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Pulmonary tumor embolism from breast cancer diagnosed by selective aspiration cytology using a Swan-Ganz catheter

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ABSTRACT

We describe a case of pulmonary tumor embolism (PTE) from breast cancer diagnosed by selective aspiration cytology using a Swan-Ganz catheter. A 60-year-old woman was referred to Hamanomachi Hospital because of increased levels of tumor markers. The patient complained only of slight exertional dyspnea and a dry cough. Due to breast cancer, she had undergone a mastectomy followed by radiation and chemotherapy one year earlier. Positron emission tomography scanning with CT images revealed no evidence of malignancy. Repeated chest CT images showed emerging wedge-shaped nodules in the subpleural zones of the left lower lobe with diffuse ground-glass opacities in the bilateral lower lobes. The D-dimer level was negative. Pulmonary perfusion scintigraphy showed multiple small wedge-shaped defect areas on the peripheral sides of the bilateral lungs. Suspecting PTE, we performed selective aspiration cytology from the left pulmonary arteries. Cancer cells were detected from selected branches of left A8 and A9. Morphology and immunostaining led to a final diagnosis of PTE of recurrent breast cancer. Pulmonary embolism of cancer is a progressive, fatal condition with challenging diagnosis. Selective aspiration cytology with a Swan-Ganz catheter is a useful, less invasive option in patients with suspected PTE.

1. Introduction

Pulmonary tumor embolism (PTE) was first described in 1937 by Brill et al. as a disease in which tumor cells occlude small arteries with thrombi, rapidly leading to pulmonary hypertension and right heart failure [1]. PTE has a poor prognosis because it leads to respiratory and circulatory failure in a short period of time, and is difficult to diagnose before death due to its rarity and the lack of characteristic findings in chest radiographic imaging [2]. In the present report, we describe a case of PTE due to breast cancer. Pulmonary artery aspiration cytology was used to isolate cancer cells, leading to a final diagnosis of PTE from breast cancer, resulting in initiation of chemotherapy.

2. Case presentation

A 60-year-old woman underwent a partial right mastectomy plus sentinel node biopsy for right breast cancer one year earlier. The pathological stage was pT1N1M0, with ER(0%), PgR(0%), HER2(Score 0). She received 4 courses of epirubicin and cyclophosphamide, followed by 4 courses of docetaxel as postoperative chemotherapy and radiation therapy six months earlier. Body CT imaging four months earlier showed no evidence of recurrence or metastasis. Positron emission tomography (PET) scanning with CT images three months earlier revealed no evidence of malignancy. CEA and CA 15–3 were elevated at 358.8 ng/mL and 22.7 U/mL, respectively, one month earlier. A biopsy of the right mammary gland was negative, and a contrast-enhanced CT scan did not reveal the primary lesion of the malignancy.

The patient was then referred to the Department of Respiratory Medicine. At the outpatient clinic, she complained of exertional dyspnea (modified Medical Research Council grade 1) and a dry cough. She was never a smoker. The interview revealed no exposure to mold or birds. Her respiratory condition was almost normal, with a respiratory rate of

