Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.8558-21
Intern Med 61: 3611-3615, 2022
http://internmed.jp

【 CASE REPORT 】

Successful Rescue of Life-threatening Hemoptysis Caused by Pulmonary Tuberculosis Bridging with Extracorporeal Membrane Oxygenation

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Abstract:

Massive hemoptysis is a fatal complication associated with pulmonary tuberculosis (TB). It can lead to severe respiratory failure. Extracorporeal membrane oxygenation (ECMO) is a life-saving technology that is rarely indicated for bleeding disorders. We herein report a 26-year-old man who presented with severe respiratory failure caused by massive hemoptysis with pulmonary TB. Transcatheter artery embolization was successfully performed with venovenous ECMO support. The hemostatic procedure allowed concomitant anticoagulant use, and neither bleeding nor thrombotic complications occurred throughout the clinical course. Administering the appropriate hemostatic procedure with subsequent management, including anticoagulant therapy, supported ECMO application in a case of bleeding.

Key words: extracorporeal membrane oxygenation, tuberculosis, massive hemoptysis, transcatheter artery embolization, anticoagulant therapy

(Intern Med 61: 3611-3615, 2022)
(DOI: 10.2169/internalmedicine.8558-21)

Introduction

Extracorporeal membrane oxygenation (ECMO) is a type of prolonged mechanical cardiopulmonary support indicated for acute severe cardiac or pulmonary failure that is refractory to conventional management (1).

Since uncontrollable bleeding is a relative contraindication for ECMO, hemorrhagic disorders should be carefully considered, and a multidisciplinary approach is warranted. Previous reports have documented the indication of ECMO for bleeding disorders, such as severe trauma (2), diffuse alveolar hemorrhaging (3), and massive hemoptysis (4). In those cases, the concomitant use of anticoagulants was controversial and varied among reports. Therefore, the treatment strategy for ECMO should be considered by experts.

We herein report a case of severe respiratory failure due to massive hemoptysis caused by pulmonary tuberculosis (TB). The patient successfully underwent transcatheter artery embolization (TAE) with venovenous (VV) ECMO for respiratory support, resulting in withdrawal after five days. Adequate monitoring and hemostatic treatment allowed for the safe management of bleeding disorders with ECMO.

Case Report

A 26-year-old Japanese man complaining of bloody sputum was admitted to the previous hospital. The patient was diagnosed with pulmonary TB based on the presence of multiple nodules and a granular shadow on chest computed tomography (Fig. 1A, B), as well as a positive acid-fast bacilli test in the sputum sample. Upon initiating anti-TB therapy, the patient developed hemoptysis (100 mL). Despite conservative treatment, the frequency and amount of hemop-

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Received: August 23, 2021; Accepted: February 20, 2022; Advance Publication by J-STAGE: April 9, 2022
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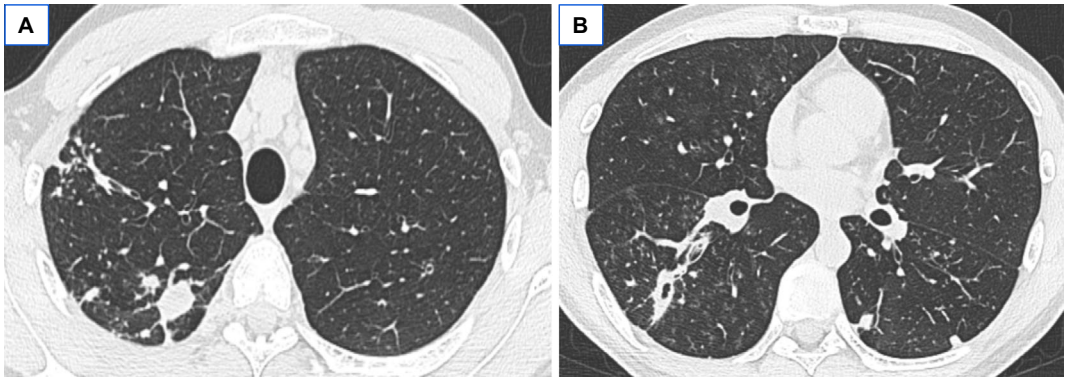

