Acute Myocardial Infarction Associated with Small-size Lung Cancer in a Young Woman

Kenji Mizumura¹, Toshio Sugane¹, Shunsuke Ozaki¹, Hiroshi Ohta², Yutaka Kouzu¹, Akiko Sekiyama¹, Hisato Hiranuma¹, Masahiro Terakado¹, Maki Sato¹, Tetsuo Shimizu¹, Tomoko Kobayashi¹, Noriaki Takahashi¹ and Shu Hashimoto¹

Abstract

A 34-year-old woman visited our hospital with chest pain and was diagnosed with acute myocardial infarction (AMI) on admission. Echocardiography revealed the presence of complex masses in the aortic valve. As serum tumor marker CA19-9 was elevated, she was screened for malignant disease. A computed tomography (CT) scan revealed a solitary pulmonary nodule, but because the nodule was small and non-specific, CT follow-up was considered appropriate. However, she developed hemorrhagic stroke in the short term and was subsequently diagnosed with lung adenocarcinoma. Clinicians should be on alert for the occurrence of AMI in patients with small-size lung cancer.

Key words: small-size lung cancer, acute myocardial infarction, nonbacterial thrombotic endocarditis, CA19-9

(DOI: 10.2169/internalmedicine.50.4610)

Introduction

Cancer patients are often in a hypercoagulable state and are susceptible to nonbacterial thrombotic endocarditis (NBTE). All complications of NBTE lead to severe damage of multiple organs and result in a poor outcome. NBTE, which is typically associated with far-advanced or late-stage malignancies (1, 2), causes various emboli; however, the incidence of myocardial infarction (MI) among patients with NBTE is generally low.

In this article, we describe a rare case of acute MI (AMI) associated with small-size lung cancer in a young woman. At first admission, we did not consider that an aggressive diagnosis for malignant diseases was required, because her lung nodule was small and non-specific. However, even this early lung cancer caused NBTE and AMI. If both elevated serum CA19-9 levels and hypercoagulability are detected, the presence of malignancy is possible and an aggressive diagnosis for malignant diseases should be sought.

Case Report

A 34-year-old woman presented with chest pain. She had never smoked and there was no record of cardiac abnormalities in her past medical history. Physical examination findings on admission were as follows: height, 155 cm; body weight, 46.5 kg; body temperature, 36.7°C; blood pressure, 150/90 mmHg; and pulse, 80 beats per minute. Her consciousness was alert. On auscultation, respiratory and cardiac sounds were normal, with no abnormal sounds noted. Laboratory findings on admission are shown in Table 1. Renal, hepatic function and APTT were normal, however, prothrombin time (PT) was prolonged and D-dimer level was high. The rapid troponin T was also positive. AMI was strongly suspected on the basis of an abnormal electrocardiogram with ST-segment elevation in leads V₂-V₅. As coronary angiography showed total stenosis of the left anterior descending (LAD) coronary artery (Fig. 1), she underwent emergency percutaneous coronary intervention. As echocar-
ings were consistent with NBTE.

The prevention of further embolisms. Histopathological find-

ingic embolism, she underwent aortic valve replacement for

hemiparesis. Magnetic resonance imaging (MRI) of the

brain showed an infarct in the left middle cerebral artery ter-

риторity (Fig. 5). Since the infarct appeared to be a cardio-

diagnostic, she was diagnosed with NBTE. Although she had mis-

carried twice, antiphospholipid antibodies were not present.

The serum tumor markers, CEA, SCC, CA125, and CA19-9

were evaluated, but only serum CA19-9 was elevated (202

U/mL). She was screened for malignant diseases by chest

radiography and computed tomography (CT) scans, which

revealed a solitary pulmonary nodule 10 mm in diameter

(Fig. 3A, 4A), while an abdomen CT scan showed only a

nodule by CT follow-up was considered to be appropriate,

because in addition to the small and non-specific nature of

the nodule, serum tumor markers other than CA19-9 were

normal. At this point, warfarin anticoagulant therapy was in-

stituted.