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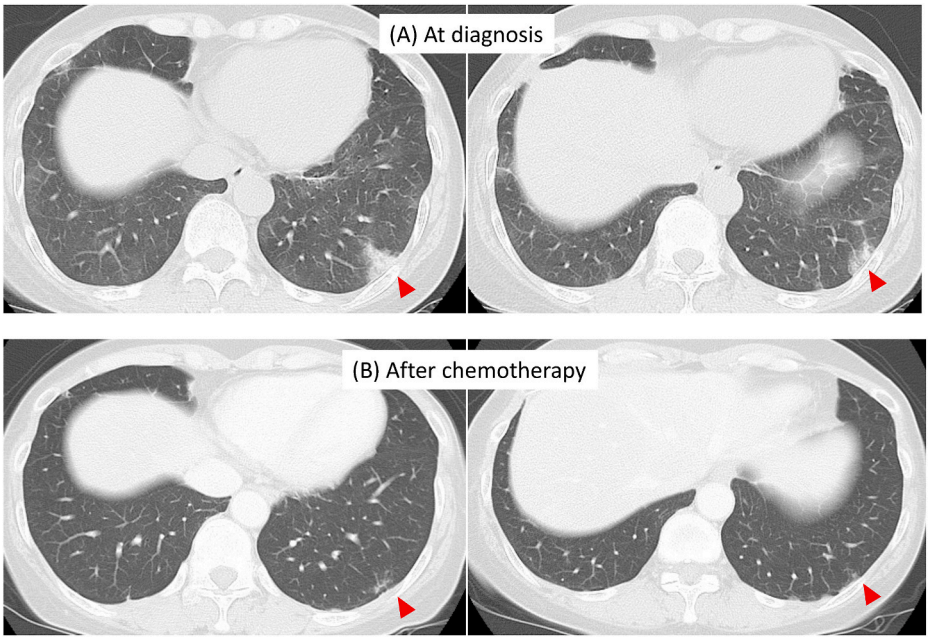

Fig. 1. Chest CT images of the patient.
(A) At diagnosis of pulmonary tumor embolism. Emerging wedge-shaped nodules in the subpleural zones of the left lower lobe (arrowheads) and diffuse ground-glass opacities in both lower lobes were detected. (B) Two and a half months after the diagnosis of PTE. The patient received three cycles of paclitaxel and bevacizumab. Chest CT images revealed shrinkage of multiple wedge-shaped nodules and disappearance of ground-glass opacities.

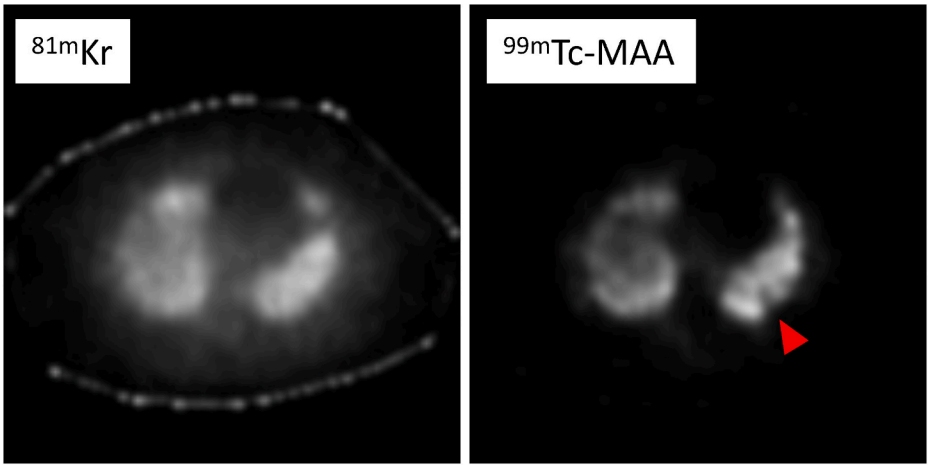

Fig. 2. Pulmonary perfusion-ventilation scintigraphy.
Pulmonary ventilation scintigraphy (^{81m}Kr) showed no abnormalities, whereas pulmonary perfusion scintigraphy (^{99m}Tc-MAA) showed multiple small wedge-shaped defect areas (arrowhead) on the peripheral sides of both lungs.

