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LETTER TO THE EDITOR

Management of an adult patient with sickle cell disease and acute chest syndrome by veno-venous extracorporeal membrane oxygenation

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Dear Editor,

A 21-year-old male patient of a sub-Saharan African descent with homozygote sickle cell disease (SCD) on hydroxyurea therapy was transferred from another hospital to our institution with acute respiratory failure. He had a history of multiple vaso-occlusive crises, salmonella sepsis with multiple organ failure, intracranial bleedings requiring surgical evacuation and bone infarction of hips and vertebral bodies. Initially, he had presented at his local hospital with a pain crisis and was treated with fluids and intravenous opioids. Nonetheless, he developed an increasing loss of vigilance and hypoxemia as well as purulent sputum within 1 day. Anti-infective therapy with piperacillin/tazobactam was initiated. Lab chemistry showed intravascular haemolysis, thrombocytopenia and acute renal failure. Upon referral to our institution, the patient was intubated due to respiratory failure and required norepinephrine at a dose of 1000 μg/h to maintain an acceptable mean arterial pressure (MAP) > 50 mmHg. Ciprofloxacin was added to the empiric anti-infective regimen to account for possible atypical pneumonia. Chest X-ray showed extended bilateral consolidations (Fig. 1a). Working diagnosis was infection-triggered very severe acute chest syndrome (ACS) with acute respiratory distress syndrome (ARDS). After initial cardiopulmonary stabilisation, the patient showed progressive multiorgan failure including cardiac failure, anuric renal failure and liver failure (Table 1). To overcome global respiratory insufficiency with a Horowitz index of 56 despite optimised conventional ventilatory support (BIPAP, FiO2 1.0, PEEP 12 cm H_2O, P_{max} 29 cm H_2O, Freq 20/min, I:E 1:1) veno-venous extracorporeal membrane oxygenation (vv-ECMO) was initiated. Subsequently, bronchoalveolar lavage returned PCR-positive for rhinovirus as well as Chlamydia pneumoniae. Echocardiography showed a severely reduced left ventricular function with an ejection fraction of less than 20% so that dobutamine was added to noradrenaline to maintain adequate MAP. Renal replacement therapy was initiated via sustained low-efficiency daily dialysis (SLEDD). Hb electrophoresis showed an HbS proportion of 96% and blood smear microscopy showed a sickle cell proportion of 9‰. Red blood cell exchange was thus performed daily over 3 days until HbS levels reached 9%. By these measures, cardiopulmonary stabilisation was achieved and the patient was successfully decannulated after 7 days and subsequently could be extubated after 14 days. Chest X-ray showed complete resolution of the pulmonary consolidations (Fig. 1b). Renal function remained impaired with elevated creatinine values of up to 9 mg/dl, however, no further dialysis was required after 18 days as electrolytes were normal, urea levels only mildly elevated to 80 mg/dl and diuresis was restored. The patient was transferred to our intermediate care unit and subsequently to the haematology ward, where hydroxyurea therapy was restarted. The patient reported blurred vision, and ophthalmologic examination revealed a beginning glaucoma as well as sickle cell retinopathy, which required vessel photocoagulation. The patient was discharged 4 weeks after admission in good condition and preparations for allogeneic stem cell transplantation were initiated.

Our report demonstrates the successful use of vv-ECMO in an adult SCD patient with very severe ACS. Due to global migration, SCD has become more frequent in Western Europe [1] and ACS remains the leading cause of death in adult SCD patients [2]. ECMO is an established intervention to manage severe ARDS patients with continued respiratory insufficiency despite conventional mechanical ventilation [3, 4]. Currently, reports on the use of ECMO in SCD have mainly derived from paediatric patient populations and only a few reports on adult patients are available [5–7]. Given the high frequency of comorbid conditions in adult patients with ACS

