

SEVERE ENCEPHALITIS IN AN INFANT WITH COVID-19: A CASE REPORT

Aspazija Sofijanova ^a, Olivera Jordanova ^a, and Khalaf H. Hasan Hivi ^b



Submitted: 2/10/2020; Accepted: 24/4/2021; Published: 21/9/2021

ABSTRACT

Encephalitis is a severe condition that consists of neurological dysfunction caused by inflammation of the brain tissue. Etiological factors for the occurrence of this condition include infectious and non-infectious causes.

CASE REPORT

A nine-month-old infant was referred to the hospital in a convulsive state, fever, and disturbed consciousness to the hospital objectives. From anamnestic information, the infant has been febrile for two days with protracted vomiting started just before admission at the hospital. At admission, the infant looked toxic with fever, shortness of breath, weak reaction to painful stimuli, and generalized tonic-clonic convulsions. He was admitted to the Isolation Unit by the protocol of the hospital. Laboratory investigations were done. Due to the persistence of the seizure, a CT scan of the brain was performed. It was showing dilated lateral ventricles, with intraventricular masses and pronounced internal hydrocephalus. The results of SARS-COV-2 from the infant were positive as well as the grandmother. The infant was intubated immediately and put on mechanical ventilation SIPPV.

CONCLUSION

SARS-CoV-2 infection may cause severe clinical symptoms, neurological manifestations, and encephalitis in infants.

Keywords: *Severe encephalitis, infant, COVID-19.*

^a University Children's Hospital– Skopje, North Macedonia

^b Pediatric Teaching Hospital-Iraq, College of Medicine, University of Duhok, Kurdistan Region, Iraq.

Correspondence: dr_gargary@uod.ac

INTRODUCTION

Encephalitis is a severe condition that consists of neurological dysfunction caused by inflammation of the brain tissue⁽¹⁾. Etiological factors for the occurrence of this condition include infectious and non-infectious causes^(2, 3). The exact cause of this condition is often unknown, but the most common infectious causes are viruses. The viruses that can cause encephalitis include Varicella-Zoster virus, Epstein-Barr virus, Herpes simplex virus (HSV type 1 and 2), Enteroviruses, Rubella, West Nile virus, and Rabies⁽²⁻⁴⁾. Encephalitis can also be caused by a bacterial infection such as Tuberculosis, Syphilis, Lyme disease, or after an infection caused by parasites such as Toxoplasmosis⁽⁵⁾. Non-infectious causes include an autoimmune reaction in the body, which occurs when the body's immune system produces antibodies against brain tissue^(6, 7). Diagnostic tests required to confirm the diagnosis include blood tests, bronchoalveolar lavage or sputum, urine and stool tests, EEG, lumbar puncture, X-ray, computed tomography scan (CT scan), and magnetic resonance imaging (MRI)^(8, 9). The treatment of viral encephalitis consists of antiviral drugs, supportive therapy such as; monitoring cardiac and respiratory function and respiratory support, intravenous fluids, anti-inflammatory drugs, and anticonvulsant drugs⁽¹⁰⁻¹²⁾.

Human Coronaviruses (CoVs) can be found in the human population, and they can cause respiratory, enteric, hepatic, and neurological diseases^(13, 14). A novel coronavirus appeared in December 2019 in Wuhan, Hubei province of China, with severe pneumonia causes⁽¹⁵⁾. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the third human coronavirus known to co-opt the peptidase angiotensin-converting enzyme 2 (ACE2) for cell entry⁽¹⁶⁾. SARS-CoV-2 cell entry is dependent on its 180-kDa spike (S) protein, which mediates two essential events: binding to ACE2 by the amino-terminal region and fusion of viral and cellular membranes through the carboxyl-terminal region⁽¹⁷⁾. Infection of lung cells requires host proteolytic activation of the spike at a polybasic furin cleavage site⁽¹⁸⁾. The lung pathology in severe disease is different from the earlier pneumonitis, with progressive loss of epithelial-endothelial integrity, septal capillary injury, marked neutrophil infiltration, complement deposition, intravascular viral antigen deposition, and localized intravascular coagulation⁽¹⁹⁾. The virus binds to the angiotensin-converting enzyme 2 (ACE2) receptor, located in the epithelium

of the small intestine, respiratory tract, kidney cells, respiratory tract, the vascular endothelium throughout the body throughout the central nervous systems. Angiotensin-converting enzyme 2 (ACE2) receptor is expressed in astrocytes, oligodendrocytes, neurons, and concentrated in ventricles. Posterior cingulate cortex, olfactory bulb, substantia nigra, and middle temporal gyrus. Most patients with SARS-CoV-2 manifest a respiratory infection followed by sore throat cough, fatigue, shortness of breath, and respiratory distress. In addition to these effects on organic systems, more extensive studies published by China and France show that as many as 36% of patients with this infection develop neurological symptomatology. SARS-CoV-2 can cause a wide range of symptoms from other organ systems such as the gastrointestinal tract, manifested by diarrhoea and vomiting, blood clotting disorders, and heart damage⁽²⁰⁻²²⁾.

