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Veno-venous extracorporeal membrane oxygenation in devastating bacterial pneumonia: a case report and review of the literature

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Abstract

Background Bacterial pneumonia is one of the most common causes of acute respiratory distress syndrome. In fulminant cases, when mechanical ventilation fails, veno-venous extracorporeal membrane oxygenation is required. However, this method is still associated with significant mortality and a wide range of potential complications. However, there are now many case reports of good outcomes even in patients with prolonged extracorporeal oxygenation, as in our rather complicated case report.

Case presentation Our case report describes a complicated but successful treatment of a severe, devastating bacterial pneumonia in a 39-year-old European polymorbid woman with a rare form of diabetes mellitus, which had been poorly compensated for a long time with limited compliance, in the context of a combined immunodeficiency that strongly influenced the course of the disease. The patient's hospitalization required a total of 30 days of veno-venous extracorporeal membrane oxygenation therapy and more than 50 days of mechanical ventilation. Numerous complications, particularly bleeding, required seven chest drains, two extracorporeal membrane oxygenation circuit changes, and one surgical revision. The patient's mental state required repeated psychiatric intervention.

Conclusion It is possible that even the initially severely damaged lung parenchyma can develop its regenerative potential if suitable conditions are provided for this process, including a sufficiently long period of extracorporeal membrane oxygenation.

We believe that this case report may also contribute to the consideration of the indications and contraindications of extracorporeal support. The authors also discuss the limitations and risks of prolonged veno-venous extracorporeal membrane oxygenation support and periprocedural anticoagulation strategies.

Keywords VV–ECMO, Bacterial pneumonia, Bleeding, Case report

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Background

Pneumonia remains a leading cause of death in adults worldwide and is the leading cause of death in children under the age of 5 years [1]. The development of extracorporeal membrane oxygenation in the last decade and under the pressure of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has allowed us to expand the treatment options for patients with very severe disease who fail conventional therapies, including mechanical ventilation (MV).

The case report presented here describes a case of complicated therapy of disintegrating bacterial pneumonia requiring prolonged veno-venous extracorporeal membrane oxygenation (VV–ECMO). The treatment was complicated by a combined immunodeficiency due to a rare form of diabetes mellitus, which was poorly compensated for a long time.

Case presentation

A 39-year-old European woman was admitted to the intensive care unit (ICU) of our department with bacterial disintegration pneumonia after a previous 8-day hospital stay. Prior to admission, the patient had been suffering from fever for approximately 1 week with increasing shortness of breath.

The patient was chronically treated for long-term poorly compensated diabetes mellitus (DM) type maturity-onset diabetes of the young (MODY) with polyneuropathy of the lower extremities and diabetic visceral neuropathy, chronic lymphocytic thyroiditis and depressive syndrome.

Admission chest X-ray revealed pneumonia with bilateral pleural effusions (Fig. 1). Bedside transthoracic echocardiogram (TTE) ruled out congestive heart failure with good systolic function of both ventricles and a large left pleural effusion with consolidation of the lung parenchyma.

Chest computed tomography (CT) scan showed extensive atelectasis of both lungs dorsally and basally with gross enlargement and edema of airless lung tissue and a negative bronchogram. Gas-filled cavities in the left lung wing were described as a sign of incipient decay (Fig. 2A, B).

Streptococcus pneumoniae was cultured from the patient's tracheal aspirate, exudate, and urine. A combination of cefotaxime (2 g intravenous every 6 hours), clindamycin (600 mg intravenously every 8 hours), and fluconazole (400 mg intravenously per day) was prescribed in consultation with the local antibiotics center.

Fluconazole was chosen given the dramatically progressing infection and suspected immunodeficiency in decompensated DM.

