INTERNAL MEDICINE

□ CASE REPORT □

A Rare Case of Septic Pulmonary Embolism Caused by Infection-associated Catheter Removal in a Patient with Hodgkin's Lymphoma

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Abstract

As a reflection of the considerable increase in the number of cancer patients treated with chemotherapy, indications for the use of implanted venous catheters are rapidly growing. However, in some cases, implanted venous catheters induce unwelcome complications. We herein report a rare case of septic pulmonary embolism (SPE) caused by local infection-associated catheter removal during the administration of ABVd combination chemotherapy consisting of adriamycin, bleomycin, vinblastine and dacarbazine in a patient with Hodgkin's lymphoma of the mixed cellularity type. During the course of treatment with chemotherapy administered via implanted venous catheters, think it is crucial to monitor for the potential occurrence of SPE.

Key words: septic pulmonary embolism (SPE), implantable venous catheter, catheter removal, malignant lymphoma, HTLV-1

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Introduction

Septic pulmonary embolism (SPE) is a disorder characterized by the embolization of thrombi containing pathogens admixed with fibrin originating from an infected site into the venous circulation, leading to implantation in the vascular system of the lungs (1-3). The primary causes of SPE include drug abuse, right-sided infectious endocarditis and septic thrombophlebitis of the internal jugular vein, also known as Lemierre's syndrome (4, 5). Of note, recent reports have highlighted the use of indwelling central venous catheters (6) and an immune-compromised state associated with AIDS or organ transplantation as pathophysiological background factors for SPE. According to microbiologic studies, the most common pathogens for SPE are coagulase-negative Staphylococcal species, particularly *S. epidermidis*, followed by *S. haemolyticus* and *S. aureus* (7). In the present case, however, no pathogens were detected in the blood or removed catheter. Commonly accepted principles for the treatment of SPE include the prompt empiric administration of intravenous antibiotics (8), the detection and removal of any potentially infected devices and surgical intervention to remove the collection purulent fluid (9). We herein report a rare case of SPE caused by infection-associated catheter removal in a patient with Hodgkin's lymphoma.

Case Report

A 64-year-old man with Hodgkin's lymphoma (mixed-cellularity type, clinical stage IIA) and a human T-cell leukemia virus-1 carrier status was treated with ABVd chemotherapy (adriamycin: 25 mg/m^2 days 1,15; bleomycin: 9 mg/m^2 days 1,15; vinblastine: 6 mg/m^2 days 1,15; dacarbazine:

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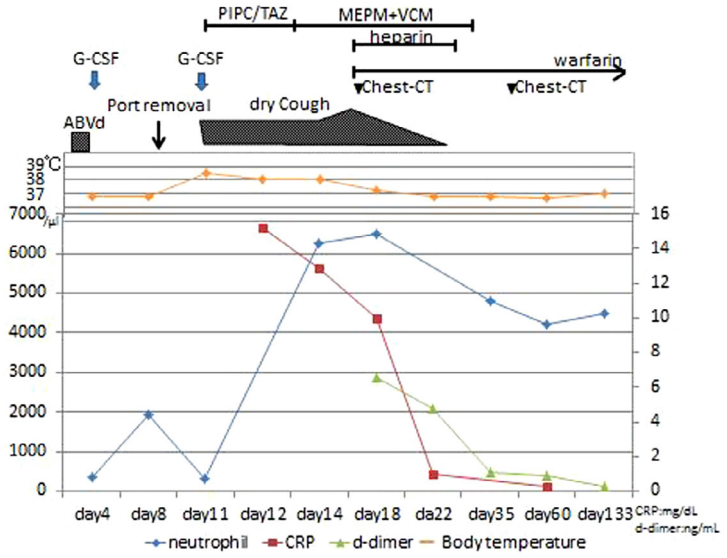

