

Successful Mobile ECMO In COVID-19 and Varicella Patient: Case Report

Andrijevic A^{1,2*}, Carapic V^{1,2}, Gavrilovic S¹, Matijasevic J^{1,2}, Andrijevic I^{1,2} and Batranovic U¹

¹Intensive Care Unit, Institute for pulmonary diseases of Vojvodina, Sremska Kamenica, Serbia

²Medical faculty, University of Novi Sad, Novi Sad, Serbia

*Corresponding author: Andrijevic Ana, Intensive Care Unit, Institute for pulmonary diseases of Vojvodina, Sremska Kamenica, Serbia



ARTICLE INFO

Received:  December 20, 2021

Published:  January 10, 2022

Citation: Andrijevic A, Carapic V, Gavrilovic S, Matijasevic J, Andrijevic I, Batranovic U. Successful Mobile ECMO In COVID-19 and Varicella Patient: Case Report. Biomed J Sci & Tech Res 40(5)-2022. BJSTR. MS.ID.006519.

SUMMARY

Up to this date the World Health Organization had recorded more than 270 million confirmed cases of SARS CoV-2 infection, with over than 5 million deaths. Many hospitalized patients developed critical illness, requiring extracorporeal membrane support. In Serbia, there is only one center with experience in this technique. Some patients develop severe form of acute respiratory distress syndrome and cannot be transferred to reference hospital just by using conventional mechanical ventilation. This case reported successful treatment and first interhospital transport in Serbia of severe SARS CoV-2 and primary varicella co-infection using extracorporeal membrane oxygenation.

Keywords: Extracorporeal Membrane Oxygenation; Mobile ECMO; Covid-19; Acute Respiratory Distress Syndrome; Varicella

Background

Last year declaration of the coronavirus outbreak as pandemic by World Health Organization was followed by rising number of patients infected with SARS-CoV-2 requiring hospitalization and intensive care unit (ICU) admission [1]. Although mechanically ventilated patients fulfilled criteria for acute respiratory distress syndrome (ARDS) by Berlin definition of ARDS [2], some distinctive features of SARS-CoV-2 infection made this ARDS more difficult to treat [3]. The Surviving Sepsis Campaign Guidelines released in January this year suggested to use venovenous ECMO in mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, use of rescue therapies and proning [4].

Case Presentation

We present the case of thirty-nine-year-old male patient, without other pre-existing conditions, who was admitted to remote

University Hospital due to the bilateral covid pneumonia, proven by PCR analysis of nasopharyngeal swab. During the sixteen-days hospitalization period he was treated with oxygen therapy, corticosteroids, tocilizumab, and other supportive therapy. On the day of the planned hospital discharge, fever appeared as well as maculopapular rash on the skin of the face and in the oral cavity. Additional anamnestic data revealed that a few days prior to the hospital admission the patient's children suffered from chickenpox. Serological enzyme-linked immunosorbent assay confirmed high levels of Varicella Zoster IgM antibodies and acyclovir treatment was initiated. The patient's condition rapidly deteriorated, respiratory failure required invasive mechanical ventilation, including the trial of prone position, with PaO₂/FiO₂ ratio of 85. Hypotension was bridged with the use of vasopressors. Severe refractory hypoxemia with Murray Score for Acute Lung Injury of 3.5 was the indication for VV-ECMO.

ECMO circuit was set by ultrasound guided placing of stiff wires in the right jugular vein and right femoral vein, followed by radiographic confirmation of adequate wire positions. Next, the cannulas were placed and the ECMO procedure with ultraprotective mechanical ventilation (Volume Control Ventilation, Tidal Volume 280ml, PEEP 12cmH₂O, RR 12, FiO₂ 0.6, plateau pressure 22cmH₂O) was started. On Day 3, after the hemodynamic stabilization was achieved, the patient was transferred to our ICU. Although ECMO transports are considered as high-risk and complex, this was the first interhospital transport on ECMO in Serbia and it went neatly. Team members included an anesthesiologist accompanied by ICU physician and ICU nurse. No staff has been proven infected during transport. The duration of the transport, defined by the time of leaving the hospital until arriving to our ICU, was not greater than 15 minutes. Potential ECMO transport complications were reduced by using our previously made ECMO checklists for interhospital transport.

For the time while VV-ECMO was performed the patient tailored anticoagulation was done with use of heparin, with targeted APPT-R of 1.5-2.0. Functional antithrombin III level was always above 80%. We did not observe any thrombotic circuit complication, nor bleeding. Platelet count were at the bottom level of normal range. Native lung shunt was 37% at the beginning, while membrane lung shunt was 23% and there were no major deviations in shunt percentages during the procedure. On the eleventh day of ECMO procedure, ECMO weaning was successfully done. Specimens submitted for microbiological testing at admission were negative. However, ICU stay was accompanied by *Acinetobacter cloaceticus* ventilator associated pneumonia treated with combined intravenous and nebulized colistin. Direct therapy led to significant clinical improvement within 24 hours. The day after ECMO weaning the patient was extubated. Nevertheless, severe ICU delirium along with urosepsis appeared so the patient was reintubated.

