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Case Report

Posterior reversible encephalopathy syndrome on COVID-19 [☆]

Sidharta Suwanto, MD, Widiana Ferrriastuti, MD^{*}

Department of Radiology, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Academic General Hospital, Surabaya, Indonesia

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ABSTRACT

For the time being, COVID-19 has been endemic and presents a varied neurological picture. Moreover, one of the remarkable neurological pictures is posterior reversible encephalopathy. It is a neurotoxic state which is considered a rare manifestation; however, it is essential to recognize. It originates from the disturbance of the blood-brain barrier which causes vasogenic edema and most commonly occurred in the parieto-occipital regions. Thus, we presented a case of a patient diagnosed with COVID-19 infection with posterior reversible encephalopathy syndrome (PRES) as shown at the brain MRI examination. It was categorized as a form of brain disorder in COVID-19.

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Introduction

Acute respiratory syndrome coronavirus (SARS-CoV-2) may stimulate multiple organ systems to react differently and, at worst, can affect the central nervous system. Posterior reversible encephalopathy syndrome (PRES) has also been associated with COVID-19 infections and several cases have manifested the correlation between these entities. Furthermore, the symptoms of PRES have various presentations, for example, headache, unconsciousness, seizures, and loss of vision. The main feature of this disease is the emergence of edema in the white matter, especially occurring in the posterior parietal and occipital region of the cerebrum [1].

In addition, several factors associated with PRES are described in Table 1. A wide variation of symptoms includes

visual impairment such as the followings; blurred vision, homonym hemianopsia to cortical blindness, loss of consciousness which ranges from confusion to coma, nausea, vomiting, and brainstem problems. In contrast to a more frequent generalized status epilepticus, nonconvulsive status is uncommon [2]. Furthermore, postmortem examination demonstrated the coexistence of parenchyma brain edema associated with neuronal damage. This notion conveyed that coronavirus (COVID-19) has a similar manifestation.

Case report

We discovered the posterior reversible encephalopathy syndrome (PRES) in a 7-year-old girl presented with a history of

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^{*} Corresponding author.

E-mail address: widiana-f@fk.unair.ac.id (W. Ferrriastuti).

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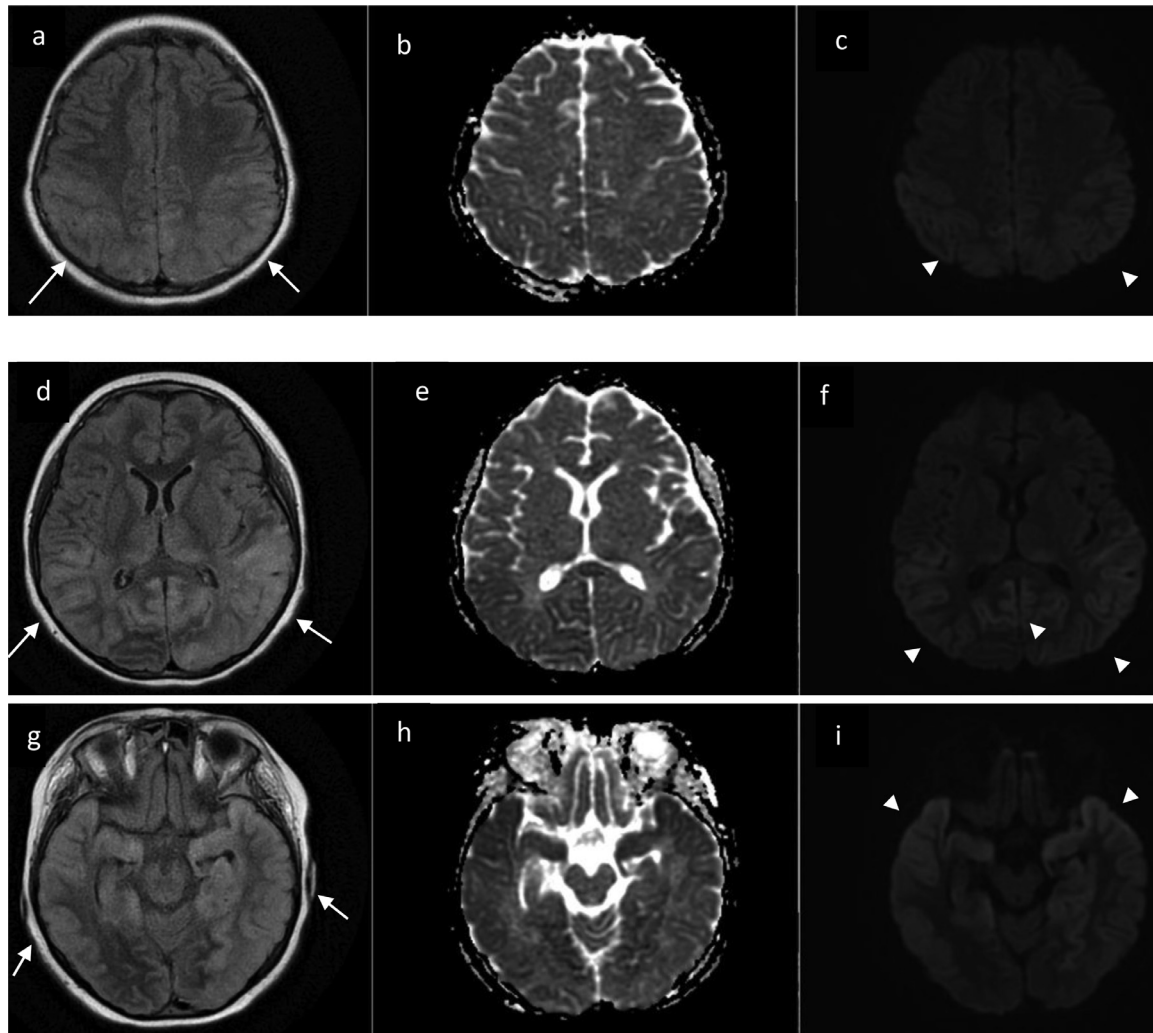


