



(CASE REPORT)



Acute cerebral infarction due to severe COVID-19, bacterial meningitis due to *Pseudomonas stutzeri*, mild loculated pericardial effusion due to MIS-C

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Abstract

Neurological involvement was common in children and adolescents with Coronavirus disease-2019 (COVID-19) related hospitalization and is mostly transient. A spectrum of life-threatening neurologic involvement infrequently occurred and was associated with more extreme inflammation and severe sequel. We reported a patient male, seven months old with chief complaint of fever since 1 month before admission. The patient was diagnosed by confirmed case COVID-19 with a positive RT-PCR SARS-CoV-2 swab. He had some contact with his parents that had confirmed with COVID-19 before. The patient also complained with focal seizures in the left extremity with decreased of consciousness. The seizure always repeated every day for 1 week with the same pattern. Patient also complain of nausea and vomiting every time he has been breastfed. There is no changes of the lips and oral cavity, no cutaneous rash, no red eyes, no swelling or edema on extremities. Non-contrast head CT-Scan revealed large area of acute cerebral infarction. Echocardiography revealed mild loculated pericardial effusion and cerebrospinal fluid cultured result revealed *Pseudomonas stutzeri*. After 3 weeks discharged from the hospital, the patient underwent a head MRI examination and the results revealed chronic ischemic cerebral infarction and communicating hydrocephalus. The patient was planned to undergo a VP shunt as a treatment for hydrocephalus. The neurological involvement can occur in children and adolescents with COVID-19. The range of severe neurologic complications including peripheral nerve disorders, focal CNS disease and diffuse CNS involvement, make it likely that multiple mechanisms underlie this wide spectrum of disease.

Keywords: SARS-CoV-2; COVID-19; Children; Neurological involvement

1. Introduction

Coronavirus disease-2019 (COVID-19) has been defined as a global health crisis since it was firstly reported in Wuhan, China in December 2019 and it has rapidly spread and affecting over 200 countries worldwide. There are children account for 1-5% of diagnosed COVID-19 cases in the world. At the time of writing, in Indonesia, the number of virologically confirmed COVID-19 positive cases is 32,033 (1,883 deaths) as per the Ministry of Health [1,2]. A large retrospective study of 2,142 confirmed or suspected COVID-19 infections in children reported to the Chinese Center for Disease Control and Prevention, it is showed milder clinical manifestations in children. Similar morbidity data in United States showed that 2,572 (1.7%) of 149,082 reported cases of COVID-19 infection occurred in pediatric patients [1].

Neurological involvement was common in children and adolescents with COVID-19 related hospitalization and is mostly transient. The range of severe neurologic complications including peripheral nerve disorders (GBS and variants), focal CNS disease (ischemic stroke due to large vessel occlusion, cerebral venous sinus thrombosis, and focal cerebral arteriopathy), and diffuse CNS involvement (CNS infection, ADEM, severe encephalopathy with white matter and corpus callosum lesions, and acute fulminant cerebral edema) make it likely that multiple mechanisms underlie this wide

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spectrum of disease [2,3]. An important line of research pertains to the question of whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is neuroinvasive. There are several mechanisms of infection with the SARS-CoV-2 virus which are believed to involve the neurological system. Similar to SARS-CoV-2, the molecular mechanisms underlying cell invasion by SARS-CoV-2 are related to the capacity of the virus to bind to angiotensin-converting enzyme 2 (ACE2) receptors [3].

A spectrum of life-threatening neurologic involvement infrequently occurred and was associated with more extreme inflammation and severe sequel. Long-term follow-up of pediatric patients with COVID-19-related neurologic involvement is needed to evaluate effects on cognition and development [2,4].

2. Case report

A 7 months old boy was referred from S hospital with chief complaint of fever that went up and down since 1 month before admission. The patient was admitted to S hospital on the fifth day of fever, with the highest temperature was 40°C. When arrived at S hospital, the patient was diagnosed with confirmed case COVID-19 with a positive RT PCR SARS-CoV-2 swab. He had some contact with his parents that had confirmed with COVID-19 before. There were no respiratory symptoms (cough, runny nose and shortness of breath).

