Received: 24 February 2023 | Revised: 5 June 2023 | Accepted: 3 July 2023

DOI: 10.1002/ccr3.7709

CASE REPORT

Clinical Case Reports Open Access WILEY

VV-ECMO as bridge and safety net for successful therapeutic polypragmasy in a case of influenza-triggered near-fatal asthma

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Key Clinical Message

In near-fatal asthma, the combination of ECMO therapy and isoflurane application via an intensive care ventilator with an anesthetic conservation device represents a therapeutic combination in seemingly hopeless clinical situations.

Abstract

We report a case of an adult patient with near-fatal asthma, who was implanted venovenous extracorporeal membrane oxygenation in an extern hospital before transfer to our tertiary center. After 13 days and various therapeutic approaches, including inhaled isoflurane therapy via an anesthetic-conserving device, the patient was decannulated and extubated 3 days later.

KEYWORDS

asthma, extracorporeal membrane oxygenation, mechanical ventilation, respiratory failure

1 | INTRODUCTION

Bronchial asthma is characterized by chronic airway inflammation, and bronchial hyperreactivity leading to variable and fully reversible airway obstruction. Respiratory failure can occur during exacerbation and status asthmaticus is used to describe a particularly severe, sometimes therapy-refractory asthma attack. Even though progress has been made in therapeutic management, reducing the frequency and severity of attacks, about 2 million asthma-related presentations are reported in US emergency rooms.[1] Intensive care is required in about 10% of all reported cases, and ventilation in about 2%.[1,2] In a few cases, mechanical ventilation is insufficient to ensure sufficient gas exchange. In these cases, extracorporeal membrane oxygenation (ECMO) offers a rescue therapy until the status asthmaticus can be interrupted by drug therapy.[3–5] Inhaled ß-mimetics, anticholinergics, and

systemic corticosteroids are primarily used to treat airway obstruction in acute asthma attacks.[6] Intravenous magnesium may be given adjuvantly[7]; if sedation is required, ketamine may provide additional bronchodilation.[8,9] The beneficial use of volatile anesthetics such as halothane and isoflurane in asthma has been discussed but remains controversial.[10]

2 | CASE REPORT

A 55-year-old female patient (169 cm, 65 kg, BSA 1.75 m^2) presented to the emergency department (ED) of an external hospital with dyspnea and known non-allergic asthma under therapy with inhaled beclometasone/formoterol. On admission, the patient reported that the symptoms had worsened over a 5-day course of oral antibiotic therapy. In the ED, inhaled and intravenous beta-mimetics were administered as well as iv steroids and morphine. Within a few hours after admission, a rapidly progressive respiratory deterioration occurred, and the patient required tracheal intubation.

After intubation, sufficient decarboxylation was not achieved with highly obstructive expiratory flow curves reflecting severe bronchospasm. Despite increased driving pressure, systemic paralysis, and a low respiratory rate, sufficient ventilation was no longer possible in the short term, which led to severe respiratory acidosis (pH 6.98) due to hypercapnia (pCO_2 137 mmhg) with accompanying circulatory instability. To allow safe inter-hospital transport to our center, venovenous (V-V) extracorporeal membrane oxygenation (ECMO) (Cardiohelp, Getinge, Germany) was implanted on-site by a team of our clinic using the Seldinger technique without any vascular complications (24 FR drainage cannula in the left femoral vein and 17 FR return cannula in the right internal jugular vein). Anticoagulation with activated clotting time (ACT)-guided continuous iv-Heparin (target range between 160 and 180 sec) was initiated directly after ECMO-implantation.

Immediately after the transfer, we performed a chest X-ray (Figure 1) and a CT scan (Figure 2), which showed marked pulmonary hyperdistension, bronchus wall thickening, bi-pulmonary bronchus wall edema, and mucoid impactions. ARDS-like patterns or infiltrates, on the other hand, were not visible. Bronchoscopy ruled out mucoid obstruction of the visible bronchi and showed only mild mucosal redness while echocardiography revealed mild right ventricular dilatation with no signs of acute decompensation. Although PCR diagnostics from a bronchial lavage showed influenza a, we considered the findings to be consistent with influenza a-triggered near-fatal asthma

