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Multidisciplinary Rehabilitation for Severe Respiratory Failure Due to Dasatinib-Induced Pulmonary Toxicity: A Case Report

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Patient: Female, 60-year-old
Final Diagnosis: Chronic myeloid leukemia
Symptoms: Respiratory failure
Clinical Procedure: —
Specialty: Rehabilitation

Objective: Unusual clinical course

Background: Tyrosine kinase inhibitors (TKIs) are effective for chronic myeloid leukemia (CML), but they may cause pulmonary toxicity, including pleural effusion. In severe cases, respiratory failure requiring mechanical ventilation can occur, and weaning from the ventilator may be difficult. Although multidisciplinary rehabilitation strategy may be necessary for favorable outcomes and physical function in such situations, it has not been well described.

Case Report: A 73-year-old woman with CML was responding well to TKI treatment, but prolonged pleural effusion as an adverse effect led to home oxygen therapy 9 years after diagnosis. She was admitted with acute type II respiratory failure (pH: 7.076, PaO₂: 181.1 mmHg, and PaCO₂: 213.3 mmHg) triggered by pneumonia and required intubation and mechanical ventilation. Rehabilitation began the day after admission and advanced progressively. Extubation was considered impossible due to persistent hypercapnia, so a tracheostomy was performed on day 11. A structured multidisciplinary rehabilitation program was continued throughout the acute and recovery phases. Her physical function gradually improved, although without complete ventilator weaning. She regained independent ambulation and achieved a Barthel index score of 100. Daytime ventilator support was discontinued, while nocturnal ventilation was maintained. After caregiver training and coordinated discharge planning, she was discharged home on hospital day 105 with nighttime mechanical ventilation.


Conclusions: Early and coordinated multidisciplinary rehabilitation can facilitate functional independence and home discharge, even when complete ventilator weaning is impossible, in patients with cancer treatment-related pulmonary toxicity. Collaboration across specialties may be essential in managing complex cases of prolonged respiratory failure.

Keywords: Rehabilitation • Leukemia • Tyrosine Kinase Inhibitors
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Introduction

Chronic myeloid leukemia (CML) makes up approximately 15% of all leukemias in adults [1]. Although many patients die following acute transformation, tyrosine kinase inhibitors (TKIs) such as dasatinib markedly improve survival rate [1]. Nonetheless, dasatinib has several adverse effects, including pulmonary toxicity leading to pleural effusion and pleurisy [2-4]. These conditions may lead to restrictive ventilatory impairment [5], and in severe cases, type 2 respiratory failure [6].

Cases of hypercapnic respiratory failure often require mechanical ventilation, and prolonged ventilator dependence may occur, particularly in those with underlying chronic respiratory dysfunction [7]. Because patients on mechanical ventilation typically require bed rest, initiating early rehabilitation is crucial to prevent functional decline [8]. Early rehabilitation during mechanical ventilation may help address deconditioning and treatment-related functional decline in patients with cancer and is safe when conducted under the careful supervision of a multidisciplinary team [9].

Recently, multidisciplinary care, which integrates the expertise of specialists from diverse fields to manage patients with complex needs, has become increasingly important [9]. For patients requiring long-term mechanical ventilation and concurrent rehabilitation, such collaboration is essential to determine individualized treatment plans, design appropriate rehabilitation programs, and provide comprehensive discharge support [10,11]. However, such multidisciplinary rehabilitation approaches in patients with cancer treatment-related pulmonary toxicity requiring long-term ventilatory support have been poorly described. For patients with cancer, a good performance status is necessary to continue chemotherapy; therefore, it is essential to maintain a favorable condition for discharge home and for post-discharge activity levels.

Here, we report a case of dasatinib-induced pulmonary toxicity complicated by chronic respiratory failure, in which multidisciplinary rehabilitation was associated with recovery of functional independence and discharge home despite incomplete ventilator weaning.