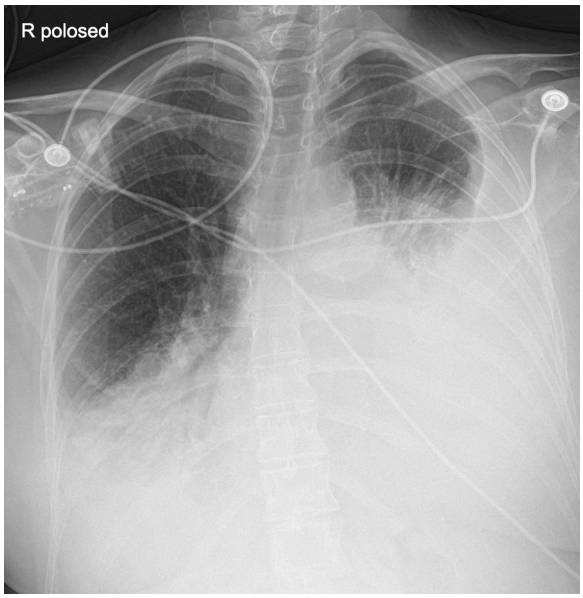

Fig. 1 Bilateral pneumonia with bulky fluidothorax on admission chest X-ray

On admission to our ICU, the patient was connected to VV–ECMO support via the right-sided internal jugular vein (15F) and right-sided femoral vein (23F). The cannulae were inserted by the puncture-dilatation method 36 h apart after connection to MV.

The indication for VV–ECMO was progressive hypoxia with hypercapnia when the capacity of mechanical ventilation was exhausted. Prone ventilation was not performed due to rapidly developing circulatory instability with high norepinephrine support at 0.8 ug/kg/min combined with maximal vasopressin dose and positive fluid balance.

The initial setting of the ECMO machine was as follows: fraction of inspired oxygen (FiO2 1.0), sweep gas flow (SGF) 4l/minute, and blood flow (BF) 2.8 l/minute. At the same time, MV parameters were adjusted to bilevel positive airway pressure (BiPAP), FiO2 0.5, peak inspiratory pressure (Pinsp) 20 cmH_2O; pressure support (Psupp) 10 cmH2O; respiratory rate (RR) of 12 breaths per minute; positive end-expiratory pressure (PEEP) 7 cmH2O; and tidal volume (TV) was about 250 ml.

With these parameters, there was an improvement in oxemia with PaO_2 9 kPa and a reversal of hypercapnia to $PaCO_2$ values around 5kPa.

As a tension pneumothorax developed in the left pleural space, a chest tube was placed (Fig. 3). The following day, a right chest tube was also inserted to drain the significant fluidothorax. Follow-up bedside TTE showed extensive consolidation of the left lung wing and