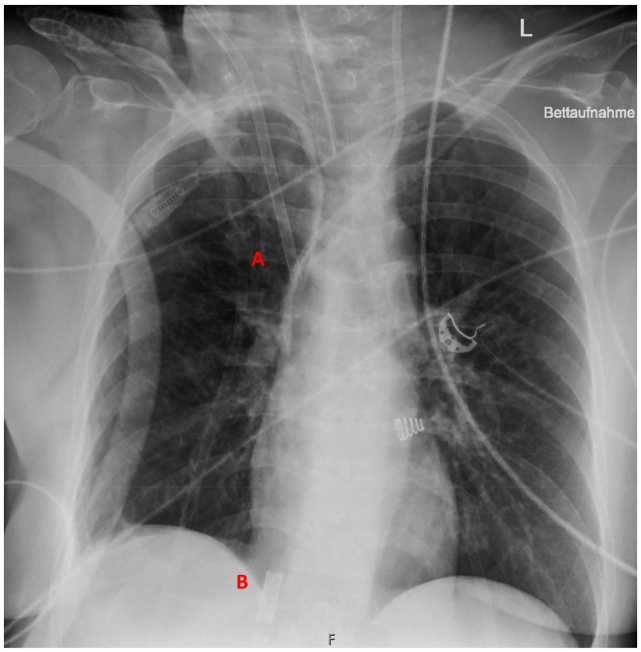

FIGURE 1 Chest X-ray on admission showing pulmonary hyperinflation without ARDS-typical infiltrations. (A) Jugular ECMO cannula, (B) femoral ECMO cannula.

than influenza-ARDS and continued anti-inflammatory therapy with high-dose corticosteroids.

We also used various bronchodilators, namely continuous infusions of reproterol, inhaled ipratropium, and salbutamol as well as magnesium, ketamine, and montelukast. Additional therapy with theophylline was discontinued after only a few hours due to the occurrence of supraventricular tachycardia. Unfortunately, despite of this multilayered therapy and an ultra-low respiratory rate of ~6 per minute, we could not achieve tidal volumes of more than 50 mL. As there was no tendency for improvement in the short term, we initiated additive volatile anesthesia with isoflurane via an anesthetic conserving device (ACD) (SedaConDa® system Sedana Medical Germany GmbH). After a few hours of additional volatile anesthesia, we observed an increase in tidal volumes of up to 250 mL (3.8 mL/kg Predicted Body Weight) with subsequent de-escalation of the ECMO therapy (Figure 3).

As there was no further improvement within the following days, we re-initiated theophylline on day 5 with resounding success resulting in normalized exhaled tidal volumes (Figure 3) without obstructive flow patterns. In the further course, a short-term pulmonary deterioration due to a respirator-associated superinfection with E. coli was noticeable. After this had completely regressed under antibiotic therapy (see time course of CRP and lactate in Figure 4), ECMO was removed without complications on day 14. Three days later, the patient was successfully

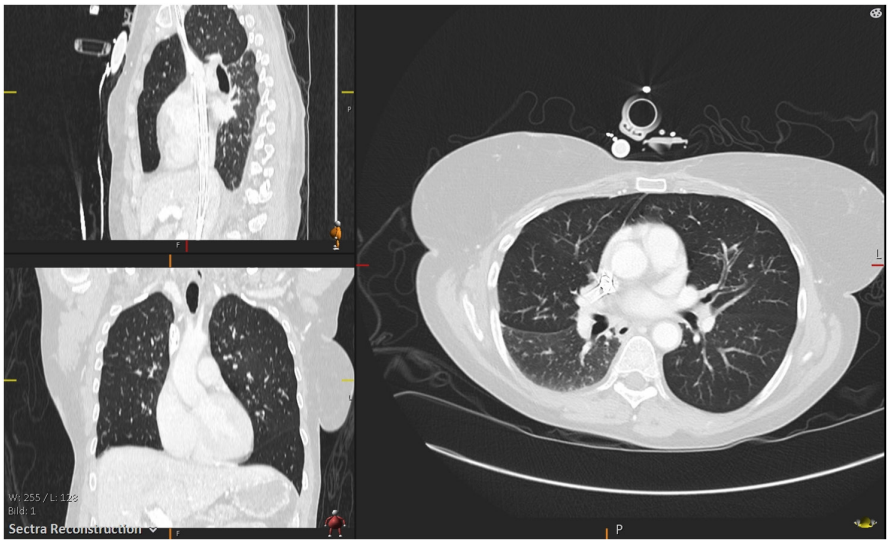

FIGURE 2 Computed tomography of the chest on admission showing pulmonary hyperinflation, bronchus wall thickening, bi-pulmonary bronchus wall edema, and mucoid impactions.