Case Report

Medical History and Initial Treatment Course

A 73-year-old woman was diagnosed with CML in 2012, and dasatinib was prescribed. She achieved complete hematologic response and maintained a major molecular response. In 2018, a chest X-ray revealed pleural effusion, with increased pleural effusion observed in December 2019. Consequently,



Figure 1. Chest X-ray at admission.

supportive therapy with diuretics and steroids was initiated. From the end of 2020, the pleural effusion increased further, leading to the discontinued use of dasatinib and the initiation of nilotinib. In August 2021, she developed chronic pleurisy and associated dyspnea, requiring hospitalization for thoracic drainage. Only a small amount of fluid was drained, and the fluid was exudative, with suspected drug-induced pleurisy. She was discharged on home oxygen therapy and continued outpatient treatment.

In March of 2024, she was admitted to the hospital with decreased percutaneous oxygen saturation (SpO_2), and decreased level of consciousness. Vital signs at the time of admission were as follows: level of consciousness assessed by Glasgow Coma Scale was E1V1M4; blood pressure was 111/54 mmHg; heart rate was 103 beats per minute (bpm); respiratory rate was 27 breaths per minute; SpO_2 was 100% (2 L/min by nose canula); and body temperature was 36.5°C. Approximately 115 minutes after arrival at the hospital, the patient's consciousness level declined to E1V1M1, so intubation was performed and mechanical ventilation was started. X-ray imaging showed massive pleural effusion and suspected pneumonia on both sides (Figure 1). Arterial blood gas analysis showed pH was 7.076; partial pressure of arterial oxygen (PaO_2) was 213.3 mmHg; and partial pressure of arterial carbon dioxide ($PaCO_2$) was 181.1 mmHg, indicating significant carbon dioxide (CO_2) retention and acidosis. C-reactive protein was slightly elevated at 0.31 mg/dL. Therefore, she was diagnosed with

Table 1. Multidisciplinary distribution of roles.

Occupation	Responsibilities and implementation
Emergency physician	<ul style="list-style-type: none"> • Intubation and mechanical ventilation setting • Treatment of pneumonia • Spontaneous breathing trial • Informed consent for tracheotomy • Decision-making in case of emergency (consent for do not attempt resuscitation: no reintubation, no extracorporeal membrane oxygenation, no cardiopulmonary resuscitation)
Hematologist	<ul style="list-style-type: none"> • Overall treatment leader • Management of various professions, including rehabilitation prescriptions • Consideration of outcomes and treatment plans • Support for patient decision-making • Leadership of shared decision-making • Various arrangements for discharge home • Emergency response guidance for family and home healthcare providers
Otorhinolaryngology	<ul style="list-style-type: none"> • Advising on tracheostomy management and swallowing
Gastroenterology	<ul style="list-style-type: none"> • Advice on decision-making regarding gastrostomy tube placement
Medical Safety Promotion Office	<ul style="list-style-type: none"> • Advice on rehabilitation in the rehabilitation room on a mechanical ventilator (eg, feasibility, methods of transfer)
Nurse	<ul style="list-style-type: none"> • Suctioning of sputum during hospitalization including timing of rehabilitation and medication management • Daily care
Physical therapist	<ul style="list-style-type: none"> • Provision of rehabilitation aimed at expanding ADLs • Evaluation of respiratory conditions during exertion • Advice on ADLs on the ward and activities after discharge • Determination of the dose of oxygen during exertion Consultation with various professionals to enhance ADLs
Speech therapist	<ul style="list-style-type: none"> • Swallowing assessment and intervention • Leading communication methods after tracheotomy
Respiratory support team	<ul style="list-style-type: none"> • Adjustment of mechanical ventilator settings • Leadership of spontaneous breathing trial • Advice on rehabilitation program and risk management during mechanical ventilator support
Medical Engineer	<ul style="list-style-type: none"> • Mechanical ventilator maintenance • Instructions on how to use a home mechanical ventilator for the patient, her family, and medical staff
Medical Safety Promotion Office	<ul style="list-style-type: none"> • Advice on safety management during rehabilitation while on a mechanical ventilator

ADLs, activities of daily living.

acute respiratory failure and CO₂ narcosis secondary to acute-on-chronic ventilatory failure triggered by pneumonia, and was admitted to the intensive care unit (ICU).