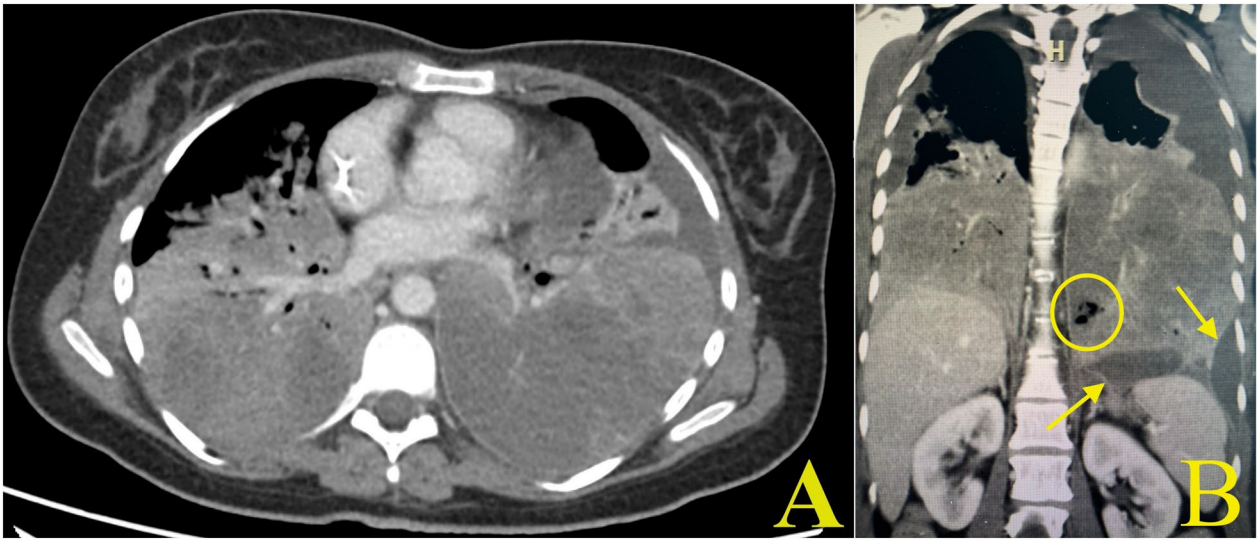

Fig. 2 Admission computed tomography scans of transverse (**A**) and frontal (**B**) sections show extensive atelectasis bilaterally with edema of the non-aerated lung tissue. There is a fluidothorax on the left (arrows) and gas cavities (circle) as evidence of a decay process

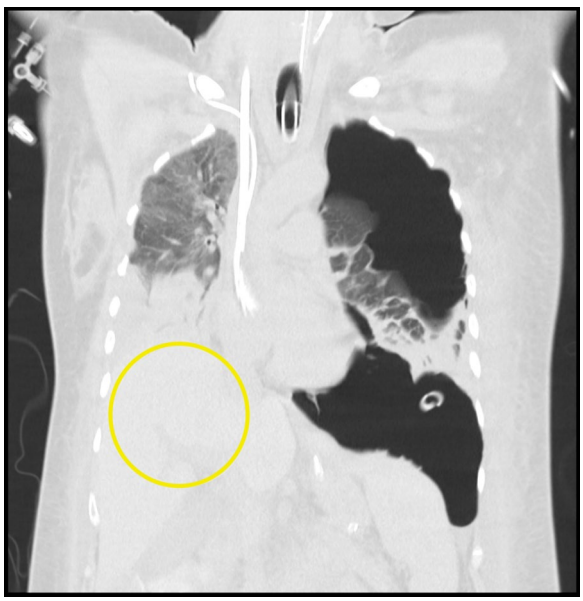

Fig. 3 Computed tomography scan showing almost complete collapse of the left lung wing due to pneumothorax. Collapsed cavities can be seen. In the right pleural cavity there is a bulky fluidothorax with an airless lower lobe (circle)

further bronchoscopy with bronchial tree clearance was performed.

The bronchial aspirate was positive for Escherchia coli and the ATB treatment was changed to a triple combination of ceftazidime (2 g intravenously every 8 hours) + clindamycin + fluconazole on the recommendation of the local antibiotic center. The ATB regimen was changed according to the current cultures and susceptibility of the bacterial strains during the follow-up hospitalization.

Bronchoscopic treatment was also required in the following days as the bronchial tree was repeatedly obstructed by mucus or bleeding.

The dose of anticoagulation by continuous intravenous infusion of unfractionated heparin (UFH) was reduced because of persistent airway bleeding, despite otherwise satisfactory coagulation parameters (activated partial tromboplasin time (APTT) 39 seconds, international normalized ratio (INR 1.11), fibrinogen 2.02 g/l, trombin time (TT) 19 seconds, activated clotting time (ACT) 160 seconds).

However, despite the substitution of coagulation factors, the airway bleeding could not be completely suppressed.

The patient's condition deteriorated dramatically on day 20 of hospitalization when she developed obstructive shock. The CT scan described the presence of bulky hematomas in both pleural cavities with mediastinal compression (Fig. 4). Laboratory data showed a significant decrease in plasma fibrinogen concentration (0.86 g/l) and platelet count (70 × 109/l). ACT was consistently around 160 seconds, even without UFH infusion, and other monitored hemostasis parameters were minimally affected. On the basis of these findings, bilateral chest tubes were indicated and the ECMO circuit was changed. Fibrinogen concentrates were administered with a plasma fibrinogen level adjusted to 2.64 g/L and platelet concentrates with a platelet count adjusted to 108 × 109/l.

