Title: Clinical spectrum of neurological manifestations in pediatric Covid-19 illness: a case series

Authors:

1. Dr Afreen Khan
MD Pediatrics
Assistant Professor, Department of Pediatrics,
HIMSR & HAHC Hospital
New Delhi

2. Dr Aparna Chakravarty
MD Pediatrics, Fellowship Pediatric Infectious Disease (Canada)
Associate Professor
HIMSR & HAHC Hospital
New Delhi

3. Dr Abhinav Jain
MD Radiology
Professor & Head of the Department, Department of Radiodiagnosis
HIMSR & HAHC Hospital
New Delhi

4. Dr Rekha Harish
MD Pediatrics,
Professor & Head of the Department, Department of Pediatrics
HIMSR & HAHC
New Delhi

5. Dr Rizwan Naqishbandi
Senior Resident, Department of Pediatrics
HIMSR & HAHC
New Delhi

6.Dr Twisha Ishani
Post Graduate Student, Department of Pediatrics
HIMSR & HAHC
New Delhi

Address of the correspondence :
Dr Afreen Khan
J-738, Gaursportswood, Noida Sector-79
GautamBuddha Nagar,
U.P.

Summary :

We describe a cohort of three patients with variable neurological presentations by SARS COV-2 infection. It includes one case each of Acute Cerebellitis, Acute encephalomyelitis and Arterial Ischemic Stroke.. To the best of our knowledge we report the first pediatric case of acute cerebellitis due to SARS CoV-2 infection.

All critically ill patients were treated with methylprednisolone pulse therapy and dexamethasone. Patient with acute cerebellitis in addition required Intravenous Immunoglobulin infusion. All the patients responded to the treatment with complete neurological recovery.

INTRODUCTION:

Since the emergence of COVID -19 pandemic, varied clinical manifestations are reported which further broaden the spectrum of illness caused by SARS CoV-2 infection. In the early phase of the pandemic most published data were on adults with SARS CoV-2 infection. Only mild symptoms like fever, cough, headache, rhinorrhoea, myalgia, sore throat etc. were reported in children [1]. It was therefore presumed that children had only mild symptoms with less hospitalisation, until April 2020 when reports from the United Kingdom described the features suggestive of incomplete Kawasaki Disease and Toxic shock syndrome in association with SARS CoV-2 infection [2]. Since then, similar presentations have been reported in children across the globe and have been termed as Multisystem Inflammatory syndrome in children (MIS-C) [3-7]. It incorporates a spectrum of presentations from mild symptoms to severe life threatening complications like respiratory failure, shock, disseminated intravascular coagulation, renal failure etc[8]. Data on pediatric neurological complications following COVID 19 is scarce and they are either reported as a part of large studies or as individual case reports. Here we report three cases with different neurological manifestations of SARS CoV-2 infection and also the first case of acute cerebellitis in pediatric age group. Consent was taken from the parents of all the cases.

CASE SERIES:

1. Acute cerebellitis (Case 1)

Eleven year old male child presented to the Emergency Department with two episodes of generalised tonic-clonic seizures. There was a history of fever, headache, vomiting and abdominal pain for last three days. On examination the child was delirious and had horizontal nystagmus, dysarthria, nuchal rigidity, features of raised intracranial tension (ICT) and shock. In view of raised ICT 3% normal saline was infused. Broad spectrum antibiotics (Ceftriaxone and Acyclovir) along with intravenous fluids, inotropes were administered. Contrast enhanced magnetic Resonance Imaging (CEMRI) brain revealed features of acute cerebellitis (Figure 1a and 1b). Initial laboratory investigations were unremarkable. Intravenous Methylprednisolone pulse therapy (30 mg/kg/day for 3 days) was started. On third day the child deteriorated neurologically however his hemodynamical parameters stabilized and was weaned off the inotropic infusion. Serial MRI revealed increasing cerebellar edema. Further laboratory evaluation showed elevated inflammatory markers along with positive COVID serology, fulfilling the criteria for MIS-C (Table-1). Other laboratory investigations were not