Clinical Course Including Multidisciplinary Rehabilitation

After initiation of a mechanical ventilator, her consciousness level recovered to E3VTM6. However, it was considered that she would not be able to wean completely off the mechanical ventilator due to hypercapnia. Therefore, difficult decision-making

and ethical considerations were required to determine the strategy, so we engaged in multidisciplinary discussions to determine the optimal interventions. Specifically, emergency physicians provided initial treatment and determined the course of action in case of sudden emergencies. Hematologists took the lead in managing the specialists in the team, determining treatment plans and supporting patient decision-making. Even in rehabilitation led by physical therapists at its core, the hematologists took the initiative in coordinating efforts—consulting with nurses, the respiratory support team, and the

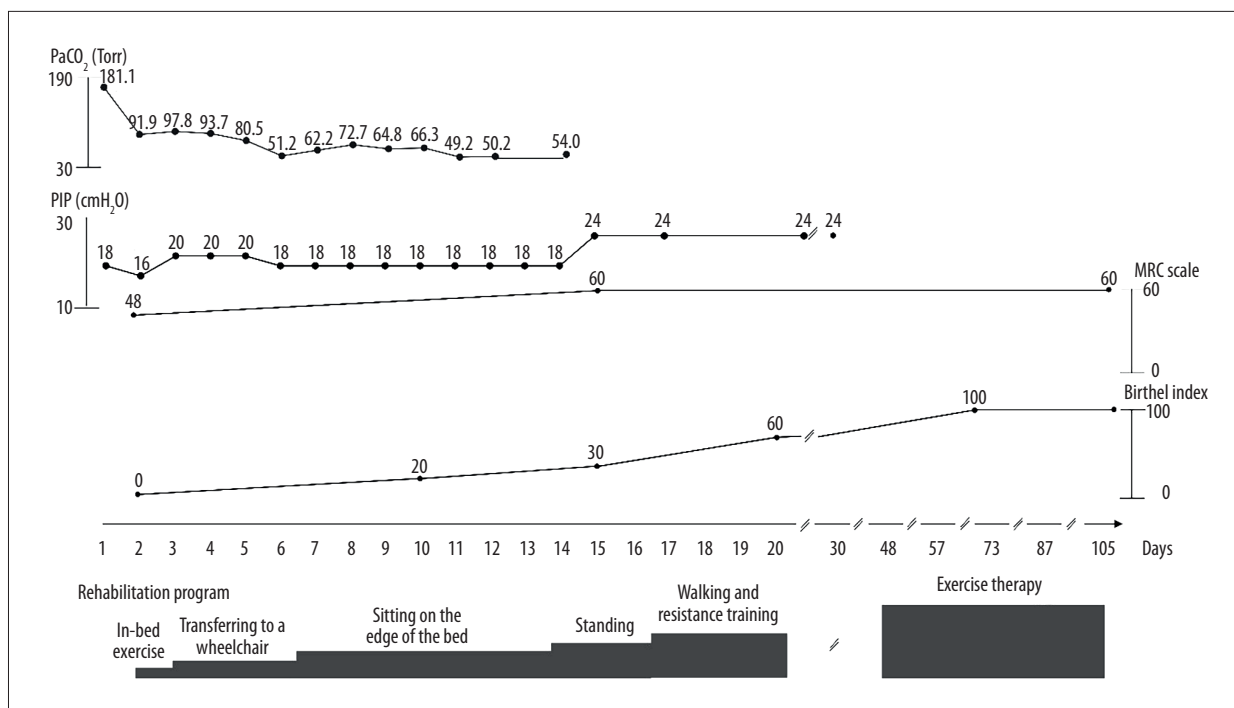


Figure 2. Clinical course. PaCO₂ decreased rapidly upon initiation of mechanical ventilation, but high levels persisted, and peak airway pressure could not be reduced. The MRC score was maintained at 48 or higher, and although the Barthel Index was initially 0, it improved throughout the rehabilitation program and eventually achieved 100. Day 30: The mechanical ventilator was changed to a home mechanical ventilator. The patient and her family started practicing how to use it. Day 48: Exercise therapy began in the rehabilitation room while on a mechanical ventilator. Day 57: During the day, the patient was successfully weaned off the mechanical ventilator and was able to spend time wearing a 1 L O₂ tracheal mask. At night, the patient continued to use the mechanical ventilator. Day 73: The Barthel index achieved a score of 100 points. Day 87: A multidisciplinary conference was held with hospital staff and community medical staff to explain and share information with the patient, her family, and specialists providing home care about precautions for living at home and responding to emergencies. Day 105: The patient was discharged from the hospital and returned home. During the day, the patient received 1 L of oxygen, and at night, the patient used a mechanical ventilator. MRC, medical research council; PaCO₂, partial pressure of arterial carbon dioxide; PIP, peak inspiratory pressure.

medical safety department regarding step-up eligibility and patient transfers outside the ward while on a ventilator. An otolaryngologist took the lead in managing the tracheostomy and swallowing, and a gastroenterologist advised gastrostomy for nutritional intake. Nurses performed daily tracheal suctioning, medication administration, and other care tasks. Physical therapists proposed rehabilitation programs and activities of daily living (ADLs) in the ward, and speech therapists led swallowing assessments and interventions as well as communication methods after tracheostomy. Medical engineers performed maintenance on mechanical ventilators, the respiratory support team led the coordination of mechanical ventilator settings and the spontaneous breathing trial, and the medical safety promotion office provided advice on safety management during rehabilitation while mechanical ventilators were being used (Table 1). Care was coordinated through regular multidisciplinary discussions, with each specialty contributing to ventilator management, rehabilitation planning, and discharge preparation.