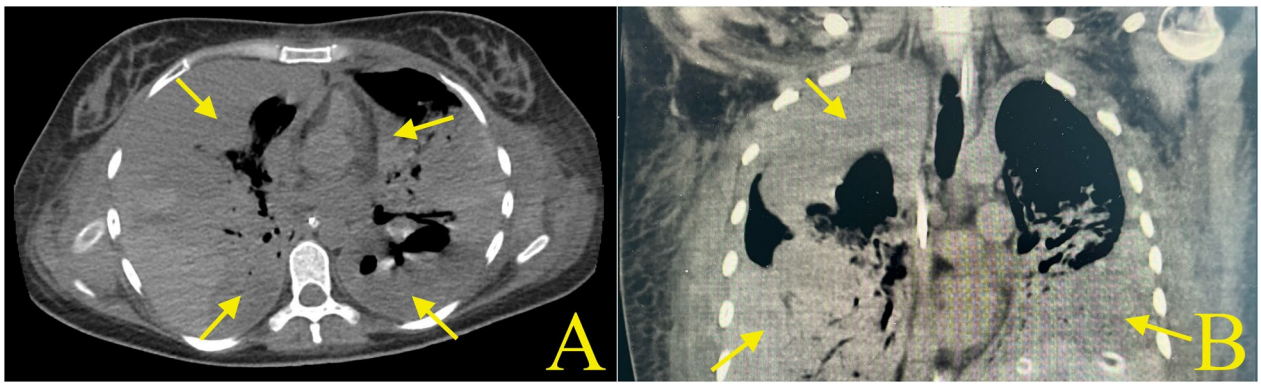

Fig. 4 Computed tomography scans of transverse (**A**) and frontal (**B**) sections clearly shows bulky clots in both pleural cavities. They are 56 mm on the right and 42 mm on the left. Both lung wings are largely airless except for the upper lobes. The mediastinum is compressed by hematomas (arrows)

From day 20 to day 21 of hospitalization, continuous UFH was resumed at a rate of 300 IU/hour (8 days without anticoagulation). On day 24 of hospitalization, tracheostomy was performed by percutaneous dilatation. On the same day, a second ECMO circuit change was required due to persistent bleeding after exclusion of other causes.

After further reduction of sedative doses, consciousness was regained on day 27. The chest tube was reinserted dorsolaterally on the right side on day 29 to drain the old hematoma.

After successful weaning, we discontinued 30 days of VV–ECMO support on day 32 of hospitalization. Weaning from VV–ECMO was performed by gradually decreasing FiO2 and SGF. At FiO2 0.21 and SGF 1 l/minute with unchanged flow through the ECMO circuit for 16 hours, weaning was terminated and the ECMO cannulae were removed.

A routine ultrasound scan revealed a spherical mass projecting into the left subphrenic space.

A bulky hematoma in the left pleural cavity was described, which dislocated the spleen ventrally and caudally on CT (Fig. 5). As the patient's clinical condition had improved, surgical evacuation of the hematoma was performed via minitoracotomy. Approximately 800 ml of old coagulum and 600 ml of fluid hemorrhagic retention were removed during surgery. The patient was completely weaned off MV after 52 days. After a further 5 days, the patient's clinical condition allowed for transfer from the intensive care unit to the intermediate care unit. The patient was discharged to home care on the day 77 of hospitalization.

The last chest radiograph before discharge showed a marked improvement in the transparency of both lung wings with persistent opacity of the lung parenchyma in the middle and lower lung fields on the right and in the middle lung field on the left (Fig. 6).