Figure 1. **Computed tomography revealed bilateral multiple granular and nodular shadows, tree-in-bud appearance, and some cavities, suggesting pulmonary tuberculosis (A, B).**

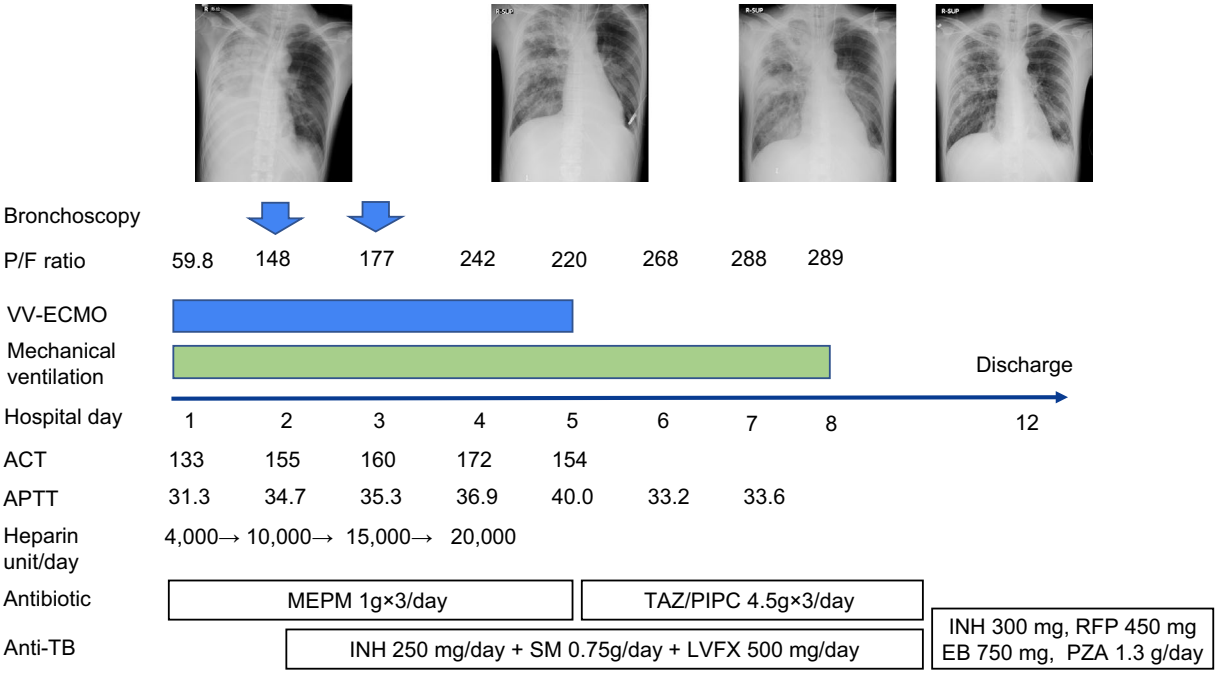

Figure 2. **The progress diagram shows the patient's clinical course during the treatment timeline. ACT: activated coagulation time, aPTT: activated partial thromboplastin time, EB: ethambutol, ECMO: extracorporeal membrane oxygenation, INH: isoniazid, LVFX: levofloxacin, MEPM: meropenem, PZA: pyrazinamide, RFP: rifampicin, SM: streptomycin, TAZ/PIPC: tazobactam/piperacillin, P/F ratio: pressure of oxygen and fraction of inspired oxygen ratio, Anti-TB: anti-tuberculosis treatment**

tysis increased, and his oxygenation worsened.