Fig. 1 – MRI FLAIR, ADC, DWI a, b, c (centrum semioval level), d, e, f (basal ganglia level), g, h, i (occipital level) showed diffuse but predominant posterior white matter, subcortical FLAIR hyperintensity (white arrow), with restricted diffusion on ADC and the presence of contrast enhancement (arrow head).

Table 1 – PRES-associated clinical conditions.

Preeclampsia
Eclampsia
Infection
Autoimmune disease
Chemotherapy for treating malignancy
Organ transplantation
Stem cell
Increase abnormality of blood pressure (hypertension)

fever and a persistent tonic-clonic seizure. These symptoms lasted for 4 days. She has isolated due to a positive PCR test with a D-Dimer laboratory result of 30,150. Thus, after being treated for 14 days, the PCR test yielded a negative result and her GCS was 235. Due to the treatment, the patient also complained of visual loss in both eyes.

In this case, MRI examination has been conducted with a high signal on the FLAIR sequence and more increased diffusion in the subcortical than the deep white matter, internal

and external capsule, and cerebellum (Fig. 1). As a result, we found a high signal with a restricted diffusion area in the deep gray matter with diffusion-weighted imaging. In addition, visible contrast enhancement developed on the posterior side of T1-weighted imaging with contrast administration (Fig. 2).

Discussion

PRES has been characterized by bilateral vasogenic edema at the brain parenchymal, predominantly in the occipital and parietal lobe [3]. It is along with the manifestations including hypertension, toxemia caused by pregnancy, uremia, chemotherapy for malignancy, and severe infection, for example, sepsis. Gram-positive bacterial and viral infections, for example, varicella-zoster, influenza A, and parainfluenza had been reported to be associated with PRES manifestations. The symptoms involve headache, dizziness, and loss of sense of smell (anosmia) and taste (hypogeusia) [4]. Moreover, the

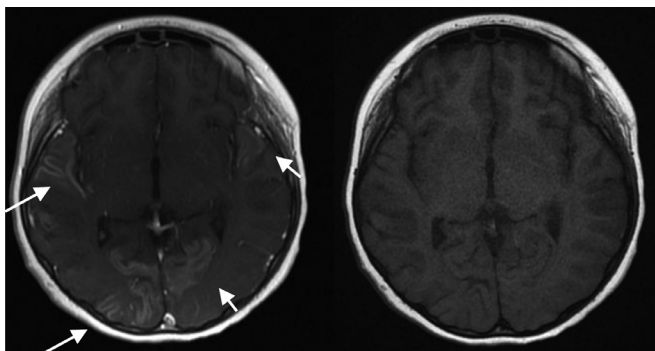


Fig. 2 – Axial MRI demonstrated contrast enhancement, predominantly posterior region (arrow).

emergence of autoregulation imbalance and endothelial dysfunction is the cause of alteration in the blood-brain barrier. It is suspected to be the pathophysiology of PRES; however, it has been under research.

