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Research Article

Disorders of blood oxygenation during extracorporeal membrane oxygenation for AH1N1 pneumonia in exacerbated chronic myeloid leukemia treated by initiation of chemotherapy

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Abstract:

Patients with severe acute respiratory distress syndrome require supportive treatment with mechanical ventilation with or without extracorporeal membrane oxygenation to maintain optimal oxygenation. Persistent inefficient blood oxygenation can be related to severity of clinical presentation, technical issues, or concomitant diseases. In this case report, man previously suffering from chronic myeloid leukemia received extracorporeal membrane oxygenation for influenza A virus subtype H1N1. Despite invasive oxygenation therapy, it was not possible to achieve amelioration of arterial blood oxygenation. After a differential diagnosis, pathological hyperleukocytosis was identified as a potential reason of oxygenation impairment, which improved after introduction of concomitant chemotherapy that lowered leukocytes count.

Keywords: extracorporeal membrane oxygenation; mechanical ventilation; acute respiratory distress syndrome; chronic myeloid leukemia

1.Introduction

Acute respiratory distress syndrome (ARDS) represents a severe form of respiratory failure characterized by bilateral pulmonary infiltrates and hypoxemia [1]. While ARDS can arise from various etiologies, including infectious pathogens such as the influenza A virus subtype H1N1 (AH1N1), its management remains challenging, particularly in patients with underlying hematologic malignancies. Chronic myeloid leukemia (CML), a myeloproliferative disorder (MPD) characterized by the Philadelphia chromosome, poses additional complexities in the treatment of ARDS due to potential complications such as hyperleukocytosis. This case report presents the clinical course and management of a patient with CML who developed AH1N1-ARDS requiring ECMO. Also, it is highlights the diagnostic and therapeutic strategies employed to address refractory hypoxemia, with a focus on the role of hyperleukocytosis in exacerbating respiratory compromise.

2.Methods

An analysis of patient's electronic and paper records was conducted. Response to treatment was closely monitored through serial arterial blood gas analysis, laboratory parameters, and clinical assessments. Improvement in oxygenation parameters and leukocyte counts served as primary outcome measures. The patient underwent multiple per day follow-up assessments to evaluate treatment response, disease progression, and potential complications. The Institutional Review Board (IRB) or equivalent ethics committee of the NCU did not approve this study because it was a retrospective case report involving a single patient. Furthermore, all data were anonymized to protect patient privacy, and the report was created solely for educational and informational purposes, adhering to ethical guidelines for case reporting without the need for formal IRB review. Patient written consent for the publication of the study was not received as he passed away.

