NEUROLOGICAL COMPLICATIONS IN PATIENTS WITH EXTRA-CORPOREAL MEMBRANE OXYGENATION (ECMO) SUPPORT

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INTRODUCTION: Extracorporeal membrane oxygenation (ECMO) is a mechanical respiratory and/or circulatory rescue therapy for severe heart or respiratory diseases otherwise untreatable with conventional therapies. Over the last several years there has been a significant increase in the use of ECMO, with an improvement in outcomes.
As a modified cardiopulmonary bypass circuit applied in the most severe patients, ECMO carries several possible complications due to the underlying disease and the extracorporeal circuit itself.
Several factors can influence the occurrence of neurological injuries:

- ❑ pre-extracorporeal life support (ECLS): e.g., hypoxia, ischemic stroke, post anoxic encephalopathy, infection with neurological involvement
- ❑ during ECLS: e.g., need for anticoagulation, reduction of platelets, coagulation imbalance, and previous ischemic injury

Neurological diagnosis is often challenging because of deep sedation, limiting the efficacy of neurological exams as well as the difficulty of obtaining imaging in critical ill patients, so that diagnosis may be delayed, with a relevant impact on intensive care unit (ICU) stay and total hospital stay.
ECMO is a complex activity, and requires substantial monetary and human resources, so the benefits of the ECMO run may be frustrated by a severe neurological complication.

METHODS: we report a case series of neurological complications diagnosed during the ICU stay for ECMO support. From October 2013 to October 2014, in our Institution, we did 25 Veno-Venous (VV)-ECMO runs and experienced neurological injuries in 6 cases. Diagnosis was achieved in 3 cases during the VV-ECMO run because of a sudden change in clinical status, while in the other 3 cases diagnosis was achieved after weaning from ECMO support because of change in clinical status or unresolved and unexplained neurological status. This study was approved according to the IRCCS-ISMETT policy on ethical standards for publication of clinical studies and in accordance with the ethical standards laid down in 1964 Declaration of Helsinki and its later amendments. Family members of the ECMO patients, in accordance with our institutional policy, gave their consent for anonymous inclusion in this study.
The spectrum of neurological complications in ECMO is quite wide, particularly we experienced intracranial hemorrhage in 4 patients, cerebral fat embolism in 1 case and acute disseminated encephalomyelitis (ADEM) in the last one. We reported demographic and clinical features of the neurologically injured patients in **Tab.1**. We propone this series in light of its heterogeneity in term of pathogenesis, insidious diagnosis and treatment decision-making. The most feared neurological complication has been intracranial hemorrhage (ICH), which results in long-term disability and/or death. Consequently, we focused particularly on this topic (**Fig.1 Case1; Fig.2 Case 3**).

RESULTS: in each case the neurological complication had a dramatic effect: ranging from brain death to prolonged ICU stay and log-term disability.

DISCUSSION: This case series has an informative impact for the neurologists who provide consultative services because they see only a small selection of these patients: most of these complications are handled by the intensive care team and not considered out of the ordinary. We firmly believe in a multidisciplinary effort treating ECMO patients, including also a neurologist in our team, whose support may be useful in those critical ill patients either in identifying earlier neurological complications or helping management when brain injuries occur. Although sedation and pharmacologic paralysis render neurologic examination and brain imaging extremely challenging, neurological monitoring has to be performed frequently, involving highly specialized neurologists and neuroradiologists well-trained in recognizing early signs of central nervous system dysfunction in order to reduce possible delays in diagnosis and treatment.

Table 1 Characteristics of all patients (mean value ± standard deviation), and description of 6 cases