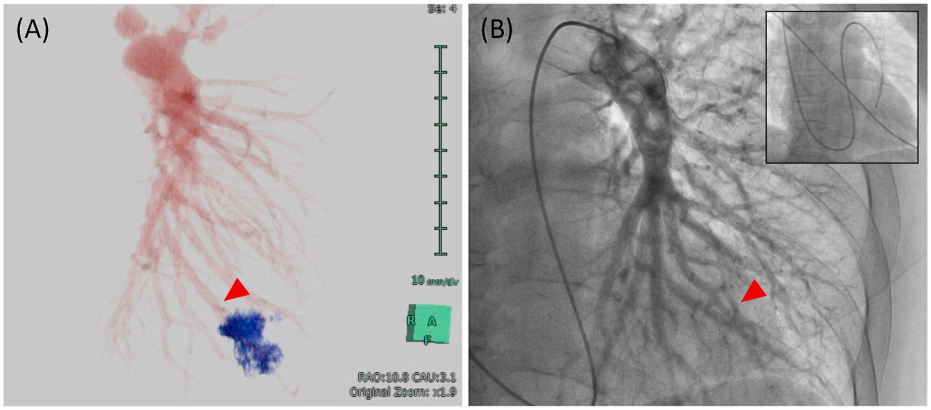

Fig. 3. Pulmonary artery aspiration cytology.
(A) 3D pulmonary artery imaging (red) reaching the nodules (blue) reconstructed from chest CT scanning. (B) The Swan-Gantz catheter was advanced and aspiration in the vicinity of each nodule was performed from selected branches of left A8 and A9. Arrowheads indicate the pulmonary artery reaching the nodules. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

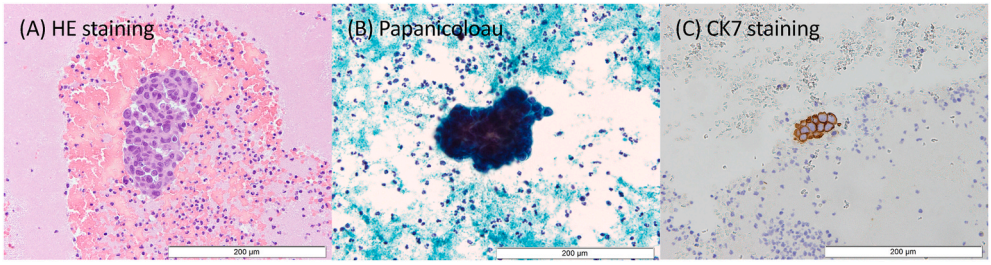

Fig. 4. Pathological examinations of cells aspirated from selected pulmonary arteries.
(A) Hematoxylin and eosin (HE) staining and (B) Papanicoloau staining showed cancer cells with a heavy accumulation having an increased N/C ratio, increased chromatin, and slightly pale cytoplasm. (C) Immunohistochemistry staining for CK7.

under 20/min and SpO_2 96% at rest. Bilateral fine crackles were detected at her back. The serum level of C-reactive protein and the D-dimer level were negative. Repeated chest CT images showed emerging wedge-shaped nodules in the subpleural zones of the left lower lobe and diffuse ground-glass opacities in the bilateral lower lobes (Fig. 1A). Suspecting a pulmonary infarction, pulmonary perfusion-ventilation scintigraphy was conducted. Pulmonary ventilation scintigraphy (^{81m}Kr) showed no abnormalities, while pulmonary perfusion scintigraphy (^{99m}Tc-MAA) showed multiple small wedge-shaped defect areas on the peripheral sides of both lungs (Fig. 2).

Since the findings were consistent with PTE, right heart catheterization and aspiration cytology of the pulmonary arteries were performed. Results of the right heart catheterization were as follows: right atrial pressure of 9 mmHg, mean pulmonary arterial pressure of 24 mmHg, cardiac index of 3.6 L/min/m^2, and pulmonary capillary wedge pressure of 15 mmHg. These results indicated no pulmonary hypertension nor circulatory insufficiency. We then performed selective aspiration cytology from the left pulmonary arteries, referring to 3D pulmonary artery imaging, reaching the nodules (Fig. 3A). We advanced the Swan-Gantz catheter and performed four aspirations in the vicinity of each nodule (Fig. 3B). Cancer cells were detected from selected branches of left A8 and A9, but not from the main branch of the pulmonary artery, nor in blood drawn from a peripheral vein.

Pathological examination showed cancer cells with heavy accumulation with an increased N/C ratio, increased chromatin, and slightly pale cytoplasm (Fig. 4A and B). Cell morphology was similar to that of cancer cells from the resection specimen of her breast cancer one year earlier. Immunohistochemistry staining revealed CK7(+) (Fig. 4C) and CK20(−). Taken together with the course of the disease and histological findings, PTE from breast cancer was diagnosed.

