Case Report

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Effective Continuous Renal Replacement Therapy and Music Therapy for a Comatose Patient with Encephalopathy: A Case Report

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Abstract

A 35-year-old woman presented with a one-week history of Covid-19 symptoms. Despite negative results for COVID-19 and influenza virus, she suffered a tonic-clonic seizure lasting one minute and experienced a subsequent decrease in the level of consciousness to 7, which further decreased to 2+T/15 accompanied by low oxygen saturation. Despite various clinical and paraclinical evaluations, no definite cause for the patient's low LOC could be determined, and various therapies and medications failed to improve her condition. Given the septic phase, two rounds of continuous renal replacement therapy were conducted, in conjunction with music therapy and reminiscence featuring the voices of her loved ones. After 48 hours from the last round of CRRT, and following 50 days of hospitalization in the intensive care unit, her LOC improved to 8+T/15. We propose CRRT and music therapy and reminiscence as possible treatment approaches for patients with unexplained coma and unresponsiveness to therapies.

Keywords: CRRT; COVID-19; Encephalopathy; Music Therapy; Sepsis.

1. Background

Differential diagnosis of encephalitis can be challenging, particularly following infectious encephalopathy resulting from viral or bacterial infections or autoimmune causes [1,2]. Antibody-mediated encephalitis is attributed to the involvement of post-synaptic receptors [3,4]. To diagnose a wide range of agents and causes of encephalitis, various clinical and paraclinical evaluations should be performed, which can sometimes yield inconclusive results. In such cases, treatment selection cannot be predetermined, and doctors must rely on their experience and evidence to determine the best possible treatment method.

Magnetic resonance imaging (MRI) is the method of choice for diagnosing encephalitis, in addition to laboratory findings [1,5,6]. In this report, we present a clinical case of a patient who showed common features of influenza or COVID-19 disease, but her clinical status became complicated with a decreased level of consciousness (LOC) without any definitive clinical and paraclinical signs or symptoms. After various evaluations, we considered her as a patient with possible encephalitis. Therefore, we treated her with different therapeutic protocols, but her LOC increased only after continuous renal replacement therapy (CRRT). However, we also applied music therapy during her deep sleep, which we believe could have aided in her mental coordination and recovery.

2. Case Presentation

We present a case of a 35-year-old female patient with no prior physical, mental, or familial medical history, no known drug or food allergies, and no recent travel within or outside the country. The patient received three doses of the AstraZeneca COVID-19 vaccine, with the last dose administered 8 months prior to admission.

The patient presented with a one-week history of headache, runny nose, sneezing, sore throat, body pain, and forgetfulness of the last 24 hours. Upon admission to the intensive care unit (ICU) on the late days of December 2022, the patient had a blood pressure reading of 116/81 mmHg, respiratory rate of 22 breaths per minute, heartbeat rate of 83 beats per minute, body temperature of 36.1ºC, oxygen saturation of 96% in room air, and non-fasting blood sugar of 128 mg/dL. The patient had a level of consciousness (LOC) of 15 on day 1 of registration.

PCR tests were conducted for COVID-19 and influenza virus upon admission, and lung and brain CT scans were performed, which showed normal results (Figure 1). However, on December 23, 2022, the patient experienced a tonic-clonic seizure for one minute, with a resulting decrease in LOC to 7 and a decrease in oxygen saturation to 75%. The patient was immediately intubated and subsequently fell into a coma. Over time, the patient's LOC continued to decrease until reaching its lowest level (LOC: 2+Endotracheal Tube/15).