Our MRI findings showed that a highly typical PRES was found with subcortical edema predominantly in the posterior region with restricted diffusion and contrast enhancement. Vasogenic edema is a characteristic imaging feature of PRES along with domination in the parietal and occipital lobes. On the other hand, it may also occur in some followings area; the watershed area, frontal lobes, inferior side of temporal lobes, basal ganglia, brain stem, and cerebellum.

A complication of PRES found in 15%-20% of cases is the emergence of bilateral micro hemorrhage. Abnormal contrast enhancement may present the parenchymal hemorrhage which becomes subacute in some patients' conditions. Eventually, cytotoxic edema portrays a restricted diffusion area in DWI [5]. In this case, this notion has been pictured in our patient. The association between PRES and COVID-19 is the notion of the rate of hemorrhage in other settings, either it is similar or has a slightly higher rate. The restricted diffusion area is commonly reported similar as well. Hemorrhage in PRES estimated as in 15-17% of patients [1]. Nevertheless, in this case, there was no hemorrhage found.

Cytokine release syndrome has been found in critically COVID-19 patients. It is a condition where a large number of cytokines in the systemic bloodstream, which is an inflammatory response due to T-cells and macrophage accumulation, have been released. Severe COVID-19 depicts a cytokine storm with; fever and elevated serum ferritin, interleukin-6 [5], and tumor necrosis factor-alpha (TNF- α) [4]. In this case, the elevated CRP value was a nonspecific test for inflammation, although IL-6 was not assessed regularly in COVID-19 cases in our center. Moreover, D-dimer was increased as it was mainly associated with COVID-19 and pro-inflammatory cytokine cascade activation in general [6].

The emergence of decreased T-cells, natural killer cells (NKC) and elevated IL-6 cause fever and multiple organ failure. Thus, excessive release of cytokines may damage and breakdown of the blood-brain barrier. PRES in post-COVID-19 patients was described through this mechanism. Furthermore, the systemic and local level of hypoxia is known to trigger this inflammation.

The development of PRES and neuroimaging findings were described in the followings presentation. Firstly, a COVID-19 infected cell which includes capillary endothelium and resulted in a rapid increment of protein S1. It is highly correlated to Angiotensin-Converting-Enzyme 2 (ACE 2) receptors. Secondly, the increase of permeability of the blood-brain barrier is a result of viral damage to its lining. It will eventually lead to loss of autoregulation of hemostatic vascular flow to the brain. In our patient, this state may yield homeostatic deterioration in the brain's blood flow, increased sensitivity to the instability of blood pressure, and brain edema. Disturbance of homeostasis can be portrayed as hemorrhages that occur due to cytokine release syndrome resulting in liver dysfunction and consumption of clotting factors. These portray as parts of disseminated intravascular coagulation. Initially, invasion of the virus into the brain triggers endothelial damage to the blood-brain barrier resulting in the S1-ACE 2 interaction and neuronal attack. Furthermore, acute necrotizing encephalopathy may originate from severe parenchyma destruction as a result from primary event of the S1-ACE 2 relationship. Even though the cytokine storm in severe COVID-19 is related to the pathogenesis of post infectious acute necrotizing encephalopathy and some cases of PRES, the correlation between those 2 is under research [5].

In this case, acute disseminated encephalomyelitis (ADEM) or acute hemorrhagic leukoencephalitis (AHEM) and PRES with micro hemorrhage as a different could be accounted into consideration in diagnosis. To the extent that our patient had no evidence of hypertension or any risk factors for PRES, those diagnoses were suitable to propose. Moreover, ADEM is considered rare and more prevalent in children. MRI imaging showed a hyperintensity signal at FLAIR sequence in gray and white matter and deep white matter with rim contrast enhancement on contrast administration. Some studies showed that there was a restricted diffusion at DWI [7]. Nevertheless, in our case, there was no characteristic of a ring or punctate enhancement in contrast administration.

Conclusion

To sum up, PRES has an excellent clinical outcome with adequate medical treatment. Nevertheless, a worse prognosis can deliver the imaging of hemorrhage or restricted diffusion area. In this case, the patient possessed vision disturbance for 9 months. MRI evaluation has not been performed until now.

Patient consent

Written informed consent was obtained from the patient for the publication of this case report.

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