Organ dysfunction can be life-threatening. Rapid clinical symptoms in pediatric patients infected with SARS-CoV-2 and neurological impairment may lead to endotracheal intubation and placement of this group of patients on mechanical ventilation⁽²⁸⁻³⁰⁾.

CASE REPORT

A nine-month-old infant referred to the hospital in convulsive status, fever (temperature 38.2) and disturbed consciousness. From anamnestic information, the infant has been febrile for two days with protracted vomiting just before admission to the hospital. Epidemiological survey for COVID-19 was false negative. At the time of admission, the infant looked toxic with fever, shortness of breath, weak reaction to painful stimuli and generalized tonic-clonic convulsions. He was admitted in the Isolation Unit by the protocol of the Hospital. The convulsion was treated with intravenous midazolam. The test of SARS-CoV-2 were done. Laboratory investigations were done: Complete blood count: Hemoglobin=105 mg/dl, Erythrocytes=4,45 x 10¹²/l, Leucocytes=10,69 x 10⁹/l, platelets=242 x 10⁹/l, Haematocrit= 31,8 %, Neutrophils=45.5%, Lymphocytes=43.5%; C-reactive protein= <0.2 mg/l; Glycaemia= 13.46 mmol/l; Sodium= 133 mmol/l, Potassium=4,3 mmol/l, Calcium=2,13 mmol/l, Phosphor=1,72 mmol/l, Magnesium=0,77 mmol/l, Chloride=106 mmol/l; Total bilirubin=1.8 umol/l; Direct bilirubin = <1.8 umol/l; AST=54 U/L; ALT= 29 U/L; LDH= 314 U/L; GGT= 10 U/L; Creatinine=41 umol/l; Urea= 3,3 mmol/l; Total protein=56 g/l, Albumin=42 g/l; CK= 206 U/L; CKMB= 49.12 U/L;

Severe Encephalitis in an Infant with COVID-19: A Case report

ABS: pH= 7.38; pCO₂=34.1 mmHg ; pO₂=90.5 mmHg; HCO₃=19.7 mmol/l; BE=-4.9 mmol/l ; sO₂=96.1 %. Urinalysis parameters were normal. Due to suspected encephalitis, a lumbar puncture was done. Ophtalmology consultation done and fortunately fundus oculi examination was normal. lumbar puncture done, CSF was obtained under pressure, clear, without elements, with proteinrachia and glycorachia. CSF biochemical analysis: Lactates = 1.70 mmol/L, Glucose 5.08 mmol/L, Proteines = 2027 mg/L PCR film array diagnostic were not isolated from the CSF a causative agent. Blood culture showed growth of Staphylococcus Aureus. Parenteral antibiotic therapy with cefotaxime and amikacin, antiviral drug, and anti convulsants. Due to the persistence of convulsive status, a CT scan of the brain was performed with the finding of enlargement of

the lateral ventricles, with intraventricular masses and pronounced internal hydrocephalus (Figure 1)

Late that day, the results of SARS-COV-2 turned positive, the grandmother who had taken care of the infant during the past two weeks. A teleconference with Geneva Children's Hospital was done; the infant had swiss citizenship. They suggested intubation as they were planning according to transfer the infant to their country by fly ambulance. That happened immediately after a few minutes with cardiac arrest and no breathing. The infant was intubated immediately and put on mechanical ventilation SIPPV. After a couple of hours, the plane came to the child using protocols for Covid 19 pandemia was transferred safely to Geneva.