As we considered that decreasing the tumor burden might

improve DIC, we initiated chemotherapy. She received che-

motherapy consisting of carboplatin (CBDCA) at 340 mg/

body on day 1 and paclitaxel (PTX) at 95 mg/body on days

1, 8 and 15. However bilateral plural effusion increased, this

regimen was considered as not effective. Chemotherapy con-

sisting of continuous carboplatin (CBDCA) at 425 mg/body

on day 1 and pemetrexed (PEM) on day 1 was initiated, but

because of severe pancytopenia after the first course, this

regimen was also withdrawn. After the recovery from pan-

cytopenia, Erlotinib (150 mg/day) was orally administered

A month after the surgery, she was hospitalized for pro-

gressive dyspnea on exertion. Chest radiography showed cardiomegaly, bilateral pleural effusions and a new pulmonary nodule (Fig. 3B). Echocardiogram imaging and chest CT revealed pericardial effusion (Fig. 2B, 4E). It was considered that the main reason for dyspnea was a diastolic dysfunction due to pericardial effusion. Diagnostic and therapeutic pericardial paracentesis under echocardiographic guidance yielded bloody effusion. Effusion yielded about 700 mL, and adenocarcinoma cells were disclosed in the cytology of the pericardial fluid. Adenocarcinoma cells were also detected after aspiration of a pleural effusion. The pulmonary nodule that was detected on first admission was slightly swollen (Fig. 4B), and a chest CT scan revealed the presence of multiple new nodules (Fig. 4C, D). Contrast-enhanced chest CT scan also revealed pulmonary embolism (Fig. 4E). The serum CA19-9 level (1,531 U/mL) was significantly elevated above the level on first admission (202 U/mL). The transbronchial tumor biopsy (TBTB) specimens from a nodule in the right S3 lesion revealed moderately differentiated adenocarcinoma cells with migration into lymphatic vessels (Fig. 6A). These adenocarcinoma cells expressed TTF-1, which is commonly used as a marker for primary lung cancer, and produced mucin (Fig. 6B, C). Findings at bone scintigraphy were positive. Based on these findings, she was diagnosed with primary lung cancer with bone metastasis (cT4N0M1, stage IV). Epidermal growth factor receptor (EGFR) gene mutation status was evaluated, but mutations were not identified by direct sequencing. At the time of hospitalization, she also displayed disseminated intravascular coagulation (DIC) and subsequently developed right toe necrosis.

After three months, the patient presented with mild right hemiparesis. Magnetic resonance imaging (MRI) of the brain showed an infarct in the left middle cerebral artery ter-

риторity (Fig. 5). Since the infarct appeared to be a cardio-

diagnostic embolism, she underwent aortic valve replacement for

the prevention of further embolisms. Histopathological find-

ings were consistent with NBTE.

<table>
<thead>
<tr>
<th>Table 1. Laboratory Data on Admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC 10400/μm³</td>
</tr>
<tr>
<td>RBC 364×10⁶/μm³</td>
</tr>
<tr>
<td>Hb 10.9 g/dL</td>
</tr>
<tr>
<td>Ht 32 %</td>
</tr>
<tr>
<td>Pt 11.3×10⁴/μL</td>
</tr>
<tr>
<td>MCV 88 fl</td>
</tr>
<tr>
<td>MCH 29.9 pg</td>
</tr>
<tr>
<td>MCHC 33.9 %</td>
</tr>
<tr>
<td>PT 61 %</td>
</tr>
<tr>
<td>PT-ratio 1.22</td>
</tr>
<tr>
<td>PT-INR 1.37</td>
</tr>
<tr>
<td>APTT 27.0 sec</td>
</tr>
<tr>
<td>D-dimer 14.8 mg/dL</td>
</tr>
</tbody>
</table>

Figure 1. Coronary angiography showed total stenosis of the left anterior descending coronary artery (white arrow).
once daily. DIC improved and she was discharged from our hospital. However, after four months of continued chemotherapy treatment, DIC developed. The patient developed respiratory failure from the difficulty in controlling pericardial and pleural effusion and died.

**Discussion**

The initiating factors in the pathogenesis of NBTE are unknown (4). Endothelial damage caused by circulating cytokines, such as tumor necrosis factor and interleukin-1, may trigger platelet deposition, particularly in the presence of an activated coagulation system (5). Generally, NBTE develops in cancer patients in the far-advanced or late stages (1, 2). However, despite small-size lung cancer without DIC, the present patient developed NBTE. Notably, her first clinical manifestation of NBTE was AMI.

