Cerebral Leukoaraiosis with Epilepsy Manifestations post Covid 19 Infection: A Case Report

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ABSTRACT

COVID-19 infection has various manifestations of symptoms. Neurological manifestations are often found in this case. We found a patient, a 50-year-old woman with no comorbidities, who confirmed mild symptoms of Covid 19 by RT PCR. One month later, the patient came to the emergency room with complaints of general tonic clonic seizure that were experienced more than 3 times a day for 1-2 minutes. Todd paralysis condition was found after the seizure took place. The results of the Covid 19 examination were negative and there were no factors that provoked the occurrence of seizures. Laboratory parameters were within normal limits. The results of the cerebral MRI examination showed the impression of cerebral (leukoaraisosis, the results of the EEG examination showed an abnormal EEG with diffuse epileptiform irritability with a normal background.

Keywords: Covid-19, epilepsy, post infection, leukoaraiosis

1. INTRODUCTION

People infected with COVID-19 also may experience neurological symptoms [1] and these neurological manifestations may occur with or without cardiovascular and respiratory symptoms [2]. Epilepsy is one of the most common, sudden, and recurrent neurological disorders, affecting about 50 million people worldwide. The exact mechanisms leading to seizures are not yet completely understood. However, the suggested mechanisms include a severe increase in neuronal excitability following an imbalance in the ion channel function, either as an increase in excitatory neurotransmitters of glutamate and aspartate or a decrease in the γ-aminobutyric acid (GABA) neurotransmitter [3]. Other causes of epilepsy include acute metabolic disorders such as hypo or hyperglycemia, electrolyte imbalance, acute neuronal damage following infection and inflammation, stroke, head trauma, mitochondrial dysfunction, hypoxia, and fever.

2. CASE DESCRIPTION

A 50-year-old woman, came to the clinic with complaints of general tonic clonic seizure, accompanied by biting of the tongue which was experienced more than 3 times in one day with a duration of 1-2 minutes. Todd's paralysis occurred after the seizure and the patient forgot the incident. There are no factors that provoke the occurrence of seizures.

One month ago, the patient confirmed Covid 19 by RT PCR with mild symptoms, without comorbidities. The results of the Covid 19 examination were negative, physical and neurological examinations were within normal limits. Laboratory results within normal

limits. The results of the cerebral MRI examination (Fig.1) showed the impression of leukoaraiosis, the results of the EEG examination (Fig. 2) revealed a diffuse epileptiform irritative abnormality with a normal background. The patient's seizure were managed with anti epileptic levetiracetam

3. DISCUSSION

COVID-19 infection may be one of the provoking factors for seizure. What's more, it is possible that some COVID-19 patients developed seizures as a consequence of other complications: viral infection, hypoxia, metabolic derangement, head injuries, neuro-logical surgeries, altered homeostasis due to organ failure and toxin exposure [4], and so on. Patients with COVID-19 and epilepsy are often accompanied by a variety of complications. 86.7% of patients (26/30) with COVID-19 and epilepsy had at least one complication, and 50% of them (15/30) had more than five complications. This was higher than the proportion of complications in general inpatients with COVID-19 from other research [5]. Some complications may occur in the recent course of COVID-19, others may have already existed as a recorded past history or even be undetected and ignored.

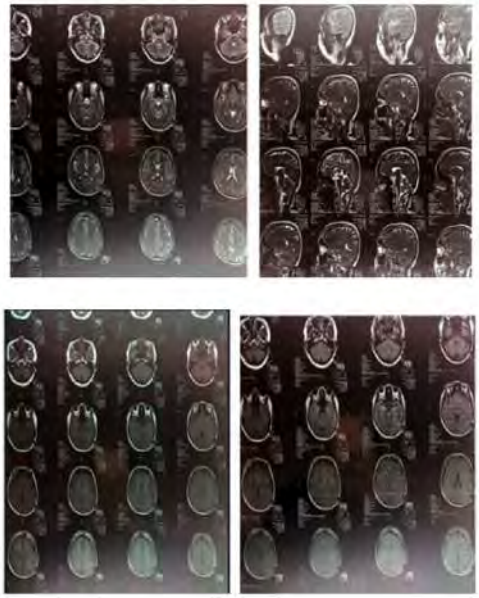
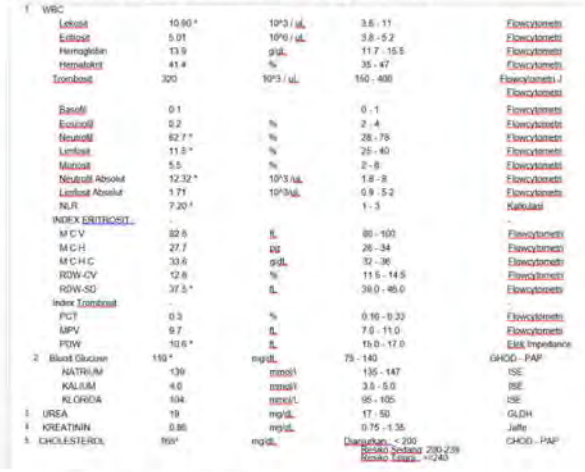


