

Received: 2021.09.15

Accepted: 2022.01.10

Available online: 2022.02.17

Published: 2022.03.21

Use of Continuous Venovenous Hemodialysis (CVVHD) in Treatment of a Polytrauma Patient with Severe Hemophilia A

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

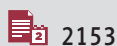
ABEF 1 **Renata Zajęzowska**ABEF 2 **Joanna Zorska**ABE 1 **Wojciech Serednicki**ABE 1 **Anna Wrzosek**ABE 1 **Jerzy W. Wordliczek**

1 Department of Interdisciplinary Intensive Care, Jagiellonian University, Medical College, Cracow, Poland

2 Center for Innovative Medical Education, Jagiellonian University, Medical College, Cracow, Poland

Corresponding Author: Renata Zajęzowska, e-mail: renata.zajczkowska@uj.edu.pl**Financial support:** None declared**Conflict of interest:** None declared

Patient: Male, 47-year-old
Final Diagnosis: Acute renal injury • bilateral pneumothorax • fractures of many bones • hemorrhagic shock • multi-organ trauma
Symptoms: Bilateral pneumothorax • hemorrhagic shock • multi-organ failure
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine

Objective: Congenital defects/diseases**Background:** There are very few reports in the literature worldwide on how to deliver continuous renal replacement therapy (CRRT) to patients with multi-organ trauma and severe hemophilia A. The aim of this case report is to describe successful multidisciplinary, intensive treatment of a patient with multi-organ trauma suffering from severe hemophilia A with the use of continuous venovenous hemodialysis with regional citrate anticoagulation (Ci-Ca CVVHD).**Case Report:** We report a case of a 47-year-old man with severe hemophilia A, who had multi-organ trauma as a result of a serious traffic accident and was admitted to the Trauma Centre of Emergency and Disaster Medicine in Krakow, Poland in critical condition. Due to elevated laboratory markers of kidney damage (creatinine 204 mmol/l, glomerular filtration rate (GFR) 32 ml/min/1.73 m²), very high myoglobin level (>1000 µ/l) associated with rhabdomyolysis, oliguria (diuresis <0.5 ml/kg/h), and overhydration as a consequence of massive transfusion of blood products and fluids, on day 2 after the injury Ci-Ca CVVHD was initiated as a part of intensive, multidisciplinary treatment. This approach proved to be successful in our patient as he was discharged from the Intensive Care Unit on day 45 after the injury in good general condition, with stable circulatory and respiratory system, without any apparent neurological deficits, and with good renal function (creatinine 50 mmol/l, GFR >60 ml/min/1.73 m²).**Conclusions:** Our case report shows that intensive, multidisciplinary treatment with implementation of Ci-Ca CVVHD may be an effective and safe method of care for patients with multi-organ trauma and hemophilia A.**Keywords:** Barotrauma • Continuous Renal Replacement Therapy • Critical CareFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/934802>

2153



2



8



Background

Continuous renal replacement therapy (CRRT) is a very useful method of dialysis, because of its unique characteristics compared with intermittent hemodialysis, which include excellent ability to precisely control fluid status and steady acid–base and electrolyte correction. CRRT provides slow and relatively gentle treatment, and it is indicated especially in hemodynamically unstable patients [1-3].

In the available medical literature, there are only a few reports referring to implementation of CRRT in patients with multi-organ trauma and hemophilia A [4]. CRRT in patients with hemophilia A is challenging for many reasons. The major problems include high risk of complications, both during establishing vascular access and during the therapy. Placement of central vascular catheters in patients with hemophilia is associated with high risk of bleeding. It is also challenging to prevent circle clotting during CRRT on the one hand, and avoid bleeding of the patient on the other hand. Another critically important issue is how to properly supplement factor VIII in such patients taking into consideration possible losses into dialysate.

This case report presents successful multidisciplinary, intensive treatment of a patient with multi-organ trauma suffering from severe hemophilia A with implementation of continuous veno-venous hemodialysis with regional citrate anticoagulation (Ci-Ca CVVHD).