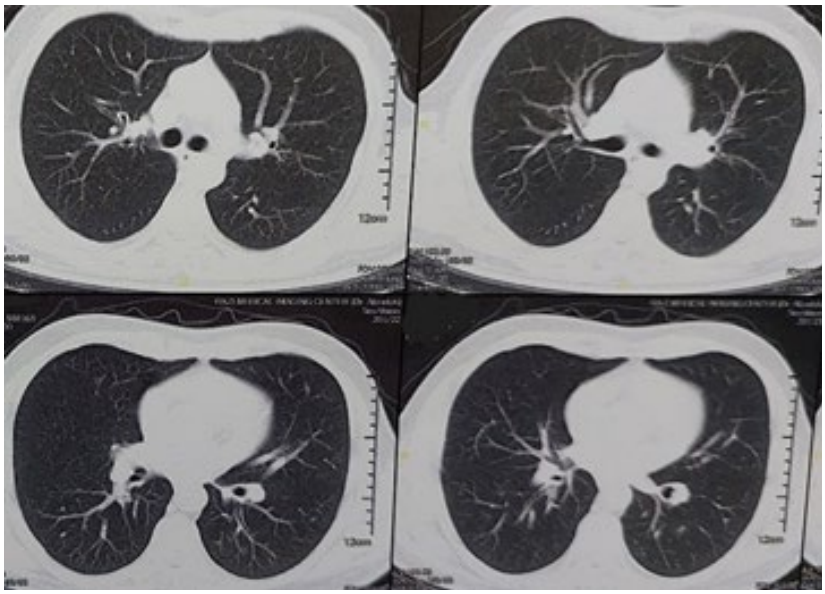

Figure 1: Chest Computed Tomography Scan Without Contrast of The Patient on Admission to the ICU; Normal Chest Computed Tomography Scan

We consulted with various specialists, including radiology, neurology, infectious disease, internal medicine, cardiology, ICU, gastroenterology, and rheumatology, regarding the patient's condition. We also conducted brain MRI (Figure 2), cervical spinal cord MRI (Figure 3), complete abdominal and pelvic ultrasound, chest ultrasound, thyroid ultrasound, carotid ultrasound, and vertebral ultrasound. All ultrasound evaluations were normal. Additionally, we performed a lumbar puncture (LP) at the patient's request, which yielded normal results (Table 1). Laboratory tests were mostly normal (Table 2), with the exception of white blood cells (WBC) (13.08×1000 cells/μL), vitamin D3 (17 ng/mL), fluorescent antinuclear antibody (FANA) (titer 1:200; positive result), D-dimer (0.6 mg/L), neutrophil percentage (77.4%), and lymphocyte percentage (14.6%) which were abnormal. Echocardiography showed that the patient had a healthy heart with an ejection fraction (EF) of 55%. Due to suspected autoimmune and unknown encephalitis, we administered intravenous methylprednisolone (1000 mg) for 7 days and performed plasmapheresis for 7 sessions, with no response from the patient, who remained in a coma with LOC 2+Endotracheal Tube/15. We then administered a single dose of rituximab (500 mg) and intravenous immunoglobulin (IVIG) (20 grams/day for 5 days). As there was no change in the patient's condition, we administered a single dose of cyclophosphamide (1000 mg).