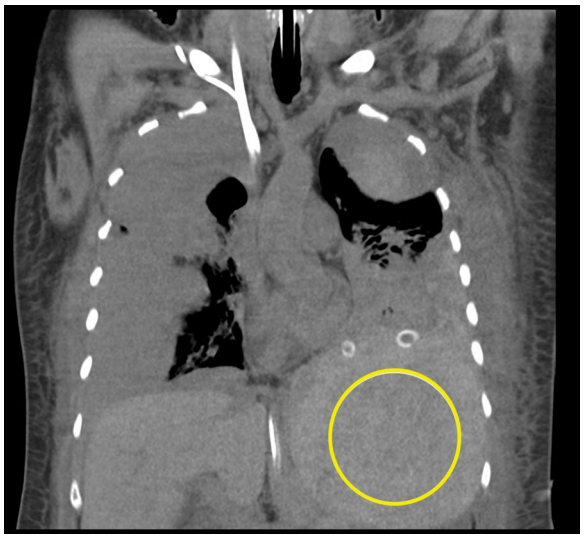

Fig. 5 Computed tomography scan showing a bulky dense hematoma in the caudal part of the left pleural cavity (circle). Partial improvement of airflow is observed in both lung wings

The follow-up chest X-ray 7 weeks after discharge showed a further improvement in transparency bilaterally (Fig. 7).

The patient was diagnosed with a complex functional immune disorder in the context of long-standing, poorly compensated DM with impaired antibody reactivity to novel antigenic stimuli during cell starvation and disruption of the body's natural barriers. She is currently attending an immunology outpatient clinic and undergoing immunomodulatory therapy.

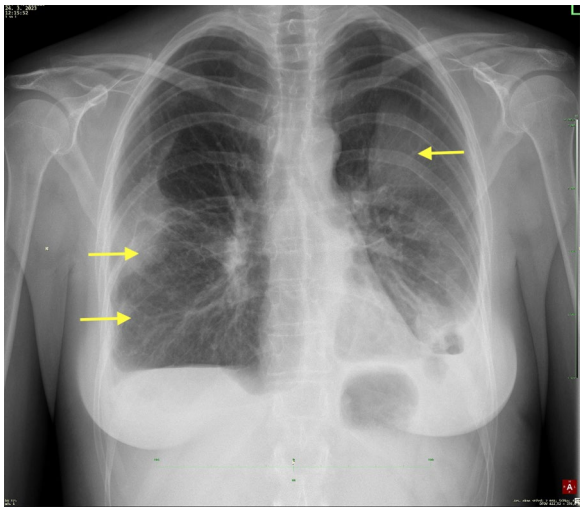

Fig. 6 Pre-dismantling chest radiographs showing improved transparency of both lung wings with persistent opacities in the lower and middle lung field on the right and in the middle lung field on the left (arrows)

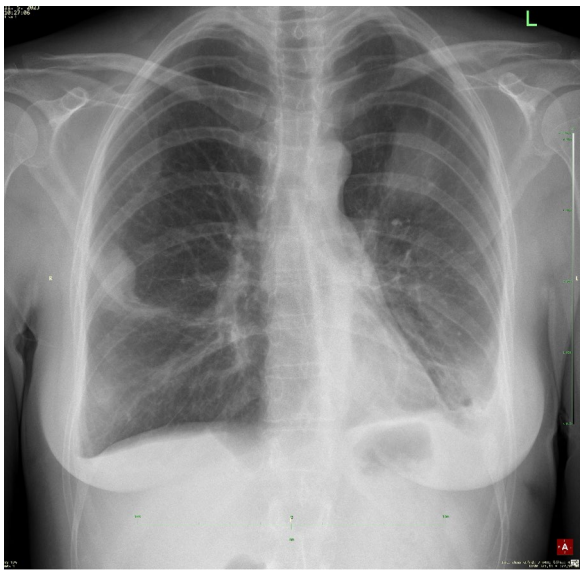

Fig. 7 Follow-up chest X-ray 7 weeks after discharge from hospital showing further improvement in the transparency of both lung wings

Discussion

We define community-acquired pneumonia as pneumonia acquired by a patient outside a hospital setting. The global incidence of community-acquired pneumonia is estimated to be 1.5–14 cases per 1000 persons per year (3.3–46 cases per 1000 persons in the elderly population) and is the fourth leading cause of death worldwide [2, 3]. The most common bacterial pathogen is Streptococcus pneumoniae [4]. This was also the case in our case report.