Three days after his admission, he was intubated, and mechanical ventilation was initiated. However, his oxygenation deteriorated rapidly, and mechanical ventilation was insufficient. Five days after admission, the patient was transferred to our hospital for the induction of ECMO and hemostatic intervention [hospital day 1 (HD#1); clinical course shown in Fig. 2]. Upon arrival, an arterial blood gas analysis revealed severe hypoxia and respiratory acidosis [pH 7.23; partial pressure of carbon dioxide ($PaCO_2$): 66.3 mmHg; ratio of partial pressure of arterial oxygen to fractional inspired oxygen (P/F ratio): 59.8 mmHg at a positive end-expiratory pressure (PEEP) of 15 cm H_2O]. He was tachycardic at 123 beats/min and relatively hypotensive at 82/38 mmHg. VV-ECMO was implemented for respiratory support, and cannulation was performed via the right jugular (PCKC-A-18, 18 French; Mera, Tokyo, Japan) and right femoral veins (PCKC-V-24, 24 French; Mera). The CAPIOX® EPS® with a non-heparin based biopassive polymer-coated (Xcoating™) membrane was applied for ECMO (Terumo, Tokyo, Japan). Intravenous albumin and noradrenaline were administered to sustain his blood pressure. Persistent pulse oximetry values >90% were obtained after establishing the VV-ECMO, following which TAE was immediately conducted via the right femoral artery approach (4-French-long sheath).

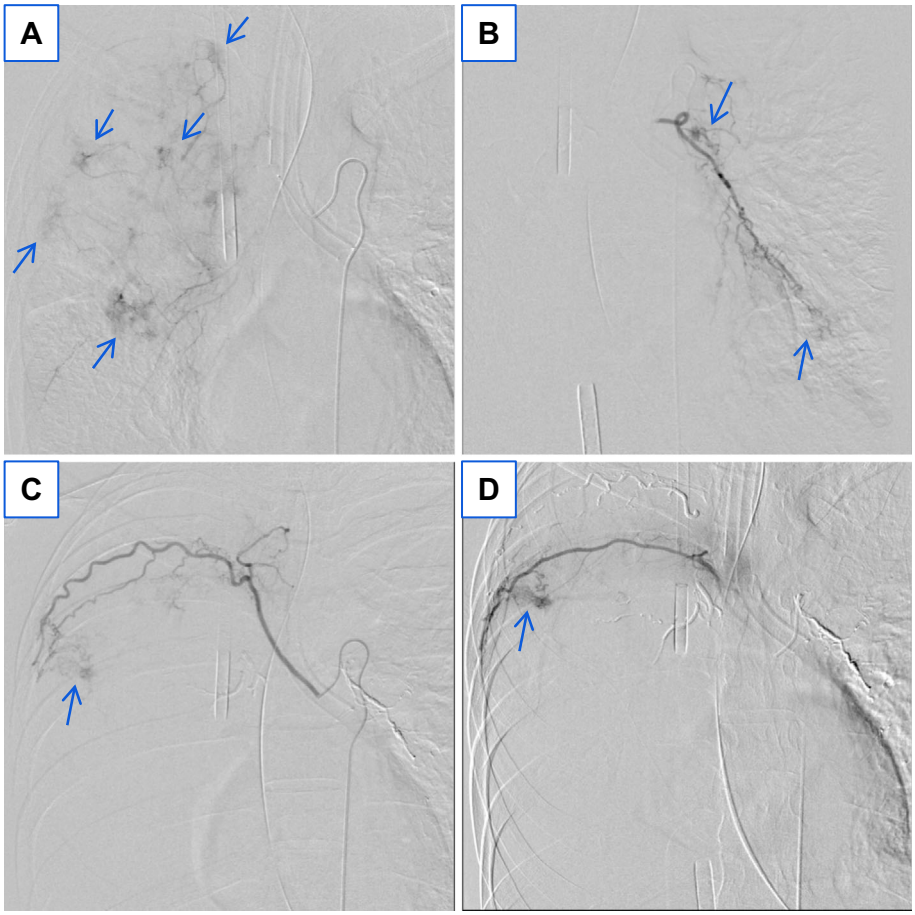

Figure 3. **Imaging of transcatheter arterial embolization; selective angiography of the right bronchial artery (A), left bronchial artery (B), and right intercostal artery (C, D) are presented. Transcatheter embolization was successfully performed at each bleeding point (blue arrows).**

Selective angiography revealed bronchopulmonary shunts, pseudoaneurysms (Fig. 3A), abnormal vessel formation in the left bronchial artery (Fig. 3B), and abnormal vessels in the right fifth to seventh intercostal arteries (Fig. 3C, D). The involved lesions were successfully embolized with n-butyl-2-cyanoacrylate.