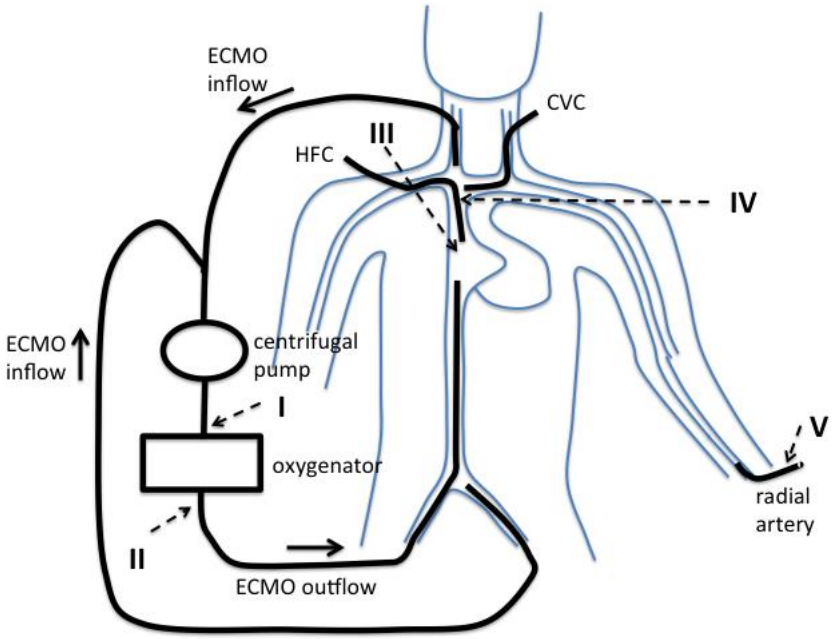
3.Results

A 42-year-old male was admitted to a University Hospital intensive care unit (ICU) due to increasing hypoxia and severe ARDS caused by viral AH1N1 pneumonia (confirmed by PCR test). The patient was previously managed for 1 day in a county hospital and was transferred to a hospital of a higher reference as his condition worsened. Additionally, he presented with exacerbation of chronic myeloid leukemia (CML) with hyperleukocytosis (360 000-480 000/mm^3), detected by blood tests and bone marrow examination. At admission, the patient fulfilled all the criteria of severe ARDS and was treated with intensive conventional therapy consisting of mechanical ventilation, positioning therapy, and infection control [1, 2]. Antibiotic therapy consisting of imipemene/cilastatin, linezolid, caspofungine, colistine, sulfamethoxazole/trimethoprime, oseltamivir and acyclovir was carried out from the beginning until the 12th day of treatment, when oseltamivir was discontinued, and linezolid was switched to vancomycin. This composition of antibiotic therapy was continued unchanged until the end of the patient's treatment. The treatment plan included implementing ECMO if conventional therapy did not improve patient's condition due to multiple relative contraindications: duration of mechanical ventilation, neoplastic disease, PaO_2/FiO_2 = 140-190 and oxygenation index OI = 15 – being outside the ranges recommended by the Polish Society of Anesthesia and Intensive Care[3]. His clinical condition improved for the first 8 days of ICU stay, allowing for consideration of extubation, followed by noninvasive ventilation within a short-term treatment plan. On the 9 th day of ICU stay, sudden aggravation of clinical condition, with increasing hypoxia prompted the decision of initiating veno-venous ECMO therapy that, unexpectedly, did not improve blood oxygenation (Table 1). Despite high flows of blood (4.6 L/min on centrifugal pomp) and gases (10 L of 100% O_2/min on oxygenator), no more than PaO_2 56 mmHg was achieved (from radial artery, Figure 1, point V) not allowing for induction of minimal, ultraprotective ventilation[4, 5]. ECMO parameters remained unchanged during the time of treatment: Blood flow on the centrifugal pump was set at 4 L/min (besides day 9, before chemotherapy, when it was set at 4.6 L/min) and gas flow on the oxygenator was set at 10 L/min of 100% L O_2.

Day in the ICU		**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**17**
Day of ECMO		-	1	2	3	4	5	6	7	8	9	-
Day of chemotherapy		-	-	1	2	3	4	5	-	-	-	-
Leukocytes K/mm^3		254	235	240	266	314	97	38	12	4,1	1,3	1,3
PO2	I		41								41	
	II		577	550	484				487	450	430	
	III		97	101	103	74	73	152	193	357	302	
	IV		30	34	46	48	43	40	38	45		
	V	60	58	54	65	84	70	62	57	66	61	99
FiO2 (ventilator)		1	1	1	1	1	0,9	0,55	0,5	0,4	0,3	0,35
IPAP/EPAP		22/18	22/18	22/18	22/15	25/15	25/15	20/13	17/10	17/8	14/8	SIMV, 13/6 Vt 0,45
Oxygenation index OI		33,3	34,5	37,0	28,5	22,0	23,8	14,6	11,8	8,2	5,4	3,4

Table 1: Modification of the parameters of gas exchange (partial pressure of oxygen PO2) in different places of blood samples aspiration and BGA, respiratory parameters set on the ventilator (FiO2, inspiratory pressure IPAP, expiratory pressure EPAP) during BIPAP ventilation and oxygenation index OI on consequent days of chemotherapy. Oxygenation index OI = FiO2x P_{AWmean}/PaO2, where P_{AWmean}- mean airway pressure

As the arterial oxygenation did not improve, PO2 was analysed on different levels of the patient's circulatory system and ECMO system (Figure 1) and massive oxygen consumption due to hyperleukocytosis was suspected to be the underlying reason [6]. Leukapheresis was conducted on day 9 and 10 of the ICU stay, however, it had no cytoreduction effect. Evaluating potential benefits and risks within a multidisciplinary team, a 5-day chemotherapy, based on methylprednisolone, fludrabine, fasturtek and rituximab was introduced on the 10^{th} day of the ICU stay. From day 4 of chemotherapy leukocytosis declined, preceded by improvement of oxygenation, which allowed for induction of minimal ventilation. To confirm the influence of hyperleukocytosis on the patient's oxygenation, blood was sampled from different, accessible points of the patient's circulatory system and of the ECMO circuit (Figure 1). The ECMO therapy was terminated 9 days after cannulation, when patient had normal PaO2 levels, at FiO_2 0,35 and low mechanical ventilation pressures, were possible (Table 1). ECMO therapy was interrupted after an abrupt deterioration of neurological condition secondary to intracranial hemorrhage, which was evacuated by neurosurgeons the same day. The patient's neurological condition continued to deteriorate and on day 23 of ICU treatment brain death was confirmed.



Central Picture. The placement of cannulas insertion and sample aspiration for blood gases analysis.

I. The inflow of venous blood to the oxygenator, II. The outflow of the oxygenated blood from the oxygenator, III. The right atrium (from hemofiltration cannula, distal channel), IV. Superior vena cava (from the central venous catheter, distal channel), V. Radial artery. HCF – hemofiltration catheter, CVC – central venous catheter. Blood was aspirated to ECMO by 2 27F catheters from the right internal jugular vein and left iliac vein and returned to the right atrium by right iliac vein and inferior vena cava.