Figure 1. **The port catheter was removed at day 8 of 4th ABVd chemotherapy. Nevertheless, he represented continuous fever accompanied by dry cough and chest pain. The occurrence of SPE was diagnosed by chest-CT. During the course of therapies of antibiotics and anti-coagulants, his symptoms and values for serum CRP and D-dimer were markedly improved in parallel with the amelioration of pulmonary radiographic imaging.**

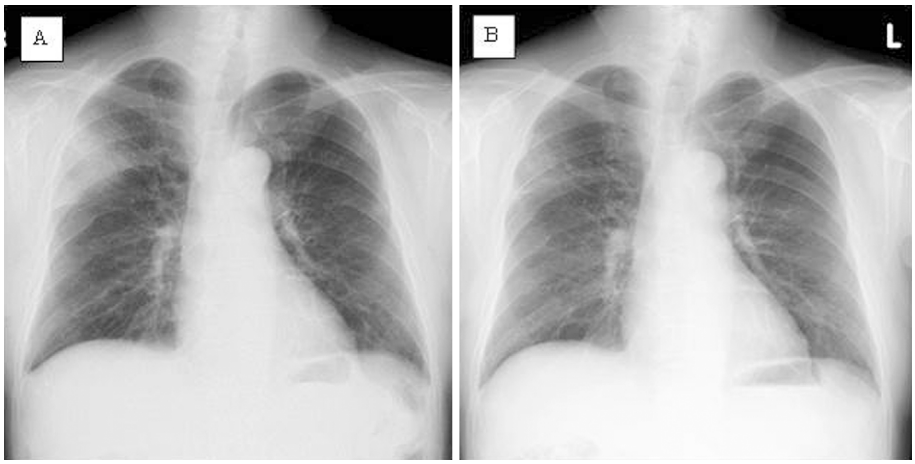

Figure 2. **A: Day 18 of 4th ABVd chemotherapy course (before the anti-coagulant therapy). Chest X-ray revealed a wedge-shaped consolidation in right upper lobe. B: Day 22. A consolidation in right upper lobe after anti-coagulation therapy was remarkably improved.**

250 mg/m^2 days 1,15). A subcutaneously implanted venous catheter was placed into the right subclavian vein. Local hematomas repeatedly appeared with an itchy sensation during chemotherapy. On interim positron emission tomography-computed tomography (PET-CT) scanning performed after the second course of ABVd chemotherapy, the patient achieved radiographic complete remission. On day 2 of the fourth course of treatment, the port of the catheter was considered to be a cause of red flaring of the skin, with burning and pressure pain. On day 8, the implanted venous catheter was exposed on the skin with odorless pus and removed (Fig. 1). The next day, the patient developed a fever with shaking chills and an occasional dry cough. His body temperature was 38.2℃, with a fast respiratory rate (24 breaths/min) and an SpO_2 of 95% on room air. A physical examination of the chest revealed fine crackles in the right upper lobe. Blood cultures for bacteria and fungi were negative. Although granulocyte colony-stimulating factor and piperacillin/tazobactam were administered, the patient's body temperature remained high. The antibiotic regimen (meropenem 3 g/day and vancomycin 2 g/day) was changed; however, his dry cough worsened on day 18, at which time a chest X-ray revealed consolidation in the right upper lobe (Fig. 2A, B). A chest CT scan demonstrated multiple bilateral areas of nodular opacity with cavitation, right pleural effusion and mediastinal lymphadenopathy (Fig. 3A, B).