After completing TAE, the hemodynamic state stabilized, and he was admitted to the intensive-care unit (ICU). Upon admission to the ICU, his oxygenation and hypercapnia improved (P/F ratio: 176 mmHg; $PaCO_2$: 41.1 mmHg). Three hours after ICU admission, on confirming the absence of rebleeding from the intubated tube, anticoagulation was initiated with intravenous unfractionated heparin (4,000 units per day) to maintain an activated coagulation time (ACT) of 150-180 s.

On HD#2, the patient was hemodynamically stable, and anti-TB therapy was initiated. However, his respiratory condition was dependent on ECMO, and the tidal volume was insufficient at 150 to 200 mL with a PEEP of 5 cm H_2O and pressure support of 10 cm H_2O. This was due to atelectasis of the right lung caused by diffuse endobronchial blood clots and ventilation-associated pneumonia. Antibiotic therapy with meropenem (3 g per day) was initiated.

On HD#2 and 3, bronchoscopy revealed a clot-filled right main bronchus and lower lobe bronchus (Fig. 4A). Upon removing the clots via suction or with biopsy forceps (Fig. 4B, C), the aeration of the right lung improved, and the tidal volume increased from 150 to 400 mL. Following airway clearance, the patient's oxygenation remarkably improved, and he was successfully weaned from ECMO on HD#5 and extubated on HD#8.

He was discharged from our hospital on HD#12 and transferred back to the previous hospital to continue the anti-TB therapy. Hemoptysis did not occur during the subsequent clinical course.

Discussion

This study reported the successful treatment of severe respiratory failure with massive hemoptysis caused by pulmonary TB. To our knowledge, this is the first report of successful TAE using VV-ECMO for respiratory support in a pulmonary TB patient. Hemostatic strategies and proper anticoagulation management were critical to the successful clinical course. Since the case was complicated by severe respiratory failure with uncontrollable hemoptysis, TAE was required. ECMO extended the time available to prepare the intervention and identify the bleeding points. Successful

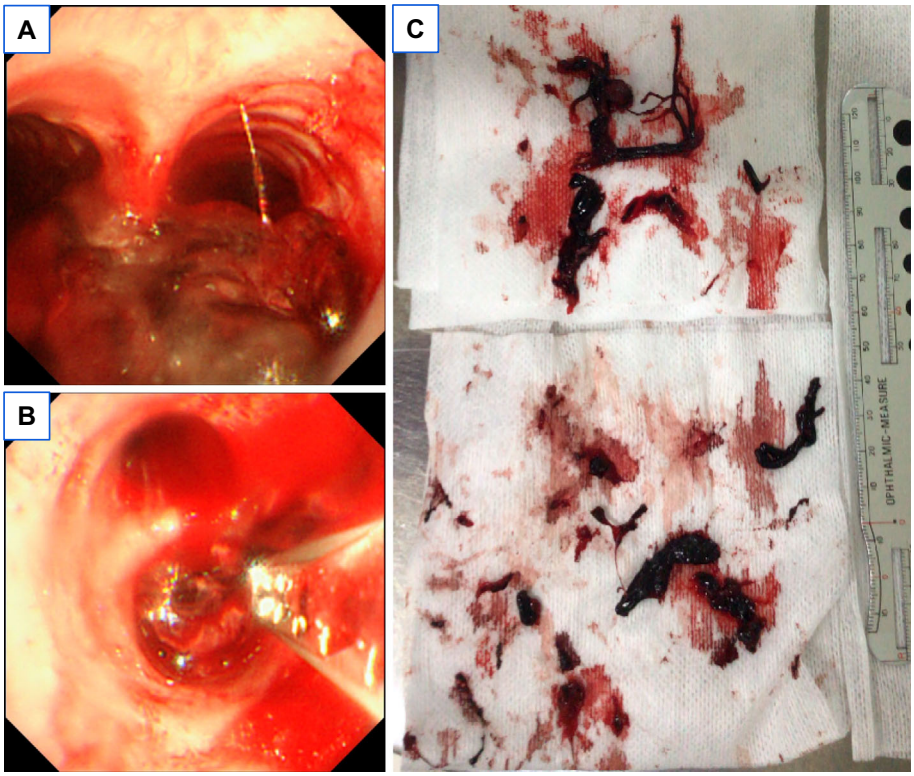

Figure 4. **Bronchofiberscopy was performed on HD#2 and #3, revealing many endobronchial blood clots (A, B). These were removed with biopsy forceps as much as possible (C).**

TAE and subsequent airway and respiratory management enabled ECMO weaning after five days and extubation after eight days. Anticoagulant therapy using unfractionated heparin was initiated immediately after TAE. No recurrent bleeding or other hemorrhagic complications was observed.