Case Report

A 47-year-old man with severe hemophilia A had multi-organ trauma as a result of a serious traffic accident. The patient was brought to the Trauma Centre of Emergency and Disaster Medicine in Krakow with symptoms of a hemorrhagic shock (hemoglobin level in the first measurement was 2.6 g/dL) and exacerbating symptoms of bilateral pneumothorax. After admission to the Emergency Department (ED), vital functions of the patient were secured (endotracheal intubation, mechanical ventilation, infusion of fluids and catecholamines), bilateral pneumothorax drainage was inserted, and emergency transfusions of packed red blood cells (PRBC) type O negative, fresh frozen plasma (FFP) type AB, fibrinogen and factor VIII were performed. Immediately after that, the patient received a CT scan, which showed severe chest trauma with multiple, bilateral rib fractures, contusion of both lungs, bilateral pneumothorax and pneumomediastinum, fractures of the pelvis, an open fracture of the right thigh, and closed fractures of the right arm, right lower leg and metatarsal bones (**Figure 1**).

Due to the need to surgically stabilize the open fracture of the right thigh and to control the bleeding, the patient was immediately transported to the operating theater. Once the fracture was externally fixated, the patient was transferred to the Intensive Care Unit (ICU), where further treatment aimed at stabilization of vital functions and correction of the hemostatic disturbances was continued. Initially, the patient required

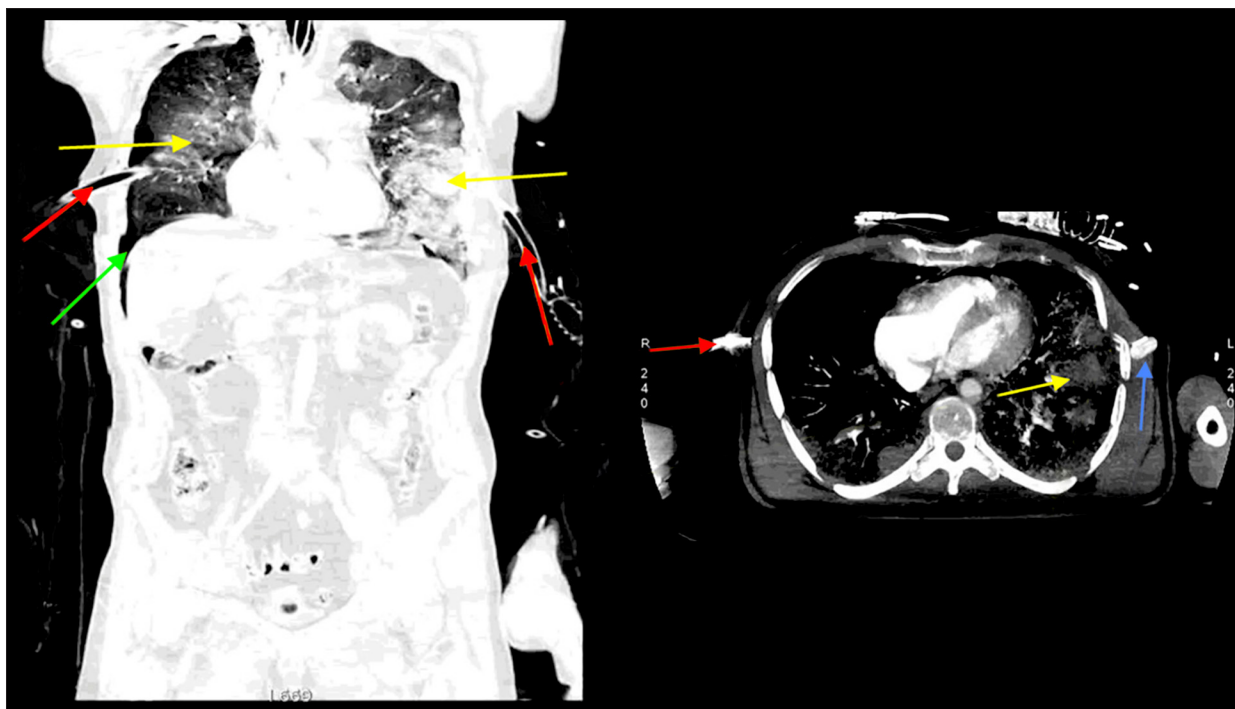


Figure 1. CT scans of first examination: yellow arrows – well-defined consolidation might correspond to the contusion of the lungs; red arrows – drains; green arrow – pneumothorax; blue arrow - broken ribs.