Typically, the major clinical manifestations of NBTE result from systemic emboli rather than valvular dysfunction. Although the common sites of embolization include the spleen, kidney, and extremities, the most significant morbidity arises from emboli to the central nervous system and coronary arteries. The incidence of MI in Japanese patients with NBTE is 7.5%, as determined from autopsy samples. Although a recent report has described the cases of four patients who had MI in association with NBTE; all four patients had late-stage malignancies. AMI associated with NBTE in small-size lung cancer is rare. Due to the absence of collateral vessels, the effects of coronary occlusion may be more severe in patients who have embolic MI. The pre-

---

**Figure 2.** A. Echocardiography imaging on first admission revealed the presence of complex masses in the aortic valve (white arrow). Ao: aorta, LA: left atrium, LV: left ventricle. B. Echocardiography imaging on the third admission revealed pericardial effusion (black arrow).

**Figure 3.** A. A chest radiography demonstrated a solitary pulmonary nodule 10 mm in diameter (black arrow) on the first admission. B. A chest radiography on the third admission (four months later) demonstrated a new nodule (white arrow) with cardiomegaly and bilateral pleural effusions.
Figure 4. A. The chest CT scan on the first admission revealed a solitary pulmonary nodule (black arrow). B. The pulmonary nodule which was detected on the first admission was slightly swollen in the chest CT on the third admission (four months later) (black arrow). C, D. Chest CT scans on the third admission showed multiple new nodules with bilateral pleural effusions (black arrows). E. Contrast-enhanced chest CT scan on the third admission revealed pulmonary embolism (white arrows). Pericardial effusion was also detected.

sent patient also developed right toe necrosis, although vascular ultrasonography did not reveal impaired arterial blood flow from the right common iliac artery to the dorsalis pedis artery. Digital ischemia with gangrene has been observed as a paraneoplastic manifestation associated with various malignant tumors, especially adenocarcinomas (9-13). As digital necrosis associated with malignancy is typically fulminating and rapidly progressive within a few days, the cyanosis of the present patient’s right toe turned to blue toe in a few days (11). The precise mechanism of this phenomenon has not been completely clarified.

Mucin produced by adenocarcinomas may be associated with disseminated microangiopathy by reacting with leukocyte and platelet selectins, resulting in the production of platelet-rich microthrombi (14). In lung cancer, the relative risk of venous thrombosis is significantly higher with adenocarcinoma than in squamous cell carcinoma. In the present patient, the lung cancer was identified as adenocarcinoma, but mucin production in the TBTB specimens was moderate (Fig. 6C). However, due to the limited number of cells vis-
Figure 5. Magnetic resonance imaging of the brain showed an infarct in the left middle cerebral artery territory.

Figure 6. A. The transbronchial tumor biopsy specimens from a nodule in the right S3 lesion revealed moderately differentiated adenocarcinoma cells (black arrows) with migration into lymphatic vessels (Hematoxylin and Eosin staining; original magnification ×200). B. Adenocarcinoma cells expressed TTF-1 (black arrow). C. Adenocarcinoma cells produced mucin (black arrows) (periodic acid-Schiff [PAS] stain; original magnification ×200).

On first admission, the serum level of the tumor marker CA19-9 of our patient was high (202 U/mL) and was markedly elevated (1,531 U/mL) on third admission (four months later). The presence of elevated CA19-9 levels in patients with lung cancer has been described. Nearly all of these patients were diagnosed with adenocarcinoma and displayed a particularly high rate of mucinous adenocarcinoma. In addition, patients with CA19-9-producing carcinoma are at a greater risk of developing distant hematogenous metastasis, as CA19-9 serves as a ligand for E-selectin and facilitates hematogenous metastasis by mediating the adhesion of circulating cancer cells to vascular endothelium.

Although we could not adequately determine the levels of mucin production in the present patient’s TBTB samples, based on the elevated serum CA19-9 levels, it is possible that her lung cancer was mucinous adenocarcinoma. As elevated CA19-9 levels have been observed in benign diseases,
the presence of malignancy in our patient remains speculative. With respect to bronchopulmonary disease, high serum CA19-9 levels in bronchiectasis, pulmonary mycobacterium avium-intracellulare infection, and interstitial pneumonia have been reported. In a case similar to the present case, a solitary pulmonary mass shadow and high CA19-9 level due to nontuberculous mycobacterial disease was also reported. However, if both elevated serum CA19-9 levels and hypercoagulability are detected, the presence of malignancy, particularly mucinous adenocarcinoma, should be suspected. As mucinous adenocarcinoma generally progresses rapidly, a diagnosis should be aggressively sought even if the detected lesion is small and non-specific.

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

References