Fig 1 Cerebral MRI Leukoaraiosis

Fig 2. EEG abnormal diffuse iritative epileptiform with normal background



1	WBC				
	Lekosit	10.90 *	10^3 / uL	3.6 - 11	Flowcytometri
	Eritrosit	5.01	10^6 / uL	3.8 - 5.2	Flowcytometri
	Hemoglobin	13.9	g/dL	11.7 - 15.5	Flowcytometri
	Hematokrit	41.4	%	35 - 47	Flowcytometri
	Trombosit	320	10^3 / uL	150 - 400	Flowcytometri / Flowcytometri
	Basofil	0.1		0 - 1	Flowcytometri
	Eosinofil	0.2	%	2 - 4	Flowcytometri
	Neutrofil	82.7 *	%	28 - 75	Flowcytometri
	Limfosit	11.8 *	%	25 - 40	Flowcytometri
	Monosit	5.5	%	2 - 8	Flowcytometri
	Neutrofil Absolut	12.32 *	10^3 /uL	1.8 - 8	Flowcytometri
	Limfosit Absolut	1.71	10^3/uL	0.9 - 5.2	Flowcytometri
	NLR	7.20 *		1 - 3	Kalkulasi
	INDEX ERITROSIT :	-			-
	MCV	82.6	fL	80 - 100	Flowcytometri
	MCH	27.7	pg	26 - 34	Flowcytometri
	MCHC	33.6	g/dL	32 - 36	Flowcytometri
	RDW-CV	12.8	%	11.5 - 14.5	Flowcytometri
	RDW-SD	37.3 *	fL	39.0 - 46.0	Flowcytometri
	Index Trombosit	-			-
	PCT	0.3	%	0.10 - 0.32	Flowcytometri
	MPV	9.7	fL	7.0 - 11.0	Flowcytometri
	PDW	10.6 *	fL	11.0 - 17.0	Elek Impedance
2	Blood Glucose	110 *	mg/dL	70 - 140	GHOD - PAP
	NATRIUM	139	mmol/l	135 - 147	ISE
	KALIUM	4.0	mmol/l	3.5 - 5.0	ISE
	KLOREDA	104	mmol/L	95 - 105	ISE
3	UREA	19	mg/dL	17 - 50	GLDH
4	KREATININ	0.86	mg/dL	0.75 - 1.35	Jaffe
5	CHOLESTEROL	169*	mg/dL	Diangurkan : < 200 Berisiko Sedang 200-239 Berisiko Tinggi : >=240	CHOD - PAP

Fig. 3 Laboratory examination within normal limit

The mechanisms behind COVID-19 associated seizure are also not fully understood [6]. A growing number of studies have reported a possible association between seizures and COVID-19 through multiple pathways, including direct neuroinvasion of the SARS-CoV-2 virus via olfactory neuron axonal transport and hematogenous spread via disruption of the blood brain barrier [7]. Other indirect factors may also contribute to the cause of seizures in COVID-19, including features such as hypoxia, multiorgan failure, and metabolic derangements typically seen in severe diseases. After penetration of the blood–brain barrier, the virus can slow cerebral microcirculation, possibly through the creation of a hypercoagulable state. This

allows increased interaction of SARS-CoV-2 with the endothelial receptors and receptors on glial tissue [8]. The interaction at the glia may predispose patients to seizures as seen in other neurological diseases [9].