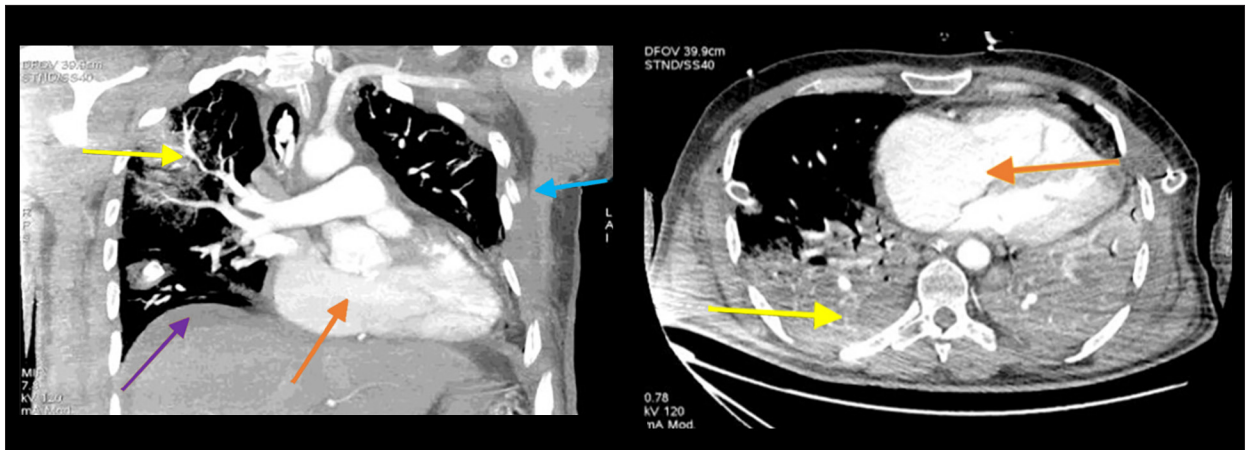


Figure 2. Control CT scans (on day 3): yellow arrows – consolidations might correspond to a contusion of the lungs; orange arrows – heart enlarged in the transverse dimension; blue arrow – broken ribs; purple arrow – fluid in the abdominal cavity.

ventilation with high oxygen concentrations (fiO_2 0.7-0.8), infusion of high doses of norepinephrine, and transfusion of further units of factor VIII, PRBC, FFP, platelet concentrates (PC), and fibrinogen.

Findings of the CT performed on admission to the ICU included: a massive contusion of both lungs, normal echocardiographic image of the left heart with the ejection fraction (EF) of 55%, while the image of the right heart showed dilatation and overload with mildly elevated pulmonary artery pressure, moderate tricuspid insufficiency, and a 30-mm-wide inferior vena cava. Due to elevated laboratory markers of kidney damage (creatinine 204 mmol/l, glomerular filtration rate (GFR) 32 ml/min/1.73 m²), very high myoglobin level (>1000 µ/l) associated with rhabdomyolysis, oliguria (diuresis <0.5 ml/kg/h), overhydration as a consequence of massive transfusion of blood products and fluids, further need for transfusion of PRBC, FFP, PC, fibrinogen, and factor VIII to ensure hemostasis, and need for enteral and parenteral nutrition in the subsequent days, on day 2 after the injury, renal replacement therapy was initiated in the form of continuous veno-venous hemodialysis with regional citrate anticoagulation (Ci-Ca CVVHD). The initial settings of CVVHD parameters were: blood flow 120 ml/h, dialysate flow 2000 ml/h, and ultrafiltration 150 ml/h.

On day 3, the patient's exacerbating symptoms of hemodynamic instability prompted us to increase the norepinephrine dosage. Echocardiography findings included acute tricuspid valve dysfunction with fourth-degree regurgitation and a detached fragment of the papillary muscle, further increase in the size of the right ventricle and the right atrium, presence of regurgitation in the pulmonary trunk, and progressive enlargement of the inferior vena cava. The patient was consulted by cardiac surgeons, who decided that a surgical intervention using cardiopulmonary by-pass was unadvisable at the moment due to the serious condition of the patient (Figure 2).