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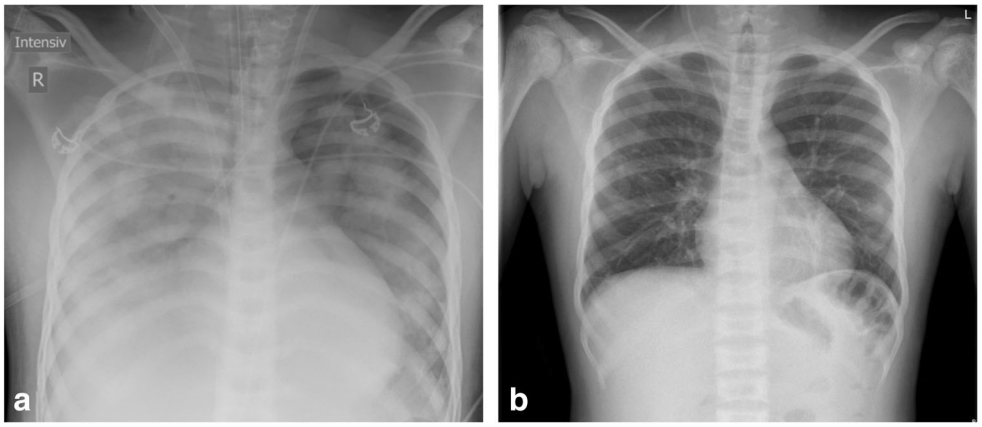

Fig. 1 Chest x-ray on admission, day 1 (**a**). The patient was intubated and a venous cannula was inserted in the right internal jugular vein, the other cannula was placed in the right femoral vein [not visible]. Chest x-ray on day 22 (**b**). The patient is extubated and decannulated, a central venous catheter was placed in the right internal jugular vein.

due to pre-existent organ damages caused by vaso-occlusion such as chronic heart failure, chronic kidney disease and pulmonary hypertension, the use of ECMO in this group of patients is challenging. ECMO frequently causes haemolysis due to the continuous extracorporeal blood flow which can potentiate vaso-occlusive crises in SCD patients. Moreover, chronic anaemia in SCD patients can be a challenge since the efficacy of ECMO highly depends on sufficient Hb levels and, therefore, frequent red blood cell transfusions are required. In our case, transfusion management was complicated due to the presence of alloimmunization with anti-Fy^a, anti-S and anti-E antibodies. Therefore, extended antigen matching prior to each transfusion was necessary and compatible donors had to be called in by the blood bank to ensure supply with compatible red cell concentrates. A priority consisted in the prevention of sickling and hyperhaemolysis during ECMO by avoiding triggers like hypoxaemia, hypercapnia and acidosis. We decided to initiate therapy with vv-ECMO to allow optimal medical treatment of vaso-occlusion which we judged to be the central driver of the patient's poor condition. However, given the coexistent cardiogenic shock in our patient, we considered switching to veno-arterial ECMO as a backup strategy if the cardiac dysfunction would not resolve upon improved oxygenation and erythrocyte exchange. A further challenge of the use of ECMO in SCD patients is the necessity of anticoagulation to maintain continuous flow within the ECMO circuit. In our case, the patient had experienced cerebral bleedings 3 months prior to the current admission. Eleven percent of SCD patients have already experienced strokes at the age of 20 years [8], so there is a high risk of haemorrhagic transformations in this group of patients. In our case, careful monitoring of coagulation parameters several times daily allowed sufficient control of haemostasis so that no major haemorrhages or clots in the ECMO filter occurred during hospitalisation.

Table 1 Laboratory data at ICU admission

Parameter	Reference range	Value
Sodium	135–145 mmol/l	139
Potassium	3.6–4.8 mmol/l	5.5 ↑
Chloride	94–110 mmol/l	105
Glucose	74–109 mg/dl	97
Calcium	2.04–2.59 mmol/l	1.72 ↓
Phosphate	0.81–1.45 mmol/l	1.25
Albumin	35–52 g/l	18 ↓
Creatinine	0.50–1.10 mg/dl	2.18 ↑
Urea	< 50 mg/dl	47
Uric acid	3.4–7.0 mg/dl	4.8
GOT	< 50 U/l	4004 ↑
GPT	< 50 U/l	1558 ↑
gGT	< 60 U/l	43
Bilirubin	< 1.2 mg/dl	4.4 ↑
CK	< 190 U/l	7349 ↑
LDH	< 250 U/l	4776 ↑
Haptoglobin	0.3–2.0 g/l	<0.2 ↓
CRP	< 5.0 mg/l	149 ↑
PCT	<0.1 μg/l	160 ↑
Leukocytes	4.4–11.3 G/l	6.1
Haemoglobin	13.5–18.0 g/dl	11.6 ↓
Thrombocytes	150–400 G/l	79 ↓
INR		2.6
APTT	< 36 s	79

In summary, this report presents the successful use of ECMO support in a patient with severe ACS. Given the multiple organ dysfunctions caused by SCD, management of ACS with ECMO is challenging but feasible. Further research is needed to evaluate the indications, management and outcomes of ECMO in patients with SCD and ACS.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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