Rehabilitation was initiated on the second day after admission. Major clinical courses, including trends in peak airway pressure, PaCO₂, muscle strength as assessed by the medical research council (MRC) scale, Barthel index, and the rehabilitation program are shown in Figure 2. Also, details of rehabilitation are shown in Table 2. We monitored blood pressure, heart rate, respiratory rate, SpO₂, and end-tidal CO₂ tension. Figure 3 shows the mean values of these variables before, during, and after rehabilitation. At the time of starting in-bed exercise, the MRC scale was 48 points, which was at the threshold of the definition of ICU-acquired weakness (ICU-AW). Because the patient was intubated, the Barthel index was 0 points. On the sixth day, sitting on the end of the bed was started, but due to discomfort caused by the intubation tube, the patient could maintain this action for only a few minutes. We attempted weaning from the mechanical ventilator, but hypercapnia did not improve. Therefore, weaning from the mechanical ventilator was deemed impossible. As a result, tracheostomy was performed on the 11th day. On the 14th day, the patient left the

Table 2. Details of the rehabilitation program.

Day 2-3; In-bed exercise	<ul style="list-style-type: none"> • Kicking and straight leg raising in supine position: 10 repetitions on each side ×1-2 sets • Ankle dorsiflexion and plantar flexion: 10 repetitions on each side ×2-3 sets • Shoulder flexion: 10 repetitions ×1-2 sets • Elbow flexion: 10 repetitions on each side ×1-2 sets
Day 4-6; Transferring to a reclining wheelchair	<ul style="list-style-type: none"> • Transfer to a reclining wheelchair with full assistance • The time was initially 30 minutes and was then extended to 2 hours • In-bed exercise was also continued
Day 7-13; Sitting on the edge of the bed	<ul style="list-style-type: none"> • Sitting at the end of the bed was initiated from a few minutes, gradually increasing the duration with the goal of 30 minutes or more
Day 14-16; Standing	<ul style="list-style-type: none"> • Standing started with 2-3 repetitions • Repetitions were increased up to 10 times
Day 17-48; Walking and resistance training	<ul style="list-style-type: none"> • Walking training began with initially 2-3 m and progressively extended within the reach of the mechanical ventilator tube • After switching to a mechanical ventilator for home use, walking distance was extended up to 200 m, which would be required for post-discharge activities such as outpatient visits • Resistance training began with 10 repetitions of knee extension and hip flexion on each side ×2-3 sets, and gradually progressed to squats and calf raises (5-10 repetitions, 1-2 sets)
Day 49+; Exercise therapy	<ul style="list-style-type: none"> • As resistance training, 10 repetitions of calf raise and squats ×2-3 sets • As balance training, 10 seconds both-leg standing and single-leg standing ×2-3 sets • As aerobic exercise, a recumbent ergometer was used with a target Borg scale of 12-13/13-14 • All of these exercises were combined and performed for a total of 40 minutes per day

