over conventional radiotherapy because of its defined range with a sharp high-dose Bragg peak [3,6,7]. This advantage not only enhanced treatment effects but also reduced the number of adverse events [1-3,6]. However, even if the damage around the esophagus can be minimized, the effects on the esophagus itself remain [8]. According to one report, 56.4% (22 of 39 cases) of patients developed esophageal ulcers after proton therapy, and five patients did not achieve healing [2]. These events occurred during observation, not during the treatment of other cancers after particle beam therapy. The two cases we have reported were very unusual in that after particle beam therapy for esophageal cancer, both patients suffered from severe esophageal ulcers induced by breast cancer chemotherapy.

Among breast cancer drugs, FEC causes more gastrointestinal symptoms such as nausea, vomiting, and gastritis than does DTX [9,10]. However, during FEC treatment, our patients did not show dysphagia. Conversely, DTX-induced dermatologic toxicity is severe and well characterized [10-12], but the cause is largely unknown. Both the skin and the esophagus originate from the ectoderm and have similar tissue structures. Therefore, we hypothesized that severe esophageal ulceration might occur just after the administration of DTX. However, there was no obvious skin disorder in our cases, and we could not prove it. Few reports [13] of patients undergoing surgery after particle beam therapy have been published, and the details of those cases are unknown; however, in our experience, fibrosis and ischemic changes in the irradiated area are severe. Therefore, if DTX induces inflammation in the gastrointestinal mucosa, particle beam irradiation can induce severe ulceration. In reports of DTX-related ischemic colitis, most patients improved if DTX was discontinued when symptoms appeared. However, some deaths were observed with continuous administration [14,15]. Fortunately, our patients could be treated with antacids; however, surgery may be necessary for delayed esophageal stricture and perforation after particle beam therapy.

Conclusion

In long-term survivors of esophageal cancer who achieve complete local response after particle beam therapy, severe esophageal ulcers and strictures may develop because of chemotherapy for cancer in other organs. For patients who have undergone particle beam therapy to the esophagus, we suggest that they be informed of the risk of severe esophageal ulcer before they undergo further chemotherapy.

Informed consent statement: The patients involved in this study gave written informed consent authorizing the use and disclosure of their protected health information.

Conflict-of-interest statement: The authors have no conflicts of interest regarding this case report.

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