On the third day of treatment, the patient complained of having seizures. The seizure was characterized by jerking in the left foot and hand with the eyes glaring upwards with a duration of \pm 30 minutes. The patient was on decreased of consciousness after seizure, the seizures were said to be repeated every day for 1 week with the same seizure pattern in the left extremity. Consciousness never fully recovered from the first seizure until the last seizure. Patient last seizure was 12 days before referred to SG hospital. The right extremity seems less active than the left. There is nausea and vomiting. Vomiting is said to appear for several days from the onset of the fever and occurs after he has been breastfed. Vomiting contains breast milk that he drunk, with a volume of 1 tablespoon per vomit, frequency of 4-5 times a day for approximately 10 days. History of profuse vomit was denied. There is no changes of the lips and oral cavity, no cutaneous rash, no red eyes, no swelling or edema on extremities.

The patient had been treated in S hospital about 23 days, the complaint is getting better but there still found some unresolved problems, so the patient referred to SG hospital. When arrived at SG pediatric emergency room, the patient was found with good consciousness, no shortness of breath, no cold, no cough, no seizures, no nausea/vomiting. Defecation and urination were said to be normal. Last urination approximately 2 hours before hospitalization. The patient is said to still have fever but with a lower peak of fever. The weakness of the right side also said to be improved.

He was never complained the same symptom like this before. No history of seizure before. There was no history of chronic disease. In previous hospital the patient was given intravenous paracetamol, ondansetron, intravenous immunoglobulin therapy (IVIG) for five days, intravenous methylprednisolone, oral azithromycin, intravenous ceftriaxone, meropenem, vitamin C oral, oral iron polymaltose complex, intravenous phenobarbital, zinc, ranitidine antiviral, valproic acid, intravenous levetiracetam, clobazam, diazepam, ventolin nebulization, oral vitamin B complex, enoxaparin injection, clopidogrel oral, and intravenous metamizole for pain.

He was looked moderately ill, the GCS was E4V5M6 (15/15) with normal regular pulse and respiratory rate. There was pale on palpebral conjunctivas, pupil reflex reactive isochor 2mm/2mm, no bulging fontanelle and no meningeal sign. The physiologic reflex was normal and pathological reflex was negative. On anthropometric status, he was well-nourished with normal head circumference/age. On laboratory examination revealed leukocytes $24.7 \times 10^3/\mu\text{L}$ (neutrophils $19.59 \times 10^3/\mu\text{L}$ (79.1%), lymphocytes $2.92 \times 10^3/\mu\text{L}$ (11.8%)), hemoglobin 9.1 g/dL (MCV 82.2 fL, MCH 25.8 pg, MCHC 31.4 g/dL), hematocrit 29%, platelets $540 \times 10^3/\mu\text{L}$. LED 65, D-dimer examination on July 19th, 2021 revealed 8590 ng/mL and August 4th, 2021 revealed 877 ng/mL. CRP on July 15th, 2021 revealed 155.72 mg/L and August 4th, 2021 revealed 237.95 mg/L. Two-sided blood culture before (July 21st, 2021) revealed no growth and cerebrospinal fluid culture (July 26th, 2021) revealed no growth. Stool examination within normal result. Cerebrospinal fluid analysis on S hospital (July 26th, 2021) revealed none and pandy reaction were positive (+++), with red color, blood was positive, mono 20%, poly 80%, erythrocyte $>50/\text{HPF}$, glucose 4, liquor cell 880 cell/uL, protein total 242.90 mg/dL. Cerebrospinal fluid analysis evaluation on SG hospital (August 7th, 2021) revealed none and pandy reaction were positive (+++), with clear color, blood was negative, mono 91%, poly 9%, erythrocyte negative, glucose 33, liquor cell 126 cell/uL, protein total 173.50 mg/dL. The result of the last thorax X-ray in S Hospital (August 4th, 2021) revealed ground glass opacity in the right lung and both hilum, the impression of pneumonia increased. Swab PCR for SARS-CoV2 results on August 4th and 5th were negative. Non-contrast head CT-Scan revealed large area of acute infarct in the left insula, capsule-ganglionic region, caudate nuclei and wedges of cortical, deep white matter of left fronto-temporal-parietal lobe as the territory of right MCA with external/ cortical watershed zones with PCA. There is also multiple focal