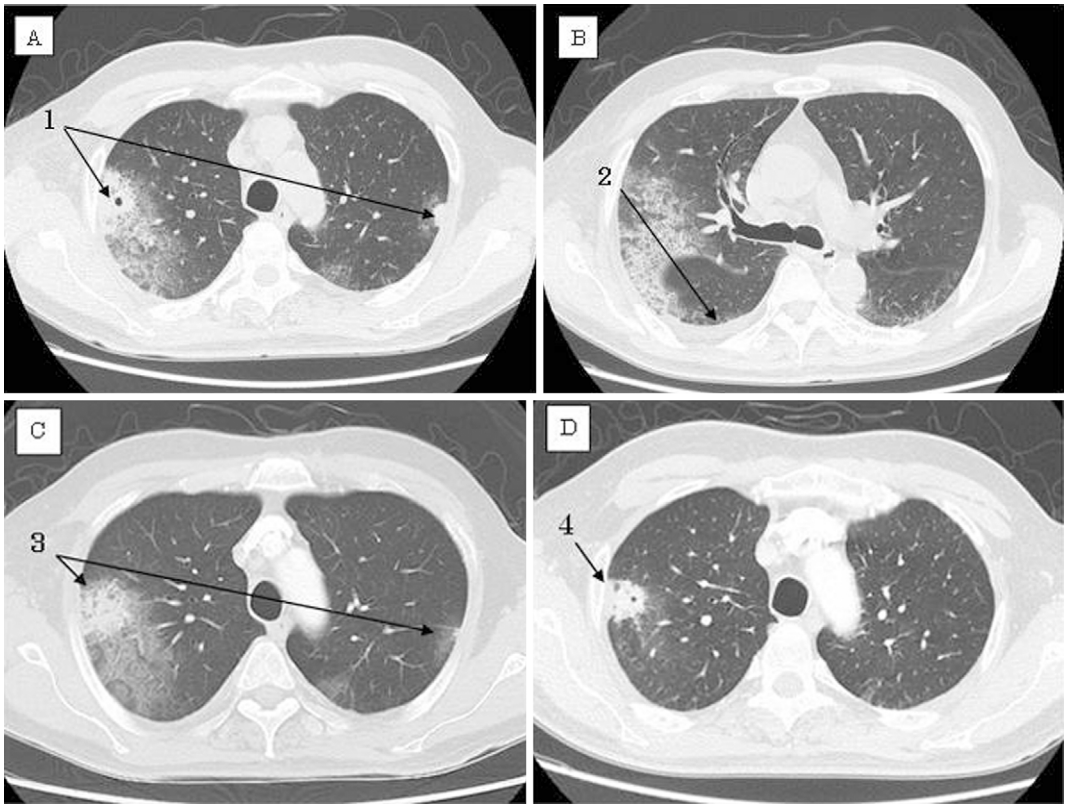

Figure 3. **A: Day 18 of 4th course of ABVd chemotherapy at the start of anti-coagulant therapy. (Arrow 1); There were subpleural opacity with a cavitation and bilateral nodular opacities. B: Day18 (Arrow 2); Right pleural effusion was detected. C: Day22 (Arrow 3); Bilateral opacities were improved by anti-coagulation therapy. D: Day38 (Arrow 4); The opacity with cavitation was remarkably improved, while feeding vessels sign still remained.**

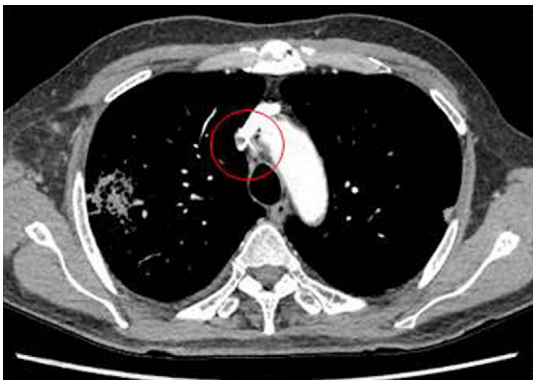

Figure 4. **At day18, enhanced chest CT findings revealed a defect area where implanted venous catheter was inserted (indicated by a circle).**