On subsequent days the treatment was continued. Due to the need for prolonged ventilation, after the preparation of the patient and obtaining optimal coagulation parameters, percutaneous tracheotomy using the Griggs method was performed. Additionally, starting on day 9, a progressive increase in bilirubin and liver enzyme levels was observed. Subsequent imaging studies (ultrasound and CT) of the abdomen showed an enlarged liver, most probably due to pathological changes secondary to heart failure. Over the next several days, the patient's condition stabilized, which made it possible to reduce the oxygen concentrations and the dose of norepinephrine. Drains were also removed from the pleural cavities. Additionally, the previously elevated liver parameters and inflammatory markers gradually declined. Due to the normalization of kidney parameters (creatinine 50 mmol/l), satisfactory diuresis, and stabilization of echocardiographic findings, CVVHD was discontinued after 14 days. The improvement in the patient's general condition made it possible to surgically stabilize the fractures. The patient was consulted again by a team of cardiac surgeons and qualified for tricuspid valve reconstruction surgery, optimally after stabilization of respiratory and hematological status.

In subsequent days, the dosage of sedatives was gradually reduced, and on day 33 after the injury, the patient was weaned from the mechanical ventilation. He was conscious, improving neurologically, and after the tracheostomy tube was replaced with the phonation one, also able to speak. At that time, he underwent intense rehabilitation. As the patient was able to tolerate a more varied diet orally, parenteral nutrition was discontinued. In laboratory tests, a normalization of liver and kidney parameters as well as a steady decrease in inflammatory markers were observed. On day 45 of hospitalization, the patient was discharged from the ICU. He was in a good general condition, conscious, without neurological deficits, with stable cardiopulmonary and respiratory functions, and with normal

kidney parameters and diuresis. He was scheduled for tricuspid valve reconstruction surgery in 3 months' time.

Discussion

Hemophilia A is an inherited, genetic, chromosome X-linked disease which causes factor VIII deficit. Clinically, the disease presents as a bleeding diathesis, and the severity of the symptoms depends on the percentage of factor VIII deficiency. Severe hemophilia A is recognized when the factor VIII serum concentration is below 1% of normal value. The state-of-the-art treatment for hemophilia A is a replacement therapy with recombinant factor VIII, with a replacement dose depending on the severity of the disease and the current clinical situation [5].

Analyzing the course of events, it should be emphasized that in our patient the crucial element of the successful treatment was an early identification of hemophilia A by the Medical Rescue Team at the site of the accident and immediate administration of factor VIII by the Team (the patient had 2000 units (U) of factor VIII in his car). Moreover, a local blood bank was promptly informed by the Medical Rescue Team, which allowed prior securing of the intended dose of factor VIII and its quick administration right after hospital admission.

Due to the severity and extent of trauma, our patient required interdisciplinary treatment with involvement of many specialists in different fields. Right after admission to the ED, advance life support was started, including tracheal intubation, mechanical ventilation, pleural drainage, catecholamine infusion and transfusion of PRBC, FFP, PC, fibrinogen, factor VIII, and crystalloids, which were continued later in the ICU. In the subsequent days the patient underwent many invasive procedures, including percutaneous tracheostomy. On the first hospital day, he had external stabilization of femoral fracture, which was followed, after stabilization of his condition, by final orthopedic surgeries. All these procedures, due to coexistent hemophilia A and coagulopathy secondary to massive bleeding, involved a high risk of bleeding and required careful preparation and transfusion of factor VIII. According to available reports in the medical literature [6] and our hematologist's recommendations, we were aiming at factor VIII levels of around 80-100%. The factor VIII requirement was calculated based on the information that administration of 1 U of factor VIII per kilogram of body weight results in a factor VIII increase of approximately 2%. Because the half-life of factor VIII is 12 h, we administered it twice a day and monitored its levels daily [6].

In our opinion, an important role in the success of the therapy was played by early initiation of renal replacement therapy in the form of Ci-Ca CVVHD. The decision to start Ci-Ca CVVHD was made because of acute renal failure secondary to shock