Patients with a severe course of community-acquired pneumonia requiring intensive care represent approximately 10–30% of all hospitalized patients with community-acquired pneumonia. The course of hospitalization in these patients is associated with higher complication rates, and overall mortality rates range from 21% to 54% [5].

Patients with DM are more likely to be hospitalized with community-acquired pneumonia, and have longer hospital stays and higher mortality rates than patients without DM [6]. In patients with DM with poor glycemic control, immune competence is impaired by a number of mechanisms. These mechanisms include inhibition of cytokine production, abnormalities in phagocytosis, or reduced immune cell function [7]. The length of hospital stay in patients with community-acquired pneumonia does not differ between DM 1 and DM 2 [8].

Our patient had MODY type DM, which was poorly compensated for a long time. Her glycated hemoglobin level was 84 mmol/mol.

MODY type DM is a group of autosomal dominant monogenic DM. The prevalence is reported to be between 1.1% and 6.5% in pediatric patients with DM. Some forms of MODY type DM are relatively mild and do not require medication, while others are well compensated with oral antidiabetic drugs or insulin [9, 10].

In patients with a very severe course of pneumonia, when conventional MV fails and in the absence of contraindications, it is appropriate to consider ECMO options. The main physiological goals of VV–ECMO are (1) reversal of hypoxemia and hypercapnia and (2) establishment of conditions for protective MV and thus protection from the deleterious effects of aggressive MV [11]. The main indication and contraindication criteria are summarized in Table 1. The duration of MV prior to ECMO connection is one of the risk factors, therefore indicated patients should be connected as early as possible [11]. The usual duration of MV-ECMO therapy is in the range of 1–2 weeks. The median duration of support in surviving patients with severe coronavirus disease 2019 (COVID-19) pneumonia was slightly longer (about 2 weeks) [12]. The maximum possible duration of support has not yet been established. There are reports of ECMO support for more than 100 days with good outcomes [13].

A common complication is bleeding. According to some studies, more than half of patients may experience bleeding during the course of therapy [14, 15]. The most common sources of bleeding are the cannula insertion site, the surgical site, and hemothorax or gastrointestinal bleeding. Fatal bleeding into the central nervous system

Table 1 Main indications and contraindications for VV–ECMO in adult patients according to the Extracorporeal Life Support Organization [26]

General indications:
1. Hypoxemic respiratory failure (PaO2/FiO2 < 80 mmHg) after optimal support including pronation (if possible)
2. Hypercapnic respiratory failure (pH 7.25 or PaCO2 > 60 mmHg) with optimal management of conventional MV (respiratory rate 35 breaths per minute and plateau pressure (P plat) < 30 cm H2O)
3. Ventilatory support as a bridge to lung transplantation or primary graft dysfunction after transplantation
Specific clinical conditions:
• Acute respiratory distress syndrome (ARDS), viral/bacterial pneumonia, and aspiration
• Acute eosinophilic pneumonia
• Diffuse alveolar and airway hemorrhage
• Severe asthma
• Severe chest trauma and pulmonary contusion
• Severe inhalation trauma
• Extensive bronchopleural fistula
• Bridge to lung transplantation or primary graft dysfunction after transplantation
Relative contraindications
• Bleeding into the central nervous system (CNS)
• Significant CNS injury
• Irreversible and disabling CNS disorders
• Systemic bleeding
• Contraindications to anticoagulation
• Immunosuppression
• Older age (threshold not specified, mortality increases with age)
• MV greater than 7 days with P plat ˃30 cm H2O and FiO2 ˃ 0.9

is rare [14, 16]. Bleeding patients had a longer ICU stay, received more transfusions, and had a longer total VV–ECMO connection time than non-bleeding patients. The bleeding group also tended to have higher hospital costs [14, 15]. Risk factors for bleeding include high APTT and low platelet count prior to ECMO and prolonged support. Kawauchi describes high APTT values during ECMO therapy as an independent factor for bleeding, whereas low platelet counts are no longer a factor.