Bacteriological analysis of urine confirmed the presence of *Enterococcus faecalis*, wherefore carbapenem was added to the therapy. After three days the patient was successfully weaned from mechanical ventilation again. Three weeks after ICU admission he was transferred to the step-down unit. Further hospital stay was accompanied with intensified respiratory rehabilitation, cough, and expectoration stimulation. With the help of a physiotherapist the patient managed to start walking and perform active exercises a week after ECMO weaning. A color duplex scan of veins and arteries of the lower extremities was performed and was described as normal, while a color duplex scan of the neck and arms showed partial thrombosis in the jugular vein where ECMO cannula was

placed. After thirty days of hospital treatment the patient was discharged home. He was recommended to use a home oxygen concentrator until the scheduled check-up as well as apixaban.

Discussion

In this paper we reported a case of SARS-CoV-2 and primary varicella co-infection resulting in bilateral pneumonia which progressed to acute respiratory distress syndrome requiring mechanical ventilation and ECMO. To our knowledge, this is the first reported case of the kind in adults with such devastating consequences. We searched PubMed, Cochrane database, Toxnet, Cinahl. Key words were varicella, COVID-19, coinfection, ARDS, ECMO. Coronaviruses belongs to a family of enveloped positive-sense single-stranded RNA viruses [5]. A novel coronavirus named Severe Acute Respiratory Syndrome Coronavirus 2 causes COVID19 [6]. As of January 2020, more than 270 million people were tested positive for SARS CoV-2, with more than 4 million deaths worldwide [7]. It was first described in Wuhan, China, and soon it led to a global health crisis. There is a long list of symptoms and signs associated with COVID-19 such as fever, dry cough, aches and pains, diarrhea, headache, loss of taste and smell, skin rash, etc.

Varicella-zoster virus is highly contagious a -stranded DNA virus that belongs to Herpesviridae family. It causes varicella (chickenpox) as a primary infection, which usually affects children under age of ten in parts of the world where vaccine against varicella is not available. Reactivation of the virus causes zoster (shingles) [8,9].

Interaction between these viruses is unknown. The immunological features of COVID19 and varicella separately are complex enough and adding tocilizumab in that equation makes pathophysiological mechanism of this case even more difficult to understand and explain. Cell-mediated immunity is necessary for fighting against viruses and bacteria. However, SARS-CoV-2 infection affects T lymphocytes, leading to immunosuppressed state [10]. Data from other study described functional exhaustion of NK and CD8+ T cells with the increased expression of inhibitory receptor NKG2A [11]. In addition to the above, humoral immune response have important role in COVID-19 infections [12].

VZV sets off robust innate and acquired immune responses [13]. While it causes mild disease in most children and healthy adults, immunocompromised patients are in risk of developing complications like pneumonia, secondary bacterial infections [14,15]. Latest published data confirmed that T-Cell mediated immune response is essential for preventing life-threatening VZV infections [16]. Other mechanisms causing immunosuppression include use of corticosteroids and IL-6-receptor-blocker

(Tocilizumab) for COVID19 treatment which occurred in early phase of hospitalization. Tocilizumab is a humanized, monoclonal, antihuman interleukin-6 (IL-6) receptor antibody. It is approved for treatment of rheumatoid arthritis, giant-cell arteritis, cytokine releasing syndrome [17-21]. Based on preliminary non-peer reviewed report from Recovery trial group Tocilizumab may improve the course of COVID-19 [22]. However, in our case, this therapy probably additionally altered immune response and enabled VZV to cause severe pneumonia. Another risk factor for severe form of disease in our patient is cigarette smoking.

Our patient did not have history of chickenpox, and he was not vaccinated against varicella. Latency time between last contact with his children and development of skin lesions was almost three weeks. Alternative diagnosis of insect bite was ruled out because he was hospitalized at the moment of appearance of skin lesions, and continuously monitored during treatment for COVID-19. Also, patient did not report any insect bites. Type and distribution of skin and mucosa lesions was typical for varicella. In adult patients admitted in ICU requiring mechanical ventilation due to respiratory failure caused by varicella mortality rate is up to 50% [23]. Treatment options are antiviral therapy (acyclovir, valaciclovir, famciclovir, brivudine, foscarnet), corticosteroids, and respiratory support. Antiviral agents have been associated with reduction of severity of the disease, but there are no large, randomized control trials to confirm this. Benefit is greater in patients who receive antiviral drugs in first 24h of skin rash appearance.

Role of corticosteroids is controversial. In some studies utilization of steroids was not associated with mortality reduction but was associated with increased risk of superinfection [24,25]. Alternative treatment option in patients who develop severe ARDS refractory to optimized conventional care is ECMO. Based on what we know today ECMO is worth of considering in patients ARDS associated with COVID-19 [23]. Also, there are several case reports on ECMO procedure in patients with severe ARDS caused by varicella. They showed that ECMO was safe and effective [26,27]. Still there is not enough data on this topic to conclude whether ECMO should be used in these patients with more confidence if needed. Interhospital transport of patients on ECMO is complex and associated with great risks. Therefore, it should be done by specialized teams with most experience to avoid complications. There are different models of organizing transportation of ECMO patients which can be considered [28]. In Serbia there are no specialized teams for interhospital transport patients on ECMO.

In our case transport was organized by team of medical experts who is responsible for treatment ECMO patients in our hospital with technical help of colleagues from Institute for emergency

medical aid Novi Sad. This case demonstrates that ECMO should be considered as rescue therapy in patients with profound respiratory failure caused by varicella refractory to standard care. Despite being complex and risky, interhospital transport patients on VV-ECMO is feasible if necessary.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2022.40.006519

Andrijevic A. Biomed J Sci & Tech Res



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