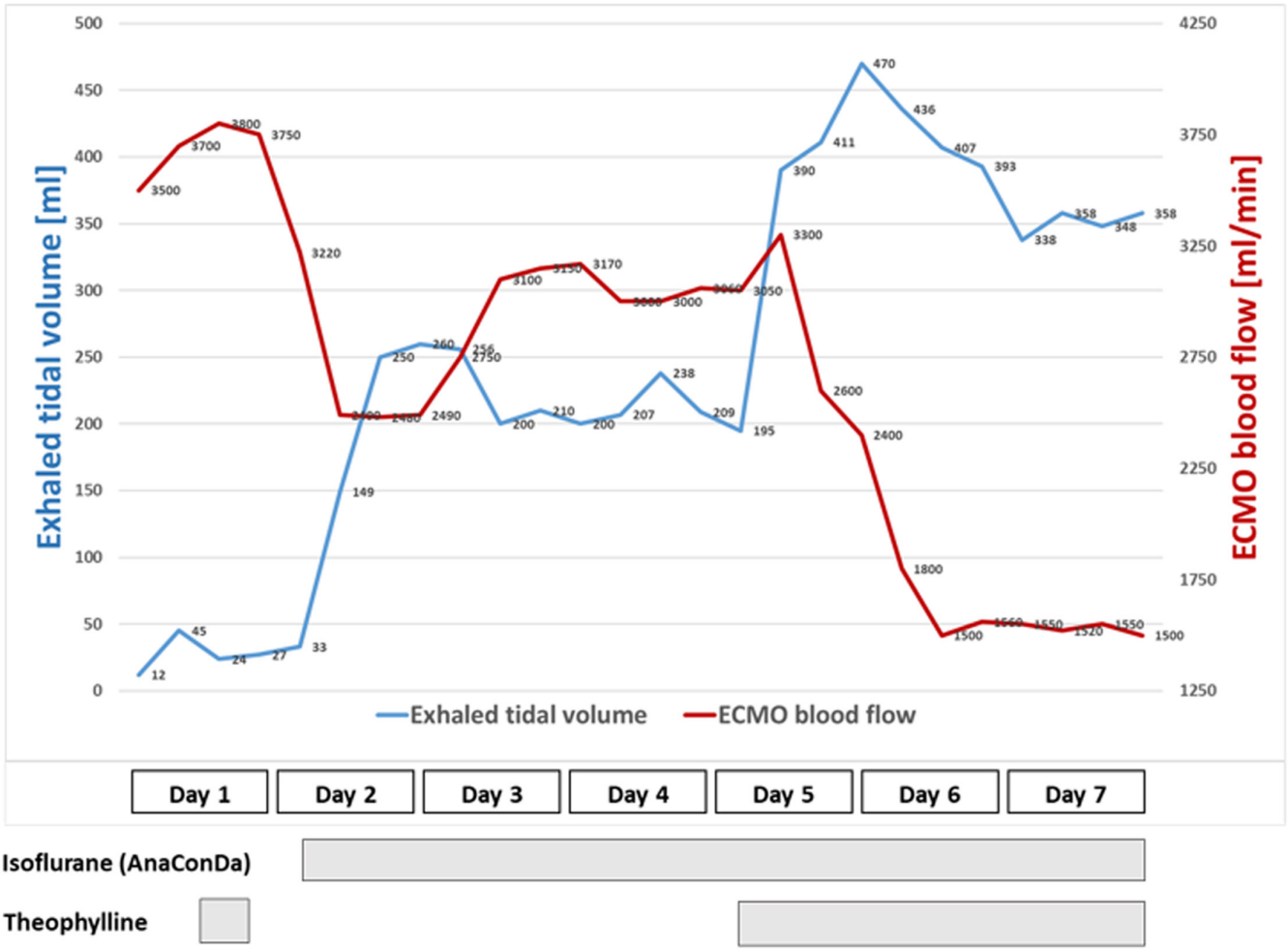

FIGURE 3 Time course of exhaled tidal volume (left y-axis, blue line) and ECMO blood flow (right y-axis, red line).

weaned from mechanical ventilation and was transferred to the pulmonary ward another 3 days later. Moreover, the patient showed up almost completely recovered 2 months after discharge at a follow-up outpatient appointment.