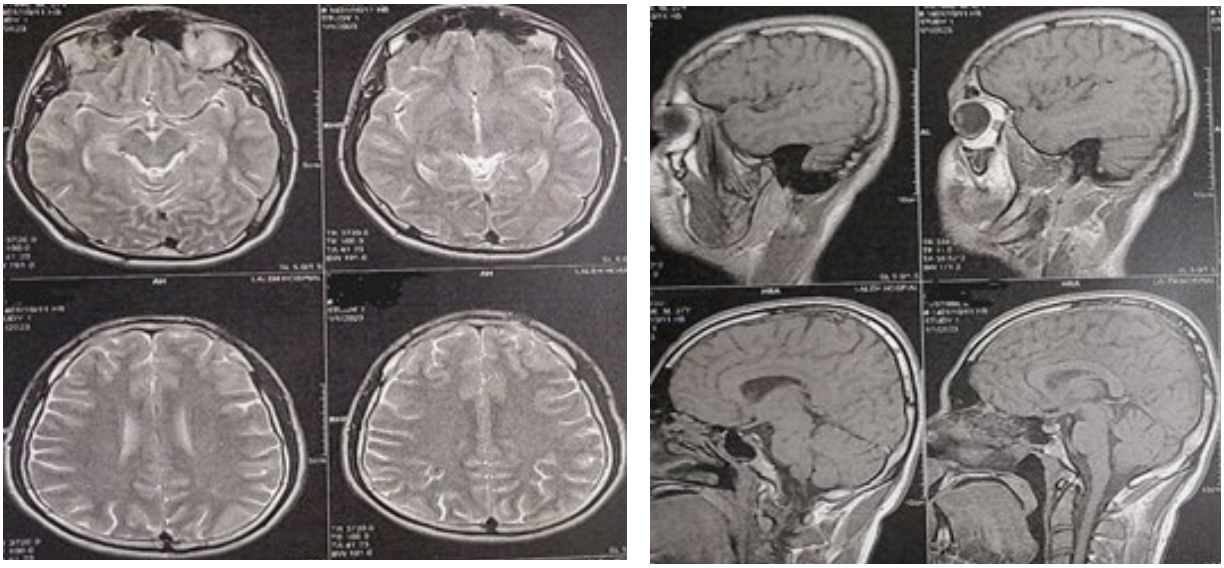

Figure 2: Brain MRI Without Contrast of the Patient; Normal Brain MRI is Present With no Evidence of Acute is Chemic/Hemorrhagic Stroke, no Evidence of Intra/Extra-Axial Mass and no White Matter Signal Changes

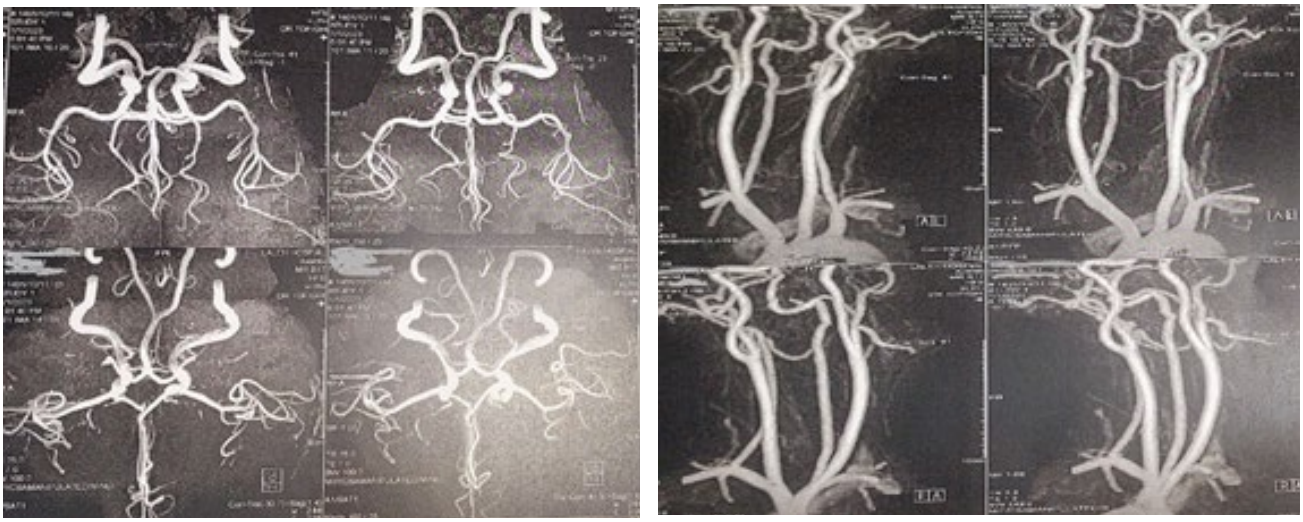

Figure 3: Patient's Brain (left) and Cervical (right) Magnetic Resonance Angiography (MRA) with Contrast; Normal Brain MRA; as it is Obvious the Supra-Aortic Arteries of Cervical Vessels are Normal

Table 1: Cerebrospinal Fluid Culture and Analysis results (a spinal tap, also known as a lumbar puncture)

Cerebrospinal Fluid Culture and Analysis	
Microbial culture	No growth
Appearance	Clear
WBC	2
RBC	-
Poly%	20
Lymph%	65
Glucose (mg/dL)	40
Protein (mg/dL)	25
LDH for CSF (U/mL)	2
ADA (adenosine deaminase)	1.6

Abbreviations: ADA; adenosine deaminase; LDH; lactate dehydrogenase, RBC; red blood cell, WBC; white blood cell