areas of acute infarct in the cortical-subcortical of bilateral frontal lobes and parietal lobes in parasagittal as the territory of ACA. Focal area of acute infarct in the right parietal lobe, cytotoxic edema with mass effect to the right lateral ventricle seen with rightward midline shift by 5,8 mm, no hemorrhagic transformation. Echocardiography revealed mild loculated pericardial effusion. Urinalysis within normal limits, second blood culture revealed no growth, and cerebrospinal fluid cultured revealed pseudomonas stutzeri, with antibiotic recommendation was Ceftazidim.

Patient was diagnosed by acute cerebral infarction due to severe COVID-19 + bacterial meningitis due to Pseudomonas stutzeri + mild loculated pericardial effusion due to MIS-C + mild normochromic normocytic anemia due to infection + well nourished. The patient was given ceftazidime, paracetamol, valproic acid, levetiracetam, clopidogrel and he also consult to the physical medicine and rehabilitation division for the physiotherapy.

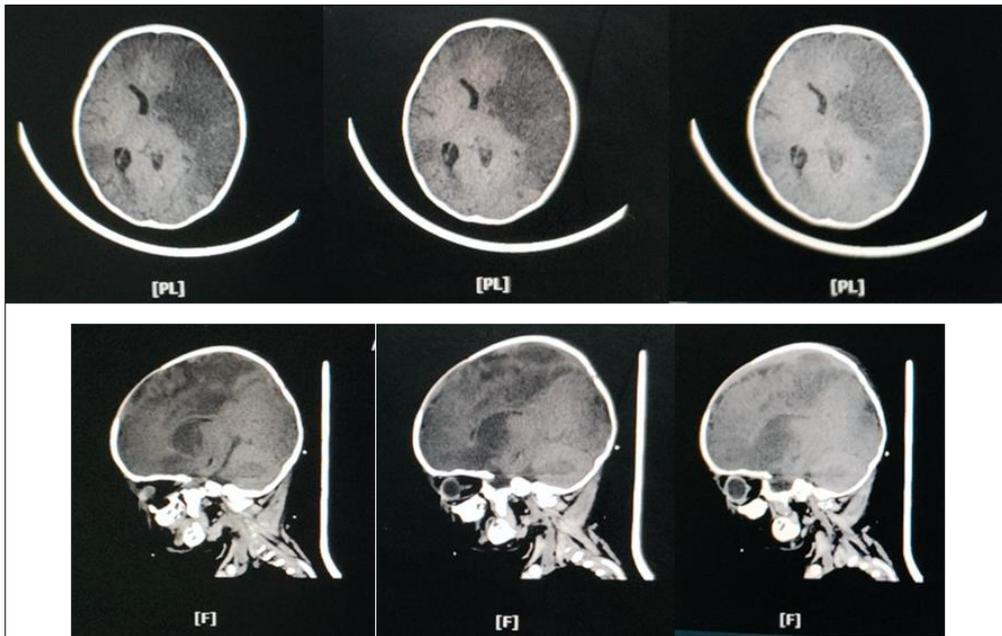


Figure 1 Head CT Scan result

After 3 weeks discharged from the hospital, the patient underwent a head MRI examination and the results revealed chronic ischemic cerebral infarction at left fronto-parieto-temporo-occipital lobe differential diagnose with encephalomalacia, leptomeningeal enhancement in the left fronto-parieto-temporo-occipital and right frontal suggests meningitis, hypoplasia of the corpus callosum, communicating hydrocephalus (left is heavier than right), mega cisterna magna. The patient was planned to undergo a VP shunt as a treatment for hydrocephalus.