	Total 25 pts	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	44 ± 12.5	22	28	47	43	42	37
BMI	27 ± 5	30	20.9	27.5	36	29.7	20.3
SAPS 2	43.5 ± 13.3	39	17	63	58	63	36
SOFA score	8.8 ± 3.4	13	6	9	9	10	12
MV pre-ECMO	6.3 ± 9	5	1	3	6	5	0
P/F	69 ± 17.7	110	104	56	50	68	40
PRESERVE score	4.5 ± 1.8	3	4	5	1	5	4
ECMONET score	6.4 ± 1.8	9.5	5	7	5.5	7.5	6.5
RESPSCORE	0.14 ± 3.5	-3	4	1	4	-3	3
Mean HTC	29.9 ± 3.2	24	26	34	29	29	27
ECMO days	16.7± 18.7	6	9	2	31	13	48
LOS	36 ± 34	20	9	2	31	47	169
Cause of ARDS		Pulmonary contusion polytrauma	H1N1 in puerperium	Interstitial pneumonia	Bacterial pneumonia	Pneumocystis pneumonia in AIDS	H1N1
Neuro injury		Cerebral fat embolism	Cerebral Hemorrhage	Cerebral Hemorrhage	Cerebral Hemorrhage	Cerebral Hemorrhage	ADEM
Treatment		Supportive therapy	Neurosurgical evacuation	No surgical indication	Neurosurgical evacuation	Neurosurgical evacuation	Plasmapheresis
Outcome	16 SURV 64%	Hosp. Discharge	Deceased	Deceased	Deceased	Hosp. Discharge	Hosp. Discharge

BMI body mass index, *SOFA score* Sequential Organ Failure Assessment score, *MV pre-ECMO* days of mechanical ventilation before ECMO run, *P/F* PaO2 ratio, *Mean HTC* daily mean hematocrit during ECMO support, *ECMO days days* of ECMO support, *LOS* total lenght of hospital stay, *Neuro injury* neurological complication recognized during or after ECMO support, *Treatment* treatment of neurological complication, *SURV* patient survived, *ADEM* acute disseminated encephalomyelitis

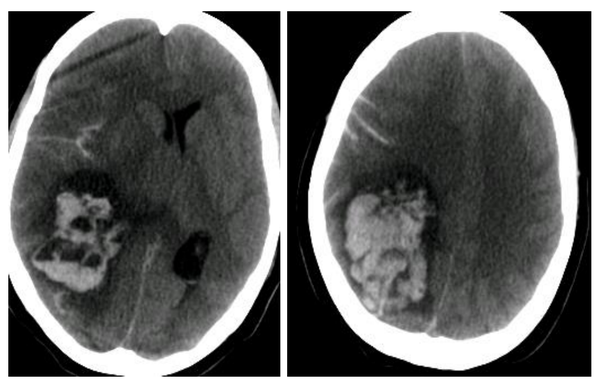

Fig. 1 Case 2: Axial non contrast CT scan shows a right parietal-occipital intraparenchymal hematoma (size: 6x5cm), surrounded by a hypodense halo corresponding to perilesional edema. The lesion is responsible of midline shifting (1.8 cm) and of the transfalcial herniation of the cingulate gyrus under the falx. The right lateral ventricle is displaced and compressed. The CT scan documents also hyperdensities in right parietal, temporal and occipital cortical sulci, consistent with acute subarachnoid hemorrhage, which involves also parasellar region and surrounds vessels of Circle of Willis.

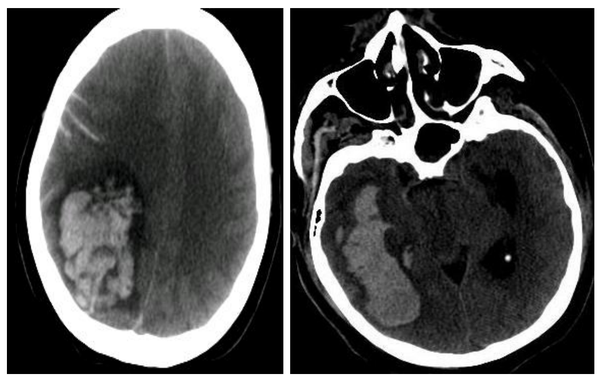

Fig. 2 Case 3: 2_CT images show large right parietal-temporal intraparenchymal hemorrhage (size: 9x6 cm). The hypodense region of oedema surrounding the hematoma may be suspicious for a large infarction with hemorrhagic transformation, with controlateral midline shift (19 mm). The intracranial lesion is also responsible for compression on right ventricular, pons, medulla oblongata, Sylvian acquedut and vertebral artery displacement. Within the intracranial hemorrhage it is evident a rounded arterial enhancement (size: 4 mm) suspicious for aneurysm.

CONCLUSION: in our ECMO center we started strict neurological monitoring involving intenstivists, a neurologist and our radiology service, but neurological complications are still an insidious diagnosis and treatment. Considering poor outcomes associated with the neurological sequelae described, our future program aims to find ways to prevent these complications.

References
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