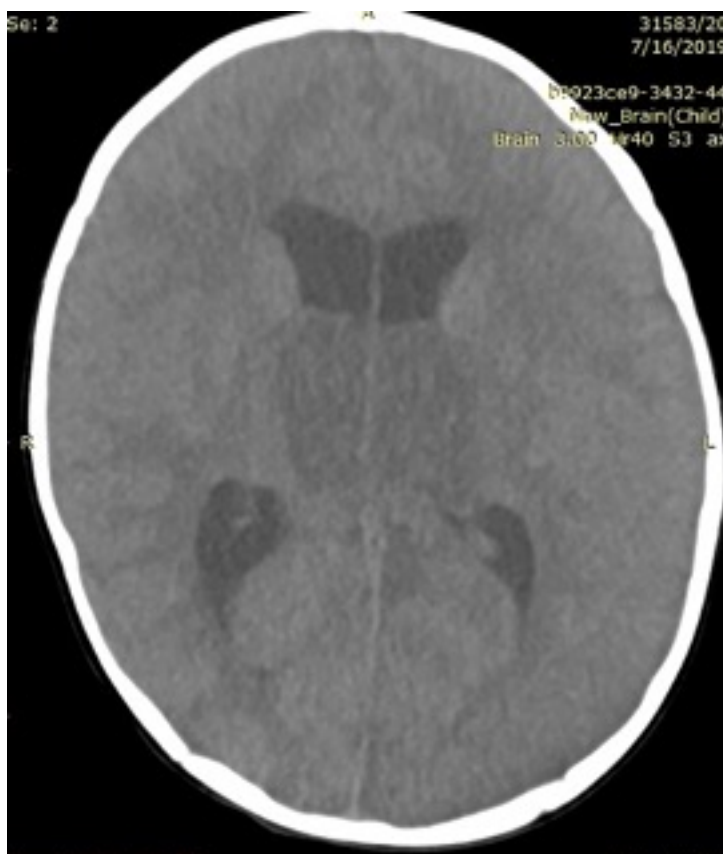


Figure 1 . CT Scan of the brain -enlargement of the lateral ventricles, with intraventricular masses and pronounced internal hydrocephalus

DISCUSSION

Infants are at higher risk of getting encephalitis due to viral infection. Symptoms of viral encephalitis in infants usually start with mild flu-like symptoms, such as fever, fatigue, weakness, headache, muscles, or joint pain. The symptoms can be much more severe and include seizures, confusion, loss of sensation and paralysis, agitation or hallucinations, muscle weakness, loss of consciousness, and coma in young children and infants, symptoms and signs encountered: tense fontanelles, poor feeding, irritability, nausea, and vomiting⁽⁷⁾. Timely diagnosis and treatment are essential because it is difficult to predict how encephalitis will affect each individual. Given the heterogeneity of the disease, epidemiological, laboratory, clinical, and radiographic examinations have required making a diagnosis and preparing the therapeutic protocol. According to previous studies worldwide, more than a third of patients with SARS-CoV-2 develop neurological symptoms. Convulsions, loss of sense of smell and taste, hallucinations, disorientation, confusion, movement disorders⁽²³⁻²⁵⁾. The SARS-CoV-2 virus can result in encephalitis, brain oedema, stroke, neurological disease, and Guillain-Barré syndrome. The immune system responds to SARS-CoV-2 infection with attacks on nerve cells, leading to muscle weakness and paralysis^(26,27). Once in the bloodstream, the brain barrier replicates and causes neurological involvement. Although most patients in the pediatric population are asymptomatic or have a mild clinical picture, in some of them, the clinical vision may deteriorate rapidly and lead to acute respiratory distress or respiratory failure. Some pediatric patients may develop severe clinical manifestations with myocardial injury or heart failure, hypoxic encephalopathy, coagulation dysfunction, shock, and acute kidney injury.

In this case, report the fast-moving of the poor child health and aggressive progression of the disease with proven SARS CO2 19 virus we were engaged with the information of this child as having severe inflammatory reaction SIRS that progressively made meningoencephalitis affecting all areas of the brain (we could not predict how long it has taken in the child body) because of poor information of the family. Still, we suppose that it has probably taken longer than two days (with fever). Encephalitis has put an infant in terrible condition and stopped circulation and breathing⁽²⁸⁻³⁰⁾.

We are talking and sharing the experience with colleagues from Swiss. We could have expected this to happen. We have performed all the procedures, including monitoring the mechanical ventilation and drug therapy. No specific drug for Covid 19 has been given.

In conclusion, SARS-CoV-2 infection may cause severe clinical symptoms, neurological manifestations, and encephalitis in infants.