Table 2: Laboratory findings during hospitalization of the patient

Blood chemistry, hematology and serological Tests					
BS (mg/dl)	130	Na (meq/L)	136.5	WBC ($\times 10^3$ cells/µL)	13.08
Hb A1C (%)	5.2	K (meq/L)	4.16	RBC ($\times 10^6$ cells/µL)	4.64
Uric Acid (mg/dl)	5.6	Calcium (mg/dL)	9.1	Hb (g/dL)	13.1
Triglycerides (mg/dl)	121	Phosphorus (mg/dL)	3.3	HCT (%)	38
Cholesterol (mg/dl)	140	Magnesium (mg/dL)	2.2	PLT ($\times 10^3$ cells/µL)	317
HDL (mg/dl)	51	Pro calcitonin (ng/mL)	<0.01	Neutrophils%	77.4
LDL (mg/dl)	119	T3 (ng/ml)	0.7	Lymphocytes%	14.6
VLDL (mg/dl)	22	T4 (µg/dl)	4.6	ESR (mm/1h)	18
Creatinine (mg/dL)	0.94	TSH (µlU/ml)	1.7	PT (seconds)	13.1
BUN (mg/dL)	13.6	Vitamin D3 (ng/ml)	17	PTT (seconds)	41
AST (U/L)	14	cTnI (ng/ml)	<0.03	INR (Ratio)	1.01
ALT (U/L)	6	D-dimer (µg/ml)	0.6	hs-CRP (mg/L)	3.10
ALP (U/L)	170	Pro BNP (pg/mL)	109	RF (RU/mL)	<2
Bilirubin Total (mg/dL)	0.3	FDP (µg/ml)	<5	Coombs	Negative
Bilirubin Direct (mg/dL)	0.1	Anti-TPO (IU/ml)	14.45	Wright	Negative
Albumin (mg/dl)	3.90	PTH (pg/ml)	25	2ME	Negative

Ammonia (µmol/L)	52				

Abbreviations; 2ME: 2-Mercaptoethanol, **ALK:** Alkaline phosphatase, **ALT:** Alanine aminotransferase, **Anti-TPO:** Anti-Thyroid peroxidase, **AST:** Aspartate transaminase, **BUN:** Blood Urea Nitrogen, **BS:** Blood sugar, **cTnI:** Cardiac Troponin I, **ESR:** Erythrocyte sedimentation rate, **FDP**: Fibrinogen degradation products, **HDL**: High-density lipoproteins, **Hb:** Hemoglobin, **HbA1C:** Glycated hemoglobin A1, **HCT**: Hematocrit, **hs-CRP:** High sensitive c-reactive protein, **INR:** international normalized ratio, **K:** Potassium, LDL: Low-density lipoproteins, Na: Sodium, PLT: Platelet, Pro-BNP: pro-blood Natriuretic peptide, **PT**: Prothrombin time, PTH: Parathyroid hormone, PTT: Partial thromboplastin time, RBC: Red blood cell, RF: Rheumatoid factor, T4: Thyroxine, T3: Triiodothyronine, TSH: Thyroid stimulating hormone, VLDL: Very low-density lipoprotein, WBC: White blood cell.

Table 3. Microbiological, urine and tracheal evaluation of the patient's samples

Blood, Tracheal, and Urine Cultures		
Blood Cultures (*1)	No growth	
Blood Cultures (*2)	No growth	
Tracheal Culture	No growth	
Urine Culture	No growth	
Urine Analysis	color	yellow
	Appearance	clear
	Specific gravity	1.020
	PH	6.5
	blood	Negative
	Protein	Negative
	Glucose	Negative
	Ketone	Negative
	Bilirubin	Negative
	Urobilinogen	Negative
	WBC (hpf)	1-3
	RBC (hpf)	0-1
	Epithelial cells (hpf)	4-5
	Bacteria	Rare
	Mucus, Yeasts, Casts	Negative

hpf: high power field

Autoimmune Encephalitis Panel Tests		**Infectious Panel test**	
Tests	Results	Tests	Results
Anti-NMDAR (Titer)	Negative	HBsAb	27
Anti-DPPX (Titer)	Negative	VDRL and Treponemal antibody	Negative
Anti AMPA1/2 (Titer)	Negative	HBsAg, SARS-COV-2 (Real-time RT-PCR), Influenza, CMV, HSV, HIV, HCV	Negative
CASPR2 (Titer)	Negative		
LGI1 (Titer)	Negative		
Anti GABAR (Titer)	Negative		