ICU. She was able to begin standing exercises on the 15th day. Moreover, walking and resistance training were started on the 17th day. On the 18th day, speech therapy was initiated with the aim of communication after tracheotomy and improvement of swallowing. Subsequently, as ADLs gradually expanded, a policy was established on the 21st day to aim for discharge to home regardless of whether weaning from the mechanical ventilator was possible or not, and on the 30th day, the mechanical ventilator was switched to one that could be used at home. On the 35th day, she achieved independent walking and toilet use while carrying her own mechanical ventilator within a private room. On the 49th day, after multidisciplinary staff shared safety management strategies, she started rehabilitation in the rehabilitation room, focusing on mobility training and instrumental ADLs training. Weaning from the mechanical ventilator also progressed gradually, and on the 58th day, she was able to spend the daytime without the mechanical ventilator and with only 1 L/min of oxygen. However, at night, CO₂ retention and dyspnea persisted when the mechanical ventilator was weaned, so we decided not to wean mechanical ventilator support and discharged her to her home where she continued to use the mechanical ventilator at night only. On the 74th day, she was able to climb stairs independently and achieved a Barthel index of 100 points. In addition, continuous walking distance improved to 200 meters. On the 87th day, nurses and social workers led a multidisciplinary conference with a visiting doctor and nurses to discuss how to deal with adverse events, precautions to take in daily life, such as

suctioning sputum, and ADLs. On the 105th day, when home renovations (installation of a power outlet for a mechanical ventilator, setting up home oxygen therapy equipment, relocation of living space, and wheelchair rental) and family training for responding to emergencies were completed, she was discharged from the hospital and returned home. After discharge, she continued to receive medical examinations from a visiting doctor and began home nursing and rehabilitation services. Although treatment for CML was discontinued at the patient's and family's decision, the physician explained that treatment could be resumed at any time if desired.

Discussion

This case describes a patient with CML who developed chronic respiratory failure associated with dasatinib-induced pulmonary toxicity and required prolonged mechanical ventilation. Although complete ventilator weaning was not achieved, the patient regained independence in ADLs and was discharged home. The key clinical feature of this case was a shift in treatment goals. Early in the clinical course, the focus was on ventilator weaning. However, because persistent hypercapnia limited further progress, the goal was redefined to prioritize functional recovery and discharge planning. This change allowed rehabilitation to proceed in parallel with long-term ventilatory support. Rehabilitation was initiated early and advanced step by step, from in-bed exercise to ambulation and ADL training. This progression was