3 | DISCUSSION

Our report illustrates the case of a patient with a status asthmaticus whom V-V ECMO stabilized. Interruption

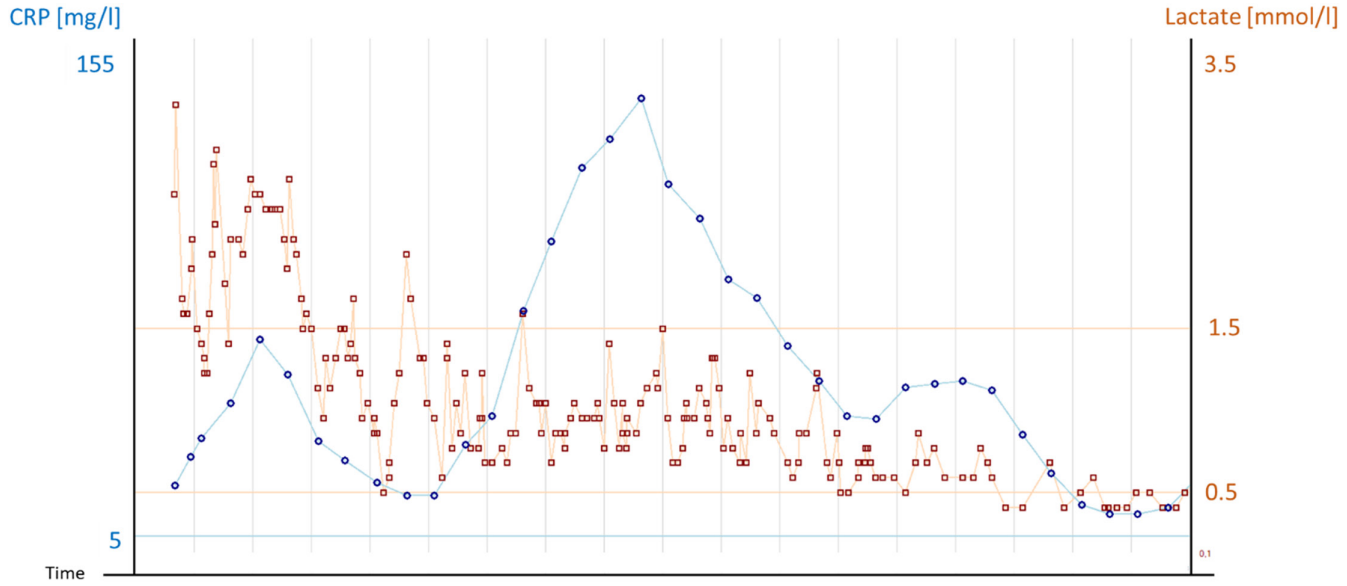

FIGURE 4 Time course of serum CRP (left y-axis, blue line) and lactate (right y-axis, brown line).

of the severe bronchospasm required multi-layer drug therapy. The time course of tidal volumes with the start of therapy suggests that the administration of isoflurane via an ACD significantly contributed to the interruption of status asthmaticus.

Literature about the use of ECMO in near-fatal asthma is limited. In a review of the ELSO register, Yeo et al. identified that asthma is a rare reason for initiating ECMO therapy as only 2.4% of all ECMO-treated patients were canulated due to a status asthmaticus.[5] Not surprisingly, V-V ECMO was by far the most common mode (93.9%) in asthmatic patients.[5] As bronchospasm in asthma is reversible, survival rates in patients undergoing ECMO because of severe asthma appear higher than in patients with other causes of respiratory failure (83.3% vs. 50.8%).[3]

As a highly resource-demanding therapy with numerous potential complications, ECMO is generally limited to specialized centers. In the case reported here, the patient did not initially present to a tertiary center offering ECMO therapy, requiring inter-hospital transfer. Transport to an ECMO center requires on-site ECMO cannulation and initiation in some clinical situations to allow for transport. The on-site ECMO implantation and transport under ECMO are generally considered safe to perform, an experience that has also been consolidated during the COVID pandemic.[11,12]