Abbreviations; Anti-NMDAR: N-methyl-D-aspartate receptor antibody, Anti-DPPX: dipeptidyl-peptidase-like protein 6 antibody; Anti-AMPA1/2: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antibody, CMV: Cytomegalovirus Antibody, CASPR2: contactin-associated protein-like 2, LGI1: leucine-rich glioma inactivated 1 antibody, Anti-GABAR: gamma-aminobutyric acid receptor antibody, HIV: Human Immunodeficiency Virus, HSV: Herpes Simplex Virus, VDRL: Venereal Disease Research Laboratory, HBsAb: Hepatitis B Virus Surface Antibody, HBsAg: Hepatitis B Virus Surface Antigen, HCV: hepatitis C virus antibody.

Immunologic tests			
Test	Results	Test	Results
F.A.N.A Fluorescent antinuclear antibody	1/200	C3 (Third Component of Complement)	100
ds DNA-G double-stranded DNA-G	<10	C4 (fourth Component of Complement)	33.9
Anti-pho (IgM) Anti-Phospholipid IgM	0.7	CH50 (Complement total blood test)	136
Anti-pho (IgG) Anti-Phospholipid IgG	1.9	Lupus Anticoagulation	33.1
Anti -Cardio (IgM) anticardiolipin IgM	5.0	A.C.E (angiotensin-converting enzyme)	25
Anti -Cardio (IgG) anticardiolipin IgG	<3.0	Anti-SSA (anti–Sjögren's-syndrome-related antigen A autoantibodies)	<3.0
ANCA antineutrophil cytoplasmic antibodies	<1/10	Anti-SSB anti–Sjögren's-syndrome-related antigen B autoantibodies)	<3.0
C. ANCA	<1/10	Beta 2 Glycoprotein (IgM)	<1.0
P. ANCA	<1/10	Beta 2 Glycoprotein (IgG)	<1.0

After 4 weeks in a coma with LOC 2+Endotracheal Tube/15, the patient's condition deteriorated into sepsis, with a blood pressure reading of 89/61 mmHg, respiratory rate of 27 breaths per minute, heartbeat rate of 130 beats per minute, body temperature of 38.9ºC, and oxygen saturation of 93%. Non-fasting blood sugar was 99 mg/dL, and laboratory results showed elevated procalcitonin (PCT) (25.1 ng/mL), high-sensitive C-reactive protein (hs-CRP) (90 mg/L), erythrocyte sedimentation rate (ESR) (36 mm/h), and WBC (21×1000 cells/µL).

In another attempt to improve the patient's condition, we initiated music therapy with wordless songs and reminiscence with the voices of her loved ones. After a week of music therapy and reminiscence, the patient's LOC improved from 2+ET/15 to 4+ET/15. Due to the septic phase, we performed two rounds of continuous renal replacement therapy (CRRT) using CytoSorb filters to purify the patient's blood. After 48 hours from the last round of CRRT, the patient's LOC improved to 8+ET/15. After 50 days of hospitalization in the ICU, the patient was transferred to the general ward with a tracheostomy and LOC of 10+ET/15. It is important to note that all paraclinical measures, such as laboratory tests and imaging, were repeated periodically, and all were normal, except during the septic phase.

3. Discussion

According to specialists, viruses are the leading cause of infectious encephalitis, with many cases having an unconfirmed etiology [1,5]. Venkatesan and Murphy (2018) have identified herpesviruses, arboviruses, enteroviruses, parechoviruses, mumps, measles, rabies, Ebola, lymphocytic choriomeningitis virus, and henipa viruses as common viral agents found in cases of encephalitis [7-10]. Therefore, it is likely that the presented case in our report is due to viral infection. Antibody-mediated encephalitis is another possible cause, but treatment with IVIG and cyclophosphamide did not yield any immediate benefits. Hence, we hypothesize that the probable cause of encephalitis in our case is a viral agent. However, it should be noted that the disease in this case may be of an unknown autoimmune type, and despite advances, the effector autoantibodies may remain unidentified.