REFERENCES

1. Hancock B. Re: Public Health and Wellbeing Amendment (No Jab, No Play) Bill 2015.
2. Kennedy PG. Viral encephalitis: causes, differential diagnosis, and management. *Journal of Neurology, Neurosurgery & Psychiatry*. 2004 Mar 1;75(suppl 1):i10-5.
3. Roos KL. Meningitis, encephalitis, brain abscess, and empyema. *Harrison's principles of internal medicine*. 2008:2621-41.
4. Fisher DL, Defres S, Solomon T. Measles-induced encephalitis. *QJM: An International Journal of Medicine*. 2015 Mar 1;108(3):177-82.
5. Larner AJ. *Neuropsychological neurology: the neurocognitive impairments of neurological disorders*. Cambridge University Press; 2013 May 2.
6. Armangue T, Petit-Petrol M, Dalmau J. Autoimmune encephalitis in children. *Journal of child neurology*. 2012 Nov;27(11):1460-9.
7. Thompson C, Kneen R, Riordan A, Kelly D, Pollard AJ. Encephalitis in children. *Archives of disease in childhood*. 2012 Feb 1;97(2):150-61.
8. Venkatesan A, Tunkel AR, Bloch KC, Laming AS, Sejvar J, Bitnun A, Stahl JP, Mailles A, Drobot M, Rupprecht CE, Yoder J. Case definitions, diagnostic algorithms, and priorities in encephalitis: consensus statement of the international encephalitis consortium. *Clinical Infectious Diseases*. 2013 Oct 15;57(8):1114-28.
9. Kneen R, Michael BD, Menson E, Mehta B, Easton A, Hemingway C, Klapper PE, Vincent A, Lim M, Carrol E, Solomon T. Management of suspected viral encephalitis in children—Association of British Neurologists and British Paediatric Allergy, Immunology and Infection Group national guidelines. *Journal of Infection*. 2012 May 1;64(5):449-77.

Severe Encephalitis in an Infant with COVID-19: A Case report

10. Ito Y, Kimura H, Yabuta Y, Ando Y, Murakami T, Shiomi M, Morishima T. Exacerbation of herpes simplex encephalitis after successful treatment with acyclovir. *Clinical infectious diseases*. 2000 Jan 1;30(1):185-7.
11. Lewis P, Glaser CA. Encephalitis. *Paediatrics in review*. 2005 Oct 1;26(10):347.
12. Zekeridou A, Karantoni E, Viacoz A, Ducray F, Gitiaux C, Villega F, Deiva K, Rogemond V, Mathias E, Picard G, Tardieu M. Treatment and outcome of children and adolescents with N-methyl-D-aspartate receptor encephalitis. *Journal of neurology*. 2015 Aug 1;262(8):1859-66.
13. Weiss SR, Leibowitz JL. Coronavirus pathogenesis. *Adv Virus Res*. 2011; 81:85164.
14. Masters PS, Perlman S. Coronaviridae. In: DM Knipe, PM Howley, eds. *Fields virology*, 6th edn. Philadelphia, PA: Lippincott Williams & Wilkins; 2013: 825-858.
15. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet*. 2020; 395: 470- 473.
16. K. G. Andersen et al., *Nat. Med.* 26, 450 (2020).
17. F. Li, *J. Virol.* 89, 1954 (2015).
18. M. Hoffmann et al., *Mol. Cell* 78, 779 (2020).
19. C. Magro et al., *Transl. Res.* 220, 1 (2020).
20. Zubair AS, McAlpine LS, Gardin T, Farhadian S, Kuruvilla DE, Spudich S. Neuropathogenesis and Neurologic Manifestations of the Coronaviruses in the Age of Coronavirus Disease 2019: A Review. *JAMA Neurology*. 2020 May 29.
21. Ye M, Ren Y, Lv T. Encephalitis as a clinical manifestation of COVID-19. *Brain, behaviour, and immunity*. 2020 Apr 10.
22. Wang HY, Li XL, Yan ZR, Sun XP, Han J, Zhang BW. Potential neurological symptoms of COVID-19. *Therapeutic Advances in Neurological Disorders*. 2020 Mar;13:1756286420917830.
23. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). *InStatpearls [internet]* 2020 Mar 8. StatPearls Publishing.
24. Singhal T. A review of coronavirus disease-2019 (COVID-19). *The Indian Journal of Pediatrics*. 2020 Mar 13:1-6.
25. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. *Pediatric pulmonology*. 2020 May;55(5):1169-74.
26. Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential faecal-oral transmission. *Gastroenterology*. 2020 May 1;158(6):1518-9.
27. Mao L, Wang M, Chen S, He Q, Chang J, Hong C, Zhou Y, Wang D, Miao X, Hu Y, Li Y. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study.
28. Cruz AT, Zeichner SL. COVID-19 in children: initial characterization of the pediatric disease. *Paediatrics*. 2020 Jun 1;145(6).
29. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Paediatrics*. 2020 Mar 1.
30. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. *The Pediatric infectious disease journal*. 2020 May;39(5):355.