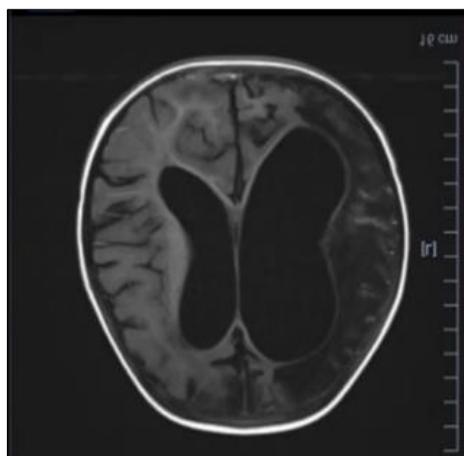


Figure 2 Head MRI result

3. Discussion

Patients with COVID-19 were classified as being asymptomatic (4.4%) or as having mild (50.9%), moderate (38.8%), severe (5.2%) or critical disease (0.6%) based on clinical features, laboratory testing, and imaging. In the children infected with SARS-CoV-2, it was observed that only a small proportion of infected children became severely or critically ill. About half of the children with COVID-19 was asymptomatic or mild cases, and several were classified as moderate due to the radiological abnormalities in spite of their mild clinical manifestations [1]. Severe disease was defined as the presence of dyspnoea, central cyanosis, and an oxygen saturation of less than 92%. Critical disease was defined as presence of acute respiratory distress syndrome, respiratory failure, or shock. Younger children were more at risk for severe illness than older children, wherein half of the children with critical disease was less than a year old [5,6]. Among the 184 children (7.2%) for whom exposure to COVID-19 information was available, 168 were (91%) infected by a positive close contact within the household or community. Among 345 pediatric patients with information on underlying comorbidities, 80 (23%) had at least one underlying health condition, most commonly chronic lung disease (including asthma), cardiovascular disease, or immunosuppression. This subset of patients and infants are more likely to require hospitalization, including intensive care [5,6].

Most children and adolescents with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have mild COVID-19 that does not lead to medical intervention. In late April 2020, clinicians in the United Kingdom reported a cluster of eight previously healthy children presenting with cardiovascular shock, fever, and hyperinflammation. On May 14, 2020, the Centers for Disease Control and Prevention (CDC) issued a national health advisory to report on cases meeting the criteria for multisystem inflammatory syndrome in children (MIS-C). Multisystem inflammatory syndrome in children associated with SARS-CoV-2 led to serious and life-threatening illness in previously healthy children and adolescents [4].

In a study, neurological involvement was common in children and adolescents with COVID-19 related hospitalization and is mostly transient. The range of severe neurologic complications including peripheral nerve disorders (GBS and variants), focal CNS disease (ischemic stroke due to large vessel occlusion, cerebral venous sinus thrombosis, and focal cerebral arteriopathy), and diffuse CNS involvement (CNS infection, ADEM, severe encephalopathy with white matter and corpus callosum lesions, and acute fulminant cerebral oedema) make it likely that multiple mechanisms underlie this wide spectrum of disease [2,3]. There are several mechanisms of infection with the SARS-CoV-2 virus which are believed to involve the neurological system. Similar to SARS-CoV-2, the molecular mechanisms underlying cell invasion by SARS-CoV-2 are related to the capacity of the virus to bind to angiotensin-converting enzyme 2 (ACE2) receptors [3].

A spectrum of life-threatening neurologic involvement infrequently occurred and was associated with more extreme inflammation and severe sequel. Future immunologic studies of cell-mediated and cytokine immune responses in young individuals may provide insight into the pathogenesis of neurologic disease in COVID-19 and MIS-C. Patients with less severe neurologic involvement could have future sequelae. Long-term follow-up of pediatric patients with COVID-19-related neurologic involvement is needed to evaluate effects on cognition and development [2].