and rhabdomyolysis and the significant volume burden placed on the patient's cardiovascular system, including both blood products and infusion fluids (crystalloids, colloids) resulting from the need to replace the blood loss and to ensure optimal tissue perfusion. Continuing Ci-Ca CVVHD also helped during the most difficult period of treatment of lung contusion and right ventricular failure, until lung and heart function improved with a concomitant decline in pulmonary vascular resistance. It should be emphasized that the decision to use Ci-Ca CVVHD in the case of our patient was a difficult one, because of the lack of our own experience in this group of patients and the scarcity of reports in the medical literature worldwide on how to deliver continuous renal replacement therapy (CRRT) to patients with severe hemophilia A [4]. The decision was made after an in-depth analysis of benefits and risks associated with potential complications. CRRT in patients with hemophilia A is challenging for many reasons. The major problems include high risk of complications, both during establishing vascular access and during the therapy. Placement of central vascular catheters in patients with hemophilia is associated with high risk of bleeding. It is also challenging to prevent circle clotting during CRRT on the one hand, and avoid bleeding of the patient on the other hand. Another critically important issue is how to properly supplement factor VIII in such patients, taking into consideration possible losses into dialysate. We decided to use regional citrate anticoagulation (RCA), because RCA compared with heparin anticoagulation is associated with significantly lower risk of bleeding, less blood transfusions, and extended life of the extracorporeal circuit [7,8]. It was especially important in our patient, because the risk of bleeding was very high due to his severe hemophilia A.

It is critically important in patients with hemophilia A to properly supplement the deficient factor VIII. As recommended by the patient's hematologist, factor VIII levels were monitored daily and the replacement doses were titrated to achieve 80-100% of serum activity in the acute phase of the disease. We had not found information in the literature on whether and to what extent factor VIII is removed during CRRT. Also, the manufacturer of the filter we used was unable to provide us with such information. Therefore, we measured serum concentration of factor VIII daily and guided the supplementation by these results. We considered it to be the only reasonable and effective way to supply the patient with the adequate dose. We observed that in order to maintain the desired serum level of factor VIII during Ci-Ca CVVHD, it was necessary to increase its dosage by an average of 15 U/kg during circuit replacement.

Our approach proved to be successful in our patient, as he was discharged from the ICU on day 45 after the injury in good general condition, with stable circulatory and respiratory system, without any apparent neurological deficits, and with good renal function (creatinine 50 mmol/l, GFR >60 ml/min/1.73 m²).

This treatment outcome was a source of great satisfaction for the whole team involved in caring for the patient, since the severity of the original injury, the patient's condition on admission, including extremely low hemoglobin level (Hb 2.6 g/dL) combined with a severe lung injury, raised serious concerns about consequences of organ hypoxia. Fortunately, multidisciplinary intensive treatment protected the patient from such an untoward course of the disease. Three months later, the patient had a minimally invasive tricuspid valve reconstruction via a right minithoracotomy with extracorporeal circulation. The procedure was uncomplicated. Currently, the patient is in a good condition and is returning to his activities from before the accident.

References:

1. Hafner S, Stahl W, Fels T, et al. Implementation of continuous renal replacement therapy with regional citrate anticoagulation on a surgical and trauma Intensive Care Unit: Impact on clinical and economic aspects – an observational study. *J Intensive Care*. 2015;3(1):35
2. Karkar A, Ronco C. Prescription of CRRT: A pathway to optimize therapy. *Ann Intensive Care*. 2020;10(1):32
3. Beitland S, Os I, Sunde K. Primary injuries and secondary organ failures in trauma patients with acute kidney injury treated with continuous renal replacement therapy. *Scientifica (Cairo)*. 2014;2014:235215
4. Sakan S, Bandic D, Peric M, et al. Renal replacement therapy in a polytraumatized patient with hemophilia. *Acta Med Croatica*. 2012;66(3):247-50
5. Coppola A, Morfini M, Cimino E, et al. Current and evolving features in the clinical management of haemophilia. *Blood Transfus*. 2014;12(Suppl. 3):554-62
6. Reinke Ch, Spodeck A, Schildhauer TA, Swol J. Haemophilia A in a major trauma patient. *BMJ Case Rep*. 2015;2015:bcr2015211694
7. Bai M, Zhou M, He L, et al. Citrate versus heparin anticoagulation for continuous renal replacement therapy: An updated meta-analysis of RCTs. *Intensive Care Med*. 2015;41(12):2098-110
8. Borg R, Ugboma D, Walker DM, Partridge R. Evaluating the safety and efficacy of regional citrate compared to systemic heparin as anticoagulation for continuous renal replacement therapy in critically ill patients: A service evaluation following a change in practice. *J Intensive Care Soc*. 2017;18(3):184-92

Conclusions

This report describes a successful treatment with Ci-Ca CVVHD as a part of multidisciplinary, intensive treatment of patient with polytrauma and severe hemophilia A. Our case report shows that such an approach may be an effective and safe method of treatment in this group of patients. However, further studies are needed to confirm our findings and to optimize this method of treatment in patients with hemophilia.

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.