Transthoracic echocardiography was performed to exclude the presence of pulmonary embolism and infectious endocarditis. Echocardiography showed normal findings and the level of KL-6 was within the normal ranges. Tests for QuantiFERON, cytomegalovirus antigenemia, β-D-glucan and Aspergillus galactomannan antigens were all negative. Notably, contrast-enhanced CT revealed a defect site lesion extending from the origin of the right subclavian vein to the right brachiocephalic vein, where the implanted venous catheter had been inserted (Fig. 4). We diagnosed the patient with septic pulmonary embolism. Although the blood cultures showed no growth of bacteria or fungi, heparin and warfarin in addition to antibacterial drugs were administered, resulting in relatively fair clinical course. The administration of heparin was ceased on day 23, and the antibacterial drugs were discontinued on day 26. Consequently, on day 31, the defect areas on enhanced CT disappeared, and the area of nodular opacity, cavitation and pleural effusion markedly improved (Fig. 3A-D). Furthermore, the levels of serum lactate dehydrogenase (LDH), C-reactive protein (CRP) and D-dimer drastically improved in parallel with the amelioration of the pulmonary radiographic imaging findings.

Discussion

Based on his symptoms and findings, including acute fever with neutropenia (WBC: 1,200/μL, neutrophil: 27%), upper respiratory symptoms, a high D-dimer level (6.6 μg/mL) and chest CT abnormalities, the current patient was diagnosed with septic pulmonary embolism (SPE). Nevertheless, although his catheter was removed in order to prevent further infectious complications, he consequently developed SPE. Only two similar cases have been reported to date (Table 1). To the best of our knowledge, this is the third case of SPE caused by infection-associated catheter removal reported in the literature (10, 11).

Table 1. Systematic Literature Review of Septic Pulmonary Embolism (SPE) Caused by Infection-associated Catheter Removal

Reference	Patient	Backgrounds	Catheter-related events	Clinical pictures
10	1 y.o female	Nutritional support with central venous catheter for intractable diarrhea	Her catheter was not removed because of the lack of other available insertion sites.	She was died of severe hypoxia due to SPE. Her culture of the catheter tip and blood grew *Klebsiella, Staphylococcus epidermidis* and *α-streptococcus*.
11	66 y.o male	Chemotherapy for multiple metastatic adenocarcinoma lung cancer	Because his catheter caused septic thrombophlebitis, it was removed.	He was rescued through intensive care. His blood culture grew coagulase-negative *staphylococcal* bacteria.

To date, only two cases have been reported.

Table 2. Summary of Major Risk Factors for Development of Central Catheter-associated Thrombosis

Risk Factors for Development of Central Catheter-associated Thrombosis
Catheter insertion site[19]
Long-term chemotherapy[20]
Sepsis[21]
Catheter exist-site infection[21]
Historogical type of cancer[22]

This may be useful for evaluating complications of pulmonary thromboembolism.

In patient with a diagnosis of catheter infection, removing the catheter within 72 hours is recommended (12). For example, Cook et al. (13) reported the management of SPE in 14 patients, in whom the catheter was removed by a surgeon. Importantly, in the febrile hematologic malignancy patients with central venous catheter, catheter-related bloodstream infection is more frequent (20.3%) than that observed in non-febrile patients (14). Contrary to our expectations, the current patient developed a fever and dry cough following removal of the catheter. Furthermore, an enhanced CT scan demonstrated a remaining thrombus surrounding the area of insertion (Fig. 4). Therefore, in this case, it is reasonable to speculate that the SPE was caused by the catheter removal procedure.

The current patient exhibited a fever, chest discomfort and dry cough starting on day 9 of the fourth cycle of ABVd combination chemotherapy. Because there were no signs of inflammation during four courses of chemotherapy, the catheter continued to be used. When the main body of the catheter appeared in the patient's skin, the surgical department advised us to observe the patient, partly because he was afebrile, but also because the terminal portion of the catheter remained intact. Therefore, at that time point, we considered the patient's clinical presentation to be a form of foreign-body reaction. As shown in Table 2, taking the patient's higher risk for SPE into account, the expeditious removal of the catheter should have been considered.

