Esophageal Cancer with an Esophagopericardial Fistula and Purulent Pericarditis

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Abstract

We herein present the case of a 56-year-old Japanese woman who developed purulent pericarditis after undergoing chemoradiotherapy for esophageal cancer. She developed epigastralgia and a fever and was admitted to our hospital. A physical examination revealed hypotension, tachycardia and pericardial friction rub. Echocardiography revealed moderate pericardial effusion. Based on these observations, the patient was diagnosed with cardiac tamponade. Computed tomography confirmed the presence of an esophagopericardial fistula. Treatment with pericardiocentesis, drainage and short-term intrapericardial administration of antibiotics relieved the patient’s symptoms. Daily rinsing through a catheter with normal saline prevented relapse of the purulent pericarditis. Esophagopericardial fistulas are so rare that their treatment is not well-established. We herein report successful palliative care of a malignant esophagopericardial fistula associated with purulent pericarditis.

Key words: esophagopericardial fistula, purulent pericarditis, palliative care

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Introduction

Every year, approximately 18,000 people develop esophageal cancer in Japan and 12,000 die from the disease (1). Advanced esophageal cancer sometimes forms malignant fistulas within airways or the mediastinum. More than half of such fistulas involve the trachea or main bronchus, which increases the risk of pneumonia (2). Meanwhile, the development of esophagopericardial fistulas, a life-threatening complication, is rarely reported (3-7). The initial symptoms include epigastralgia, retrosternal pain and fever, which overlap with the symptoms of acute pericarditis (4-7). Because some of the symptoms of esophagopericardial fistulas are similar to those of esophageal cancer and chemoradiotherapy, physicians may overlook this condition, making early diagnosis difficult. We herein present a case of esophageal cancer that developed into an esophagopericardial fistula and purulent pericarditis. These conditions were successfully treated, and we were able to relieve the patient’s symptoms, prevent relapse of the pericarditis and support the best possible quality of life for the patient for the rest of her life.

Case Report

A 56-year-old Japanese woman complained of epigastralgia and fever and was admitted to our hospital in October 2011, two weeks after undergoing combination chemotherapy with nedaplatin and docetaxel for lower esophageal cancer. She had been diagnosed with advanced esophageal cancer (squamous cell carcinoma, T3N4M0 Stage IVa) in January 2011 and had undergone chemoradiotherapy consisting of 5-fluorouracil, cisplatin and total irradiation of 60 Gy. This therapy reduced the size of the tumor and temporarily relieved the patient’s dysphagia. However, the symptoms returned in August 2011, and nedaplatin and docetaxel were administered.

The patient was 153 cm in height and 39 kg in weight. A physical examination revealed fever (37.8°C), hypotension
ment elevation in the anterior and inferior leads (Fig. 1). Electrocardiogram showed sinus tachycardia (115 beats/min) associated with concave ST segment elevation in the anterior and inferior leads (B). The magnitude of the ST elevations decreased; however, diminished QRS amplitudes associated with T-wave inversion were sustained after drainage (C).

Figure 1. Electrocardiograms before chemotherapy with nedaplatin and docetaxel (August 18, 2011; A), at the time of hospital admission due to chest pain (October 14, 2011; B) and after pericardiocentesis and drainage (October 17, 2011; C). Electrocardiogram showing diminished QRS amplitudes, concave ST segment elevation and PR segment deviations opposite the P polarity in both the anterior and inferior leads (B). The magnitude of the ST elevations decreased; however, diminished QRS amplitudes associated with T-wave inversion were sustained after drainage (C).

Figure 2. Echocardiography performed on admission. A moderate pericardial effusion (A) with many high-echoic small bodies floating in the pericardial fluid (B) was observed. The right atrium and ventricle were compressed by the effusion (A). APX: apex of heart, EFS: echo-free space, HSBS: high-echoic small bodies, LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle

(77/58 mmHg), tachycardia and pericardial friction rub. In the peripheral blood samples, the white blood cell count was increased to 16,400 cells/μL, 94% of which were neutrophils. The C-reactive protein level was also increased to 31.4 mg/dL. The creatine kinase-MB level was 3 ng/mL and within the normal range. Electrocardiogram showed sinus tachycardia (115 beats/min) associated with concave ST segment elevation in the anterior and inferior leads (Fig. 1). Echocardiography revealed a compressed right atrium and ventricle due to moderate pericardial effusion with many floating high-echoic small bodies (Fig. 2). Computed tomography (CT) confirmed the presence of an esophagopericardial fistula. The frontal part of the esophagus opened to the pericardium, and a communication was observed between the esophagus and the pericardial space. A small gas-filled space was observed in the pericardial space around the fistula (Fig. 3). Pericardiocentesis and drainage were performed, in which 350 mL of deep-yellow effusion was drained (Fig. 4). Cytology of the effusion demonstrated many neutrophils; however no malignant cells were observed.

The patient was diagnosed with purulent pericarditis due to an esophagopericardial fistula. We rinsed the pericardial space with normal saline through a multi-holed pigtail
Figure 3. Computed tomography images in the transverse plane (left column) and sagittal plane (right column). Images before chemoradiotherapy (February, 2011; A) and at the time of hospital admission due to purulent pericarditis (October, 2011; B). Wall thickening of the lower esophagus was observed without a fistula to the pericardial space (A). The frontal part of the esophagus opened to the pericardium, and a communication was observed between the esophagus and the pericardial space (arrowhead). (B) A small gas-filled space was observed in the pericardial space around the fistula (arrowhead). Pericardial effusion was observed (asterisk).

Figure 4. Pericardial effusion. A white pellet of inflammatory cells was apparent in the yellow fluid at the bottom of the tube.

The patient was unable to swallow any food due to esophageal stenosis. She received oral liquid alimentation in combination with a drip infusion and was free from both pain and fever. We left the pigtail catheter in the pericardial space and rinsed the area once a day with normal saline. Six weeks later, the patient died due to deterioration of her clinical condition.

Discussion

Approximately 18,000 people develop esophageal cancer every year in Japan (1), and about 130 new patients with this type of cancer are admitted to our facility annually (8). Our CT database shows 19 cases of fistulas caused by esophageal cancer over the past five years. Twelve cases (63%) were esophagorespiratory fistulas and six cases (32%) were esophagomediastinal fistulas. We did not find any cases of esophagopericardial fistulas in our database. A survey of the literature published in English found that 70 cases of esophagopericardial fistulas have been reported...
since 1931, 80% of which followed benign esophageal diseases (esophagitis, esophageal ulcer and injury due to ingestion of foreign bodies such as fish bones). Only 20% of the cases were caused by esophageal cancer (3-7). Given that esophagopericardial fistulas can cause purulent pericarditis and cardiac tamponade, their existence can be life-threatening. However, because there are so few case reports, treatment for malignant esophagopericardial fistulas has not been established.

Miller et al. reported that the in-hospital mortality rate of 60 patients with esophagopericardial fistulas (14 cases developed following diagnoses of carcinoma) was 83% and that early diagnosis is essential for treating life-threatening complications such as purulent pericarditis (7). The authors of some case reports have recommended that once pneumopericardium is recognized on chest radiography, esophagographic studies should be performed to diagnose possible fistulas (5-7). However, our patient demonstrated a small pneumopericardium that was not detected on chest radiography, but rather on CT only. Therefore, we question the sensitivity of chest radiography for detecting esophagopericardial fistulas in patients presenting with pneumopericardium. Rather, immediate CT should be performed once low pulse pressure and fever are detected in patients with esophageal cancer, especially following chemoradiotherapy.