Leukoaraiosis is a pathological appearance of the brain white matter, which has long been believed to be caused by perfusion disturbances within the arterioles perforating through the deep brain structures. Hypoxia-ischaemia is supposed to play a role in the aetiology of leukoaraiosis; however, it is not certain whether it is a primary or a secondary cause, i.e. whether decreased blood flow is the cause or effect of nerve cell damage. Another hypothesis focuses on blood-brain barrier breakdown and endothelial dysfunction, with haemodynamic disturbances and damage of the blood-brain barrier being interpreted as elements of endothelial dysfunction [10]. The blood-brain barrier damage is reflected by the presence of plasma proteins such as IgG, complement, and fibrinogen in patients with leukoaraiosis. Thus, it is supposed that brain damage is due to toxic effects of blood proteins on nerve cells.

The endothelial dysfunction can be

further aggravated by COVID-19-mediated RAS disruption that may result in a secondary CBF dys-autoregulation [11], leading to cerebral hypoperfusion. This has been shown in CADASIL patients with COVID-19 where CSVD lesion manifested at the cerebral internal border zone, a region that is prone to hypoperfusion. Locatelli and colleagues posited that CADASIL patients may suffer from a chronic cerebral hypoperfusion mainly from the disruption in the myogenic component of CBF autoregulation where SMCs become constricted or dilated in response to changes of transmural pressure [12].

Epilepsy is not a disease, but rather a symptom complex with a very high burden of comorbidities. Patients with epilepsy can therefore show an extremely wide variety of comorbidities and backgrounds. Thinking about the relationship between these and COVID-19 is as important for clinicians as thinking about the relationship between epilepsy and COVID-19. For example, if an individual with epilepsy is elderly, the risk of severe COVID-19 illness is higher than that in the general population, requiring more vigilant infection control measures. Furthermore, as discussed previously [13], the risk is even higher if individuals have other comorbidities that may put them at elevated risk of COVID-19. Stroke, a widely known cause of epilepsy in the elderly, greatly reduces activities of daily livings and weakens patient immunity. This could increase the risks of infection with COVID-19 and subsequent severe illness.

In most case series, EEG testing is performed following a seizure or altered consciousness, on suspicion of acute symptomatic seizures or encephalopathy. According to a study from New York that summarized the EEG findings of 111 patients with COVID-19, past medical history of epilepsy or acute symptomatic seizures prior to EEG was independently associated with epileptiform EEG findings [14]. Another study showed EEG data from 10 consecutive patients affected by COVID-19, divided into groups with good and poor prognosis, and performed quantitative EEG analysis [15]. They showed that brain reactivity was reduced or lost more often in the poor prognosis group than in the good prognosis group.

Patients with epilepsy, as with the general population, may be treated for COVID-19, and clinicians need to be aware of the potential for interactions between AEDs and COVID-19 therapies. Caution should be exercised, as interactions can either diminish or enhance the effectiveness of drugs, or

cause side effects [16]. Some combinations of AEDs and COVID-19 therapies (e.g. the combination of eslicarbazepine/lacosamide and atazanavir/ lopinavir/ritonavir) can cause potentially fatal arrhythmias, and the potential for such interactions thus requires special attention according to the Italian League Against Epilepsy (https://www.lice.it/pdf/Antiepileptic_drugs_interactions_in_COVID-19.pdf). Others, such as carbamazepine, phenytoin, and phenobarbital, should be used with caution when in combination with remdesivir, which is often used to treat COVID-19. Notably, levetiracetam has been shown to be largely unaffected by COVID-19 drugs. Consideration should be given to switching to AEDs with less potential for interactions in patients who may need treatment for COVID-19. On the other hand, changing the AED regimen has been reported as a factor associated with increased seizures [17].

4. CONCLUSION

The impact of the new coronavirus on various organs is not fully understood. This virus can cause complicated disorders of the nervous system, such as seizures and epilepsy. The destructive effect of Covid-19 on the central nervous system caused by a storm of inflammatory cytokines or the mechanism of damage to the blood brain barrier, activation of microglia can potentially cause seizures or epilepsy in post-covid-19 patients. Further research is needed to prove the exact mechanism of seizures in Covid-19 patients.

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