Kamath N et al, 2021 reported that many children and adolescents hospitalized for COVID-19 or multisystem inflammatory syndrome in children had neurologic involvement, mostly transient symptoms. A range of life-threatening and fatal neurologic conditions associated with COVID-19 infrequently occurred [3]. **In this case**, patient was diagnosed by acute cerebral infarction by head CT Scan result.

In contrast with typical adult COVID-19, MIS-C predominantly affects cardiovascular, gastrointestinal, and/or neurological organ systems and only occasionally the respiratory system. Cardiovascular manifestations, including severe circulatory failure and myocardial involvement requiring intensive care, burdens MIS-C substantially, and was dominantly present in all deceased patients. Nevertheless, the majority of patients (98.1%) survived the acute phase of MIS-C and the patients are substantially older, and represent more systemic inflammation (higher WBC counts and drastically increased CRP and IL-6), more lymphocytopenia and thrombocytopenia, and higher markers of myocardial injury (troponin and NT-pro-BNP) and coagulopathy (D-dimers). Half of the MIS-C cases that fulfilling complete Kawasaki Disease (KD) criteria was presented with shock, contrasting with non-COVID-19-associated KD shock syndrome with an incidence rate of only 3.3–7% of KD cases. Coronary dilatation (11.6%) and aneurysm formation (10.3%) are more prevalent than in appropriately treated KD (~5%), as well as mortality rates, typically less than 0.1% in KD (1.9% in MIS-C). Severe COVID-19 might be related to host immune overdrive and unbounded cytokine release. In contrast with adult COVID-19, respiratory symptoms are less common in MIS-C and primary respiratory failure does not seem a dominant cause for ICU admission. Moreover, the clinical presentation of MIS-C is mainly characterized by

systemic vasculitis, multisystem involvement, and hypercoagulation. However, although abnormal coagulation parameters are frequently reported, thrombotic or embolic events were rare, in contrast with adult COVID-19 [7].

According to Zoua H et al, 2021, the study documented three common types of MIS-C clinical presentation: persistent fever and gastrointestinal symptoms, shocked with heart dysfunction and Kawasaki disease-like syndrome. MIS-C patients proved with a marked inflammatory state were possibly associated with SARS-CoV-2 infection [8]. MIS-C criteria by IPS such as children aged 0-19 years old, fever ≥ 3 days AND accompanied by two of: (1) Rash or bilateral conjunctivitis or mucocutaneous inflammation, (2) Hypotension or shock, (3) Cardiac disorders, (4) Coagulopathy, (5) Acute GI symptoms with elevated inflammation marker ESR, CRP, procalcitonin with contact with patient or evidence of COVID-19 infection (RT-PCR, antigen, serology), and no evidence bacterial involvement as causal of inflammation [9]. In this case, patient was diagnosed by MIS-C COVID-19 in the previous hospital, patient with aged 7 months old, with fever ≥ 3 days, increase of D-Dimer, pericardial effusion, increase of CRP and LED result, with a positive result of RT PCR SARS-COV2 before.

Patients with MIS-C had prominent cardiovascular involvement, including shock, echocardiographic findings of decreased function, and coronary artery aneurysms, for which they received urgent intervention. Given the similarities between MIS-C and Kawasaki's disease, a vasculitis of childhood that can cause coronary artery aneurysms and sometimes a shock-like presentation, most patients with MIS-C were treated with intravenous immune globulin (IVIG), the standard treatment for Kawasaki's disease. Although contemporaneous studies showed clinical and immunophenotypic differences between Kawasaki's disease and MIS-C, findings of myocarditis in many patients with MIS-C also supported treatment with IVIG, given its use in clinical practice for viral myocarditis. Features of cytokine storm led to the use of dexamethasone in patients with acute Covid-19, and the frequent concurrent finding of a severe shock-like presentation in patients with MIS-C probably encouraged the use of glucocorticoids, in varying doses [4,10]. Son MBF et al, 2021 reported that among children and adolescents with MIS-C, initial treatment with IVIG plus glucocorticoids was associated with a lower risk of new or persistent cardiovascular dysfunction than IVIG alone [10]. In our case, the patient was given intravenous methylprednisolone and IVIG in the previous hospital and the clinical presentation was improved.