Patients with encephalitis may present with contradictory laboratory findings and imaging results. Brain MRI may show normal, non-specific, or severe signal changes in multifocal T2/FLAIR, while cerebrospinal fluid analysis may be normal or show non-specific findings (2, 6). Unfortunately, our facility lacks the necessary resources, such as specific diagnostic kits and anti-serum reagents, to perform molecular diagnosis of probable viral agents. Additionally, many viral agents that cause encephalitis cannot be detected due to their unspecific signs and symptoms, making diagnosis difficult. Bacterial or fungal agents were not detected in clinical samples obtained from the patient. Furthermore, the patient and her family reported no history of alcohol or toxin use. Our case has a high level of education and specializes in dentistry. Therefore, we expect that she adheres to hygiene and health considerations in her workplace and lifestyle.

Infectious diseases such as influenza and coronavirus can cause various symptoms and complications in the body. For instance, encephalopathies are the most common non-respiratory complications of influenza, presenting as seizures, ataxia, myelopathy, and delirium, typically occurring one week after the first symptoms [8]. Certain strains of influenza viruses can invade the central nervous system through infection of microvascular and endothelial cells or through the olfactory, sympathetic, vagus, and trigeminal nerves, resulting in encephalitis [9-11]. Similarly, coronavirus can also infect the central nervous system and may be associated with multiple sclerosis, as patients may exhibit demyelinating lesions and have normal cerebrospinal fluid [12,13]. Nonetheless, molecular methods have ruled out COVID-19 and influenza virus involvement in our patient.

Different treatment methods are employed for encephalitis patients, including the use of IVIG, plasmapheresis, corticosteroid therapy, rituximab and cyclophosphamide, and antibiotic therapy [5,14]. In addition to these treatments, our patient received CRRT and music therapy with reminiscence, which have not been widely used in most studies.

The patient's low LOC was treated with CRRT and music therapy with reminiscence by her family members, leading to significant remediation. We believe that CRRT played a crucial role in removing the major cause of the patient's LOC, such as viral particles, toxic materials, blocking antibodies, bacterial toxins, and any other unknown agents. Therefore, we suggest that CRRT may be a viable treatment option for patients with low LOC and unknown etiology, especially when conventional therapies such as immunotherapy, anticancer therapy, and antibiotic therapy have proven ineffective. Additionally, we propose that

music therapy and reminiscence may have a positive impact on the consciousness of patients with low LOC and can be considered as auxiliary approaches by therapeutic teams.

Listening to music activates the cortical networks of the reward circuit, resulting in emotional reward and release of dopamine, a prominent neurotransmitter in the reward system [15,16]. Positive emotional responses to music can further stimulate the limbic system, leading to additional dopamine release. Moreover, the amygdala and communication cortices may become activated during the processing of emotional responses [17]. Music can also activate the neural networks involved in episodic and semantic memory networks, and the analysis of perceptual patterns in music can stimulate and strengthen perception and cognition [18]. The fact that playing a musical instrument is a complex activity for the brain and activates almost all areas of the brain may be a key factor in enhancing cognitive functions and improving health and social interaction [16,18].

4. Conclusion

In conclusion, we hope that this case report represents a valuable treatment method for saving patients with low LOC who do not respond to conventional therapies.

Consent for Publication

Written informed consent was obtained from the patient's next of kin to publish this case report and any accompanying images. A copy of the written consent is available for review by the journal's Editor-in-Chief.

Declarations

Ethics Approval and Consent to Participate: The authors considered all the ethical considerations based on the international ethical protocols, and the ethics committee approved the work of Laleh hospital in Tehran city.

Availability of Data and Materials:

The information in this manuscript was collected from the intensive care unit of Laleh Hospital in Tehran city.

Competing Interests:

The authors declare that they have no competing interests.

Funding:

Not applicable.

Authors Contributions:

MT and AA analyzed and interpreted the patient data, performed the physical examination, and was a significant contributor to writing the manuscript. All authors read and approved the final manuscript.

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