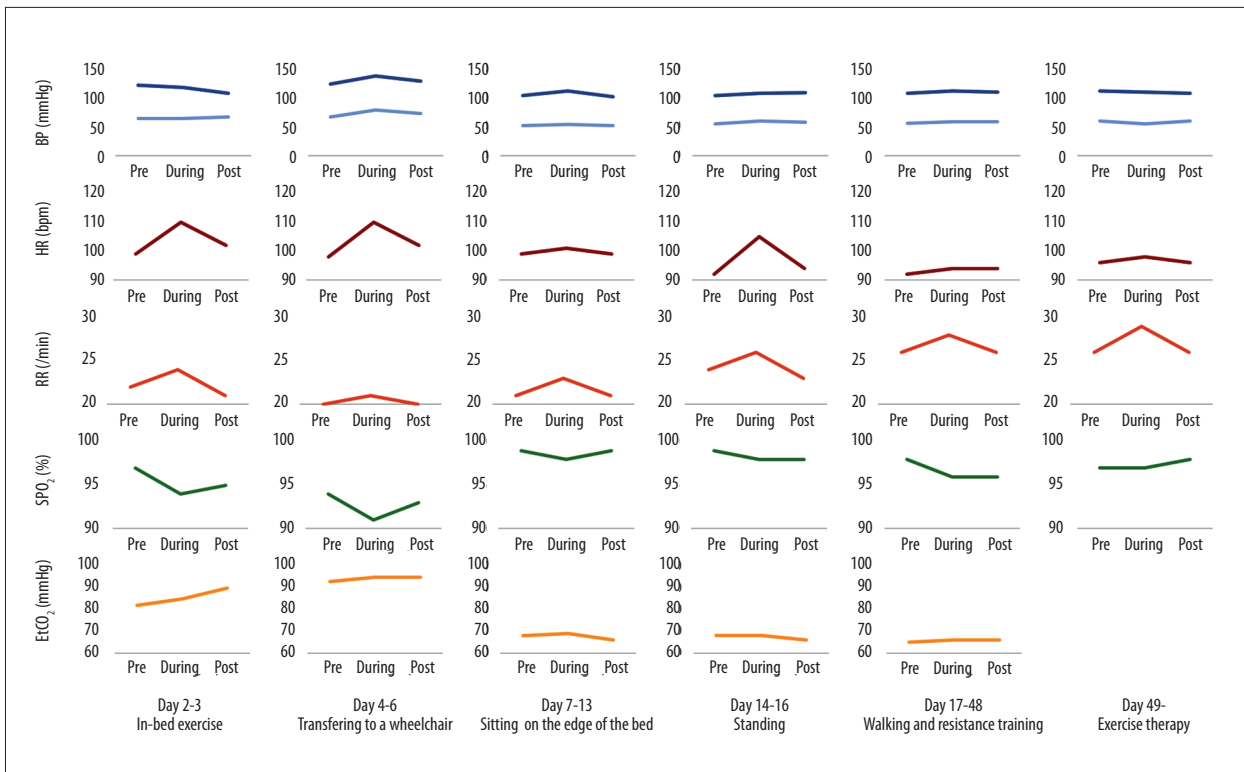


Figure 3. Changes in each parameter pre-, during, and post-rehabilitation. No significant changes in blood pressure were observed during any of the rehabilitation stages. Although heart rate and respiratory rate increased during the rehabilitation program, no adverse events occurred. SpO₂ showed a slight decrease during in-bed exercises and transfers to a wheelchair, but symptoms were minimal and the situation was deemed acceptable. EtCO₂ remained elevated until Day 6 regardless of rehabilitation but decreased from Day 7. Changes related to the rehabilitation program were largely not observed. EtCO₂ ended daytime monitoring after day 49. The values shown are means. BP, blood pressure; bpm, beats per minute; EtCO₂, end-tidal carbon dioxide tension; HR, heart rate; RR, respiratory rate; SpO₂, saturation of percutaneous oxygen.

supported by close coordination among multiple professionals, including physicians, nurses, therapists, and respiratory support staff. In particular, shared decision-making and early planning for home discharge were essential for maintaining continuity of care. Importantly, the patient's respiratory impairment persisted, and nocturnal ventilator support remained necessary at discharge. Therefore, the improvement observed in this case should be interpreted as functional recovery rather than reversal of the underlying pulmonary toxicity. This case does not establish a causal effect of rehabilitation. However, it provides a practical example of how a multidisciplinary approach can support functional independence and facilitate home discharge in patients with prolonged ventilator dependence related to cancer treatment, and we believe that it will be clinically meaningful.