Although the use of ECMO in the described case can be considered free of major complications, minor bleeding from the cannulation sites required repetitive transfusion of blood products (in total 14 red blood cells and 2 platelet concentrates). Due to the necessity of anticoagulation, bleeding is among the most common complications in ECMO therapy.[13]

While ECMO therapy provides a safety net for acute stabilization of status asthmaticus, there are several therapeutic approaches with more or less strong evidence for the underlying pathophysiology. Adjunctive medications offer possible escalation routes for severe bronchospasm refractory to inhaled ß-mimetics and systemic corticosteroids. While there is evidence for magnesium sulfate,[7] the role of ketamine or iv-administered ß-mimetics in severe asthma is still controversial.[14,15] Volatile anesthetics might offer a rescue therapy in severe asthma refractory to established drug therapy.[16,17] Mechanistically, the relief of airway obstruction by relaxation of bronchiole smooth muscles, anti-inflammatory and ß-mimetic-effects as well as histamine-antagonism and vagolytic effects are suggested.[18–20]

Evidence for the use of volatile anesthetics in acute asthma exists mainly in case reports or small single-center studies. Mostly, authors report benefits–but this beneficial effect is not unquestioned.[21] Isoflurane appears to be the preferred anesthetic because of its safety profile, but sevoflurane or halothane has also been described.[22] The use of volatile anesthetics outside the operating room is limited by organizational and structural requirements, as the use of anesthesia ventilators in an intensive care unit requires the constant deployment of trained personnel. In our case, the anesthetic conservation device enabled the administration of isoflurane via a regular ICU ventilator (Hamilton G5, Hamilton Medical). This proved a safe and convenient method, as described in previous studies.[23–25] The temporal correlation between the onset of isoflurane application and the increase in tidal volumes observed in our patient (Figure 3) makes it tempting to assume causality. Of

note, this effect occurred despite minimal initial tidal volumes, calling an effective delivery of isoflurane to the deeper airways into question.

Interestingly, Gill et al. recently reported a case in which isoflurane was applied via the ECMO circuit itself, indicating that the effect might not be limited to an administration route via the airway.[26] As expected, the combination of volatile anesthetics and ECMO for severe asthma is rarely described.[19,26,27] In these reports, volatile anesthetics were administered either via an anesthesia ventilator or, as mentioned, via the ECMO circuit.

4 | CONCLUSION

Our case report shows that ECMO therapy in life-threatening asthma can help buy time for the patient and the treating physicians. In our case, ECMO made inter-hospital transport possible in the first place. Furthermore, it was possible to build up a multi-layered drug therapy and avoid setbacks in the clinical course through the safety net of extra-corporal lung replacement. To the best knowledge, we report the first case with a combination of ECMO therapy and successful application of isoflurane via an ICU ventilator by the anesthetic conservation device in near-fatal asthma.

Our report represents one single course of treatment and cannot be generalized. Neither volatile anesthetics via an intensive care ventilator nor V-V ECMO can be considered the standard of patient care, even in severe asthmatics. Despite its increasingly widespread use, ECMO therapy remains a highly resource-consuming therapy option best discussed in an interdisciplinary team respecting risks, benefits, and contraindications.

AUTHOR CONTRIBUTIONS

Christoph Kowalewski: Conceptualization; writing – original draft. **Peter Schnürer:** Data curation; writing – review and editing. **Sabrina Kopp:** Data curation; writing – review and editing. **Johannes Windschmitt:** Data curation; writing – review and editing. **Mehmet Oezkur:** Data curation; writing – review and editing. **Marc Kriege:** Data curation; writing – review and editing. **Thomas Münzel:** Resources; software; supervision; writing – review and editing. **Joachim Kaes:** Data curation; writing – review and editing. **Ingo Sagoschen:** Resources; supervision; visualization; writing – original draft; writing – review and editing. **Johannes Wild:** Conceptualization; data curation; supervision; writing – original draft.

ACKNOWLEDGEMENTS

None. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest, especially no funding from Sedana Medical Germany GmbH.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

Written informed consent was obtained from the patient (patient's legal guardian) to publish any potentially identifiable images or data in this article. Further ethical review and approval were not required.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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How to cite this article: Kowalewski C, Schnürer P, Kopp S, et al. VV-ECMO as bridge and safety net for successful therapeutic polypragmasy in a case of influenza-triggered near-fatal asthma. *Clin Case Rep*. 2023;11:e7709. doi:10.1002/ccr3.7709