Central Message

In severe ARDS, ECMO may fail to improve oxygenation due to factors like hyperleukocytosis, as seen in a 42-year-old CML patient with AH1N1-ARDS, whose condition improved post-chemotherapy.

4.Discussion

The ineffectiveness of ECMO in ameliorating oxygenation during hyperleukocytosis could had been caused by pathological oxygen consumption in CML. After excluding the technical reasons for abnormal blood oxygenation, we considered the abovementioned phenomenon, previously described by Chillar [6]. To validate this hypothesis, we compared PO2 measured in blood samples taken from different places of ECMO machine and circulatory system of the patient

The oxygen consumption cascade in a blood sample before and after cytoreduction was not performed (PO_2 measurement immediately after sampling and after every 1 minute) as it was done by Chillar [6] due to immediate leukocyte sedimentation in blood samples, resulting in the inability to maintain blood in a liquid state allowing PO2 measurement. The improvement of PO_2 on days 2-3 of chemotherapy, before observed leukocyte reduction, can result from impairing the metabolic function of leukocytes and its oxygen intake before the definitive cell destruction [7, 8]. The effect of antimicrobial treatment does not appear to be temporally related to improved arterial oxygenation. No improvement in oxygenation in the lungs was observed until the start of chemotherapy. Modification of antibiotic therapy by the inclusion of vancomycin also seems to have no effect on the improvement of oxygenation, as a significant reduction in OI was observed already on the 11th day of treatment - 1 day after the initiation of chemotherapy but before the inclusion of vancomycin. Antibiotics in practically unchanged composition were used from the beginning throughout the patient's treatment. Only on the 12th day of treatment, oseltamivir was discontinued and vancomycin was introduced, while linezolid was discontinued. Previous reports described attempts on leukapheresis in patients treated with ECMO for respiratory failure caused by hyperleukocytosis, which enabled efficient oxygenator function. One case report presented a patient receiving induction chemotherapy for acute myelogenous leukemia concomitantly undergoing venovenous ECMO that also experienced subarachnoid hemorrhage. To our knowledge, no previous report addressed a clinical case of concomitant ARDS due to AH1N1 pneumonia with concomitant hyperleukocytosis caused by CML, requiring ECMO therapy and chemotherapy due to leukapheresis futility. The current case shows that aggressive and multimodal approach in complicated patients could be effective in the treatment of critical cases. Closer coagulation monitoring and management would be required.

Some limitations of the current case report can be outlined. PO2 measurements were not done at the end of the ECMO arterial line (before entering the iliac vein), but at the beginning of the line (after the oxygenator) (Figure 1, point II). Comparing PO_2 at the length of the ECMO arterial line could indicate the existence of a significant fall of O_2 inside the cannula, where no other sources of oxygen consumption besides blood cells can exist. While the interpretation of the results of PO_2 measurements in the other points, accessible for blood sampling (Fig 1), is not evident, the procedure can be hazardous, especially when full anticoagulation therapy is obligatory, due to the risk of perforating the cannula resulting in the need of replacement.

PO_2 in the right atrium (point III) is a function of different PO2 in blood flows form the oxygenator (PO_2 around 500 mm Hg, constant flow 4.6 L/min) and great veins (PO2 around 40 Hg, flow not possible to measure, undoubtedly variable in critically ill). So the proportions of the two blood flows were variable and the resulting PO2 was variable as well. The mean of PO2 from several samples was analyzed to overcome the problem. The difference of PO2 levels between right atrium (point III) and in the radial artery could be the best parameter reflecting blood O2 consumption. Between the two points, there are no tissues consuming O2, besides the blood itself. PO2 is physiologically lowered by venous admixture from the bronchial arteries (but there is no reason that its flow changed during treatment) and pathologically in the case of congenital heart defect (excluded by the transesophageal echocardiography). Right-left heart blood flow (if present) could even increase the radial artery PO_2 because of high oxygen levels (around 100-180 mm Hg) in the right atrium blood during ECMO therapy.

The metabolic activity of the leukemic infiltrates which are likely to occur in the lungs, and its influence on arterial oxygenation is unknown and difficult to measure.

While oxygenation index OI is not a parameter adapted for assessing oxygenation during ECMO therapy, at unchanged flows of blood (at the centrifugal pump) and gases (on oxygenator) it can correctly reflect the improvement of gas exchange[9, 10].

5.Conclusions

The clinical course, time correlation between oxygenation improvement and the decrease in the number of leukocytes can indicate hyperleukocytosis as a dominant factor determining the problems of blood oxygenation and the lack of efficacy of ECMO therapy. That can indicate the necessity to consider cytoreduction therapy in leukemic patients with hyperleukocytosis treated for ARDS.

Conflict of Interest

The authors declare that they have no conflict of interest.

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