Many adults live while using mechanical ventilators at home, but most of them are patients with neuromuscular diseases [12], and patients with respiratory failure related to CML treatment may be rare. Although the prognosis for CML has improved, long-term treatment is required, which may cause various adverse effects. One of the adverse effects of dasatinib

is lung toxicity, including pleural effusion [13]. Although some reports suggest that prolonged pleural effusion caused by dasatinib does not affect survival rates [14], chronic pleural effusion could lead to chronic pleural disease including pleurisy and pleural fibrosis [15], causing restrictive ventilatory impairment and chronic respiratory failure [5]. Severe restrictive ventilatory impairment causes type 2 respiratory failure. However, in our experience, even in this rare case where complete weaning from a mechanical ventilator was impossible, providing multidisciplinary rehabilitation and collaborating across specialties in each phase of treatment led to favorable outcomes, such as independence in ADLs and discharge to home. Dasatinib showed great therapeutic effectiveness against CML, and similar cases may be seen in the future. In such patients with cancer treatment-related pulmonary toxicity and prolonged ventilator dependence, multidisciplinary rehabilitation may support functional recovery and facilitate discharge home even when complete ventilator weaning is not achievable. Clear goal setting and coordinated care across specialties may be important in managing those complex cases. Furthermore, maintaining physical function, assessed as Eastern Cooperative Oncology

Group performance status (ECOG-PS), is important for achieving favorable outcomes and continuing medication [16], and ensuring treatment options and preserving decision-making choices is ethically important. Maintaining a good ECOG-PS is considered one of the key outcomes in cancer rehabilitation [17,18]. In this case, although the patient did not wish to continue treatment for CML at the time of discharge, it may be important to maintain high ECOG-PS levels in order to be prepared for any future changes in the patient's decision. This is important to preserve future treatment options and is required of the facility that provided the initial treatment.

Multidisciplinary interventions, which are provided across clinical fields, have been gaining attention in recent years. Multidisciplinary care is recommended in guidelines such as the cardio-oncology guidelines [19]. However, there is limited discussion in these guidelines of specific roles and responsibilities, particularly those of medical staff, and this remains an issue for the future.

In our experience, the multidisciplinary approach attempted with the contributions shown in **Table 1** was associated with favorable outcomes. In addition, although the patient stayed in the ICU for 14 days, she did not develop ICU-AW. ICU-AW is a well-recognized complication in critically ill patients, associated with prolonged immobilization and systemic inflammation, and may contribute to delayed functional recovery [20]. Although there were several risk factors, such as being an older female patient and being on long-term mechanical ventilator support [20], early multidisciplinary intervention may have helped prevent ICU-AW in our case. There are several reports that early rehabilitation prevents ICU-AW [21], and early intervention, particularly with a multidisciplinary team of professionals, may be important. In fact, a systematic review suggests that early rehabilitation is associated with a lower incidence of ICU-AW, better MRC scores, and higher Barthel index. These findings are all consistent with the present case [22].

Additionally, from the perspective of cancer rehabilitation, it has been noted that cancer rehabilitation for patients

undergoing chemotherapy is important for achieving favorable outcomes [23,24]. In this case, the smooth transition from early rehabilitation in the ICU to cancer rehabilitation may have been a good thing. However, since this is a case report, verification of the efficacy of such multidisciplinary approaches through observational studies and interventional studies is required. Also, the observed outcomes in this case may have been influenced by multiple factors, including medical management and natural clinical course, and the independent effect of rehabilitation cannot be determined. Furthermore, the present report describes the feasibility of a multidisciplinary rehabilitation approach and its association with functional recovery and home discharge, but it does not establish a causal treatment effect.

Conclusions

In summary, in a case of severe respiratory failure due to TKI-based pulmonary toxicity, multidisciplinary rehabilitation may facilitate functional recovery and support discharge to home, even when complete ventilator weaning is not achievable. It is suggested that collaboration among specialists to provide treatment, including rehabilitation, is important for achieving favorable outcomes in a case where treatment is challenging.

Department and Institution Where Work Was Done

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Patient Permission/Consent

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

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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