In the event of bleeding complications, stopping systemic anticoagulation and maintaining platelet counts above 100,000/µl and fibrinogen concentrations above 2 g/l are suggested. Higher blood flow through the ECMO circuit (that is 4–5 L/min) to prevent clot formation until anticoagulation could be resumed is also recommended [14].

Standard monitoring of therapeutic anticoagulation with unfractionated heparin is by routine APTT. One way to reduce the incidence of bleeding is to reduce the dose of anticoagulation. Although there is a large body of literature describing successful VV–ECMO therapy with low-dose anticoagulation or without therapeutic doses of anticoagulation, the Extracorporeal Life Support Organization (ELSO) does not routinely recommend this approach [17, 18]. There are currently two ongoing studies looking at VV–ECMO with only prophylactic doses of unfractionated heparin (NCT04496362, NCT04273607) [18].

The prognosis of patients requiring VV–ECMO is influenced by a number of factors. Several scoring systems (RESP score, PRESERVE score) have been introduced to assess patients. The most important factors are the age of the patient, the duration of MV before connection to VV–ECMO, and the driving pressure value during MV during ECMO therapy [19]. Mortality rate increases above 45 years of age, and indication for VV–ECMO support should be carefully considered in patients over 65 years of age, as they have a low survival rate to discharge [20].

Patients with longer VV–ECMO support were found to have lower in-hospital survival rates than those with shorter support (21% versus 60%) [21]. To date, there are not many studies that specifically describe long-term outcomes in patients with longer VV–ECMO support. However, even very long ECMO support is beneficial in patients without the development of multiorgan failure [22]. The regenerative potential of the lung parenchyma is individual. Even extensively damaged lung tissue can regain its capacity if appropriate conditions are provided for this process, including a sufficiently long duration of ECMO support [23].

More than 40% of patients discharged from hospital after VV–ECMO therapy suffered from post-traumatic stress disorder or an anxious-depressive syndrome even 1 year after connection to VV–ECMO [24]. A small monocentric retrospective study reported that up to 80% of patients were able to return to work [25].

Conclusion

Our case report demonstrates that even extensive devastating pneumonia leading to respiratory failure is potentially manageable despite conventional MV and complex resuscitation procedures. Our case required a total of 30 days of VV–ECMO support, 52 days of MV, and a total of 57 days of intensive care. During the hospitalization, chest drainage was performed seven times and the patient underwent one surgical revision. This makes the management of patients with such a diagnosis extremely costly medically, in terms of time, nursing care, and financially. This case report may help to clarify the confusion regarding indications and contraindications for extracorporeal support. We would also like to draw attention to the ongoing research into DM and its updated classification. MODY type DM tends to be diagnosed as type 1 or 2 DM in 50–90% of patients [9]. Our experience also confirms the importance of routine ultrasound monitoring in patients treated with extracorporeal methods.

Abbreviations

VV–ECMO	Veno-venous extracorporeal membrane oxygenation
DM	Diabetes mellitus
MODY	Maturity-onset of diabetes of the young
CXR	Chest X-ray
CT	Computed tomography
ATB	Antibiotics
UFH	Unfractionated heparin
TTE	Transthoracic echocardiogram
SGF	Sweep gas flow
BiPAP	Bilevel positive airway pressure

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Author contributions

Štěpán J. prepared the manuscript. Šedivý J., Kuta B., Tesařík R., Cihlářová P., Schaffelhoferová D., and Šulda M. provided comments on the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This case report did not include any new or experimental treatment; hence, approval from an ethics committee was not needed.

Consent for publications

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors have no relevant financial interests and no potential conflicts of interest to disclose.

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