After 3 weeks discharged from the hospital, the patient underwent a head MRI examination and the results revealed chronic ischemic cerebral infarction, communicating hydrocephalus (left is heavier than right), mega cisterna magna. Communicating hydrocephalus occurs when full communication occurs between the ventricles and subarachnoid space. It is caused by overproduction of cerebrospinal fluid, defective absorption of CSF such as intracranial haemorrhage or meningitis resulting in damage to the arachnoid granulations, where CSF is reabsorbed, or venous drainage insufficiency [11].

4. Conclusion

We presented a case of neurological involvement in children with COVID-19. In this case, the patient was found to have acute cerebral infarction caused by COVID-19 infection. The range of severe neurologic complications including peripheral nerve disorders, focal CNS disease and diffuse CNS involvement, make it likely that multiple mechanisms underlie this wide spectrum of disease. That is importance for early recognition by clinical presentation, laboratory also radiologic results to know the neurological involvement in COVID-19 patient because it is a life-threatening problem and was associated with more extreme inflammation and severe sequele.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There is no conflict of interests. The author reports no conflicts of interest in this work. By this statement, the author, I Gusti Ngurah Made Suwarba have no conflict of interest regarding this manuscript publication.

Statement of informed consent

Informed consent was obtained from the patient whose data mentioned in the study.

References

- [1] Balasubramaniam S, Rao NM, Goenka A, Roderick M, Ramanan AV. Coronavirus disease 2019 (COVID-19) in children - What we know so far and what we do not. *Indian Pediatr.* 2020; 57(5): 435-442.
- [2] Jha NK, Ojha S, Jha SK. Evidence of coronavirus (CoV) pathogenesis and emerging pathogen SARS-CoV-2 in the nervous system: A review on neurological impairments and manifestations. *Journal of Molecular Neuroscience.* 2020; 1-18.
- [3] Kamath N., Iyengar A., George N., and Lucykx VA. Neurologic involvement in children and adolescents hospitalized in the united states for COVID-19 or multisystem inflammatory syndrome. *JAMA Neurol.* 2021; 78(5): 536-547.
- [4] Feldstein LR, Rose EB, Horwitz SM. Multisystem inflammatory syndrome in U.S. children and adolescents. *N engl j med.* 2020; 383(4): 334-346.
- [5] Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A et al. SARS-CoV-2 infection in children and newborns: A systematic review. *Eur J Pediatr.* 2020;1-18.
- [6] Mon EY, Mandelia Y. Managing COVID-19 infection in pediatric patients. *Cleve Clin J Med.* 2020.
- [7] Hoste L, Paemel RV, HAerynck F. Multisystem inflammatory syndrome in children related to COVID-19: A systematic review. *European Journal of Pediatrics.* 2021; 1-16.
- [8] Zoua H, Lu J, Liu J, et al. Characteristics of pediatric multi-system inflammatory syndrome (PMIS) associated with COVID-19: A meta-analysis and insights into pathogenesis. *International Journal of Infectious Diseases.* 2021; 102: 319–326.
- [9] Matic KM. SARS-CoV-2 and multisystem inflammatory syndrome in children (MIS-C). *Curr Probl Pediatr Adolesc Health Care.* 2021; 51(4).
- [10] Son MBF, Murray N, Friedman K, et al. Multisystem Inflammatory Syndrome in Children- Initial Therapy and Outcomes. *N engl j med.* 2021; 385(1): 23-34.
- [11] Nelson SL. Hydrocephalus. *Medscape J Med.* 2018.