Although the precise frequency of SPE is unclear in the literature, representative symptoms of SPE include fever (36%), pleuritic chest pain (29%), sore throat (21%), coughing (14%) and hemoptysis (7%) (14). Moreover, the D-dimer level is a good indicator of the progression of pulmonary embolism (15). The sensitivity and specificity of the D-dimer level for diagnosing pulmonary embolism are 95% and 44%, respectively (15). Although the serum level of D-dimer was not evaluated before SPE in this case, it was considerably high at the onset of symptoms and improved during the course of therapy. In this context, the circulating D-dimer level was indicative of the clinical course of SPE in the present case (Fig. 1).

Although the chest X-ray findings of SPE are nonspecific (14), CT findings, such as nodular opacity, are helpful for making the differential diagnosis (14). Other pivotal findings of chest CT include multiple peripheral nodules with cavitation (85%), pleural effusion (69%) and hilar or mediastinal lymphadenopathy (31%) (14). The presence of distinct vessels reaching the pulmonary nodule has been documented to be a sign of feeding vessels (Fig. 3D). Furthermore, cavitation within nodules is commonly observed in patients with Gram-positive septic emboli (9). In the current case, CT findings, including bilateral nodular opacity with cavitation, right pleural effusion and mediastinal lymphadenopathy, were consistent with those observed in cases of SPE (Fig. 3A, B).

Anticoagulation therapy is the cornerstone of treatment for SPE (16). The chief purpose of therapy for SPE is to diminish the severity and duration of symptoms, minimize the incidence of recurrent thrombosis and decrease the risk of newly developed SPE. However, treatment does not necessarily facilitate the dissolution of a thrombus. Therefore, our patient completed an 18-day course of intravenous antibiot-

ics and a five-day course of continuous heparin infusion, followed by four months of oral anticoagulation (Fig. 1).

Although the therapeutic advantages of antithrombotic prophylaxis for cancer carriers with thrombotic complications equipped with a central venous catheter have long been controversial, the routine use of antithrombotic agents for prophylaxis is not recommended (17). However, there is a wide variety of risk factors in patients with central venous catheter-related thrombosis. The incidence of clinically overt pulmonary embolism in patients with central venous catheter-related venous thrombosis ranges from 15% to 25% (18). In cancer patients with implanted central venous catheters, five representative risk factors for thrombogenesis have been highlighted (Table 2): (a) the catheter insertion site (left>right, femoral> subclavian> jugular vein, catheter tip location in the superior vena cava> right atrium) (19), (b) long-term chemotherapy (20), (c) sepsis (21), (d) catheter exist site infection (21) and (e) the histological type of cancer (22). It has been reported that the risk of venous thrombosis in cancer patients is increased approximately seven-fold compared with that observed in healthy individuals (22). Noticeably, among a variety of cancer carriers, patients with hematological malignancies demonstrate the highest risk for venous thrombosis, after adjustment for age and sex (adjusted OR, 28.0; 95% Cl, 4.0-199.7) (22). According to multivariate analyses, catheter site infection and resultant sepsis has been shown to increase the risk of central venous catheter-related thrombosis in patients with adult acute myeloid leukemia (21). The present patient exhibited all five risk factors described above, suggesting an extremely high risk for thrombotic complications. According to previous reports, tips for preventing SPE include the following: (I) the existence of thrombi should be assessed using ultrasonography (21) or enhanced CT before removing the catheter; (II) prior to the removing the catheter, administering low-dose heparin (100 U/kg per day) for one week may decrease the incidence of SPE if thrombosis is suspected on ultrasonography (23).

Although blood culture was negative in this case, we diagnosed the patient with SPE closely related to the implantable venous catheter. Implantable venous catheters are useful devices. However, in some cases, they carry a significant risk of blood coagulation. Similar to that observed in the present patient, at the moment of catheter removal, thrombi surrounding an infectious catheter may become dislodged. Therefore, when patients with catheter-related infection exhibit respiratory symptoms, it is crucial to carefully exclude the possibility of SPE. As shown in Table 2, evaluating major risk factors for thrombogenesis is useful for preventing the occurrence of SPE.

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

Informed consent

Written informed consent was obtained from the patient for publication of this case report.

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