Massive hemoptysis is a fatal complication associated with pulmonary TB. Bleeding can occur in both active and previous TB patients. Bronchial arterial vessel ulceration in the active phase and bronchiectasis and shunt vessel formation due to a previous infection generate massive bleeding (5). Life-threatening hemoptysis requires immediate hemostatic intervention. In cases not controlled by conservative treatment, invasive procedures, such as arterial embolization or surgical resection, should be considered. TAE is the gold-standard treatment for massive hemoptysis, demonstrating a higher success rate and better safety profile than surgical treatment (6). The immediate clinical success rate of TAE reportedly ranges from 70% to 99% (6). However, the success rate was reportedly lower in TB patients than in other cause of hemoptysis due to complicated collateral formation and difficulty identifying the involved vessel (7).

Since bleeding and thrombosis are common and troublesome complications of ECMO (1), anticoagulation therapy should be carefully designed to address these factors. Conventionally, ECMO has been considered a relative contraindication for severe bleeding disorders due to the risk of further bleeding. However, accumulated experimental managements and the advent of novel devices are facilitating the use of ECMO without anticoagulation in such conditions. Recently, anti-thrombogenic surface coatings for ECMO have been widely applied in clinical practice. Bio-active coatings (e.g. heparin) exert anticoagulant effects by specifically inhibiting factors involved in coagulation and hemostasis *in vivo* (8). Bio-passive coatings (e.g. albumin, polyethylene glycol, phosphorylcholine) work by inhibiting protein adsorption, thereby minimizing the interaction between blood and foreign membranes (8). While the use of these agents does not guarantee the safety of not administering concomitant anticoagulation in clinical practice, it may be advantageous in the indication of ECMO for bleeding disorders. Indeed, in the present case using ECMO circuits with polymer-coated membranes, no thrombotic problems occurred in the early phase of introduction without anticoagulants. However, the optimal anticoagulation therapy for bleeding disorders has not been reported, and the validity of the concomitant use of anticoagulants remains controversial. Thus, conducting anticoagulation management along with ECMO requires careful monitoring and a comprehensive understanding of drug interactions.

Previous case series have reported the safety and efficacy of short-term ECMO management without systemic anticoagulant therapy. Arlt et al. reported that in a series of 10 severe trauma patients with bleeding shock, no thrombotic complications occurred during heparin-free ECMO management (9). Fina et al. also reported that short-term ECMO without systemic anticoagulation was safely managed in six patients with active bleeding or a high hemorrhagic risk (10). In contrast, in a systematic review on trauma pa-

tients undergoing ECMO, 60% of the patients received anticoagulant therapy during ECMO management (11). There have also been several reports of hemoptysis cases managed by ECMO with anticoagulation after successful arterial embolization (12). When managing ECMO for bleeding disorders, there is no consistent target range of ACT or activated partial thromboplastin time. In past reports, anticoagulation therapy was generally given with an ACT of 160-180 s as an empirical target range (13-15). In the present case, heparin was administered to achieve an ACT >150, which was less than the recommended range, for the first 12 h after embolization. Upon confirming airway hemostasis via bronchoscopy, the heparin dose was safely increased to the therapeutic range.

In conclusion, the indication of ECMO for bleeding conditions requiring hemostatic procedures needs careful consideration. However, in situations where respiratory failure is no longer tolerable, ECMO should be considered in line with hemostatic procedures. In such cases, the application of an anticoagulant-coated membrane might allow for management without anticoagulants for a short term with careful monitoring. This study showed that definite hemostasis allowed concomitant anticoagulation and ECMO in patients with bleeding disorders.

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

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