We speculate that the esophagopericardial fistula observed in our patient may have been caused by a combination of the four following factors. The first contributing factor is the location of the cancer: in the lower thoracic esophagus and anterior wall close to the pericardium of the left atrium (Fig. 3). Anatomical proximity might be the primary factor for the formation of the communication between the esophagus and the pericardial space. The second factor is the patient’s history of radiation therapy (RT), which was focused on the esophageal region close to the pericardium. RT is known to have acute and late toxic effects on the esophagus. Acute toxicity manifests itself as a reduction in cell turnover within the esophageal musculature months to years later, resulting in stricture, chronic ulcerations and, rarely, fistula formation (9). Higher-dose RT is associated with lethal toxicities. The Radiation Therapy Oncology Group (RTOG) 92-07 trial used brachytherapy boosts after treatment with 5-fluorouracil, cisplatin and 50-Gy external-beam RT. In that study, treatment-related esophageal fistulas occurred in 14% of patients receiving brachytherapy, leading to death in three cases (10). In the US Intergroup Study 0123, two RT doses (50.4 and 64.8 Gy) were compared in groups of 109 patients each (11). RT resulted in two (1.8%) and 11 (10.1%) treatment-related deaths, respectively, indicating that the higher dose was significantly more toxic. In the high-dose group (64.8 Gy), four deaths occurred at doses over 51 Gy, and one patient died from a fistula nine months after the completion of treatment at 64.8 Gy. Based on these observations, we speculate that overexposure may have caused fistula formation in our case. The third factor is persistent pericarditis after RT. The pericardium is often injured by thoracic RT in patients with breast, lung and esophageal cancer (12). Due to the proximity, chronic inflammation after RT in both the esophagus and pericardium may have caused fistula formation in our case. The fourth factor is chemoradiotherapy. Because the combined antitumor effects of chemoradiotherapy and RT are more than additive, chemoradiotherapy is currently the standard of care for treating advanced esophageal cancer. Although chemoradiotherapy has fewer local and more systemic effects compared with RT, chemoradiotherapy may have disturbed the healing of the fistula.

Purulent pericarditis is an acute and fulminating disease that is fatal if left untreated. In case series with various backgrounds, the mortality rate in treated patients has been reported to be 40%, mostly due to cardiac tamponade, infection and constrictive pericarditis (13, 14). The patient we describe here developed cardiac tamponade despite having a relatively small amount (350 mL) of purulent effusion. Therefore, we speculate that the effusion volume may have increased rapidly and compliance of the pericardium may have been impaired. We thought that the purulent pericarditis might have been complicated by mediastinitis arising from esophageal perforation; therefore, we administered imipenem/cilastatin, broad-spectrum antibiotics that cover both aerobes and anaerobes. Goodman recommends rinsing the pericardial space combined with effective systemic antibiotic therapy (14), and we were able to control the infection and hemodynamic parameters in our patient by following this recommendation.

We speculate that the aggregation of white blood cells in the pericardial effusion was the source of the high-echoic signals observed on echocardiography. Shyu and colleagues reported that aggregation of blood cells in pericardial fluid causes the formation of high-echoic bodies (15). They postulated that both the heavy blood content and the large volume of pericardial effusions contribute to this phenomenon. In our case, the pericardial effusion drained immediately after echocardiography was purulent. After we left the purulent effusion standing for 20 minutes, we observed a pellet of white blood cells (Fig. 4). High-echoic bodies were not observed again after rinsing the pericardial space. Therefore, we speculate that aggregation of white blood cells was the source of the observed high-echoic bodies.

Once infection is controlled, surgical closure is the standard treatment for benign fistulas (6, 7). We resolved the acute crisis in this patient; however, surgical closure was not appropriate for this esophagopericardial fistula because the esophageal cancer was too advanced. We rinsed the pericardial space every day to prevent relapse of the pericarditis. The patient was permitted to drink clear liquids freely, although she was not allowed to have any solid foods. Daily rinsing is sustainable care because sterile normal saline is readily available everywhere and is inexpensive. To avoid adhesion and clogging of the catheter, we did not suction the pericardial space continuously through the catheter. After
rinsing with 100 mL of normal saline, the catheter was locked with 5 units of unfractionated heparin injection to maintain patency. We believe that this method is preferable over surgical closure or stent placement and is acceptable for terminal patients. Although surgical closure is a common curative treatment for benign fistulas, we were not sure whether it was suitable for malignant fistulas in terms of quality of life or prognosis. Stent placement over a malignant fistula might seal the hole; however, the long-term performance of this procedure has not been reported. Therefore, we did not recommend surgical closure or stent placement for this patient.

In conclusion, we report a very rare case of an esophagopericardial fistula associated with purulent pericarditis. Emergent pericardiocentesis was effective for treating the acute crisis. Thereafter, an indwelling catheter was placed, and the pericardial space was rinsed every day. For terminal patients with malignant esophagopericardial fistulas and purulent pericarditis, daily rinsing is a reasonable type of palliative care.

The authors state that they have no Conflict of Interest (COI).

References