Ten days after the diagnosis of PTE, her SpO_2 deteriorated. Paclitaxel and bevacizumab were initiated as chemotherapy due to concern about progression of respiratory failure caused by PTE. After chemotherapy, her respiratory condition improved. Two and a half months after the diagnosis of PTE, chest CT imaging revealed shrinkage of multiple wedge-shaped nodules and disappearance of ground-glass opacities (Fig. 1B), indicating the efficacy of chemotherapy. The patient is continuing chemotherapy one year after the diagnosis of PTE.

3. Discussion

PTE lacks specific radiographic features, and it mimics pneumonia or interstitial lung diseases. CT findings include multifocal dilatation and beading of the peripheral subsegmental pulmonary arteries, peripheral wedge-shaped areas of opacities, and ground-glass opacities [3,4]. Peripheral areas of opacities resemble bacterial pneumonia or organizing pneumonia. Ground glass opacities resemble interstitial lung diseases. The tree-in-bud appearance is also seen on high-resolution CT of the lungs in cases of PTE [5]. It comprises small centrilobular nodules connected to multiple branching linear structures of small caliber that originate from a single stalk [6]. This is a familiar pattern in cases of endobronchial spread of infections such as *Mycobacterium tuberculosis*, non-tuberculous mycobacterium, and *Mycoplasma pneumoniae*. This tree-in-bud appearance can thus be misdiagnosed as a pulmonary infection. Therefore, the correct diagnosis of PTE was made in only 6% of patients antemortem, even in patients known to have malignancies [7]. In 2021, He et al. investigated the incidence of PTE and analyzed the discrepancy between antemortem clinical and postmortem diagnoses between 1990 and 2020 [8]. They showed 20 (3%) cases of PTE out of 658 autopsy cases with solid malignancies [8]. Out of these 20 cases, urothelial carcinoma (30%, 6/20) and invasive ductal carcinoma of the breast (4/20, 20%) were the most common primary malignancies [8]. Seven patients with shortness of breath died within 3–17 days after onset of symptoms. PTE was clinically suspected in 7 of 20 (35%) patients before death, but only 2 patients (10%) were diagnosed by imaging studies before death [8]. Despite advances in radiology, the discrepancy between the antemortem clinical and postmortem diagnoses has not improved significantly over the past 30 years [8].

There is a rare, fatal form of PTE, called pulmonary tumor thrombotic microangiopathy (PTTM), first proposed in 1990 by von Herbay et al. [9]. In cases of PTTM, widespread microscopic tumor emboli in the pulmonary arterioles cause luminal occlusion, and stimulate activation of localized coagulation and fibrocellular proliferation of endothelial cells, resulting in pulmonary hypertension [10]. In this case, we concluded that the patient had not developed PTTM, based on the lack of evidence of coagulopathy or pulmonary hypertension.

The diagnosis of PTE requires pathological proof. Transbronchial lung biopsy [11] and thoracoscopic lung biopsy [12] have been reported as methods for diagnosing PTE. However, in many cases, pulmonary hypertension is already advanced by the time of diagnosis, making lung biopsy difficult. In such cases, pulmonary artery aspiration cytology can be useful. So far, there are only a few case reports of PTE successfully being diagnosed using pulmonary artery aspiration cytology [2,13–15].

The prognosis for patients with PTE is generally poor. Banno et al. reviewed ante-mortem diagnosis and treatment of 19 cases with PTTM, in which half the cases died within a month, chemotherapy notwithstanding [11]. Chemotherapy was administered in only a few cases of PTE [16]. Therefore, early diagnosis is important, and selective aspiration cytology with a Swan-Ganz catheter is a useful option in patients with suspected PTE.

4. Patient consent for publication

Written, informed consent was obtained from the patient.

Declaration of competing interest

All authors of the manuscript declare that they have no conflicts of interest.

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