suggestive of any viral, bacterial or immunological abnormality (Table1).CSF analysis could not be performed due to persistent raised ICT. Intravenous Immunoglobulin (IVIG) infusion (2gm/kg of body weight single dose), mannitol and steroids (intravenous Dexamethasone 0.15mg/kg/dose 6 hourly) were added. Child improved gradually. Cognition improved in next four days but cerebellar signs -ataxia, dysarthria and nystagmus persisted. CEMRI brain performed on Day 7 also displayed slow resolution of cerebellar edema. Oral steroids (Prednisolone 2mg/kg/day), antiepileptic drugs, osmotic agents along with physiotherapy were continued. Steroids were gradually tapered over a period of 6-8 weeks. On follow up at four months child is stable with normal neurological examination and neuroimaging demonstrated complete resolution.

2. Encephalomyelitis(Case 2)

Seven year old female, known case of right temporal epilepsy on multiple antiepileptic drugs since 5 years of age presented with a history of high grade fever, loose stools, vomiting and throat pain for four days.

On examination she was sick, febrile with generalized erythematous rash, swollen lips and non suppurative tonsillo-pharyngitis. She was hemodynamically stable with normal systemic examination. Intravenous antibiotics - Injection Ceftriaxone 100 mg/kg/day and Clindamycin-30 mg/kg/day) along with symptomatic treatment were started. SARS CoV-2 RT PCR was negative and initial laboratory parameters were normal except renal profile suggestive of prerenal AKI. Next day she developed toxic shock syndrome. Significant laboratory parameters were leucocytosis, thrombocytopenia, raised inflammatory markers with slightly deranged renal profile and hypo-albuminemia (Table 1). Child was shifted to Pediatric Intensive Care Unit, started on inotrope (Norepinephrine @1 µg/kg/min) and antibiotics were upgraded to injection Meropenem @ 60 mg/kg/day and Vancomycin @45 mg/kg/day. Over next 36 hours the body rash and pharyngitis improved. However on day 4, there was a sudden neurological deterioration with Glasgow Coma Scale of 5/15 and poor respiratory efforts, and thus was mechanically ventilated. Chest X-ray was normal. CSF analysis was performed which did not reveal any evidence of viral/bacterial meningitis and RT PCR for COVID-19 was also negative. However, CEMRI brain suggested possibility of encephalitis with myelitis (Figure 2a and 2b) and serology for SARS CoV-2 was positive. Child met all the criteria of Multisystem Inflammatory Response Syndrome-Children (toxic shock syndrome, multisystem involvement, raised inflammatory markers, no other obvious cause of inflammation, positive SARS CoV-2 serology). In setting of MIS-C with no other explainable cause for neurological involvement it was attributed to SARS CoV-2 infection. Pulse methylprednisolone therapy (30 mg/kg/day) for 5 days followed by intravenous dexamethasone 0.15mg/kg/dose 6 hourly was started. Child was extubated after two days of ventilation. After receiving pulse methylprednisolone therapy she developed hypertension which was managed with antihypertensive drugs. She responded well to the therapy and was discharged after 16 days on oral steroids which were continued 6 weeks and stopped after tapering. At two month follow up patient had no neurological deficit.

3.Arterial Ischemic Stroke(Case 3)

Fifteen years old female with no chronic medical history presented to Emergency Department with brief history of headache and multiple episodes of generalized tonic clonic seizures in the last 24 hours. On examination child was apprehensive, sick looking, conscious and had respiratory distress. The saturation on oxygen by mask @ 6 L/min was 86%. Initial stabilization started with administration of high flow oxygen by mask with reservoir bag, intravenous fluids and antiepileptic drug. Her condition soon deteriorated and patient had gasping respiration for which she was mechanically ventilated. A probable diagnosis of severe acute respiratory infection was made. Initially the seizures were attributed to hypoxia. Complete neurological examination could not be performed as child was sedated during ventilation. Empirical antibiotics Ceftriaxone, vancomycin and Oseltamivir were started. Initial laboratory values showed total normal leucocyte count with lymphocytopenia and raised inflammatory markers (CRP, ESR, Ferritin and D- Dimer). Chest X-ray was consistent with acute respiratory distress syndrome (bilateral coalescent opacities predominantly in the lower zones and parahilar location) but 3 subsequent samples from nasopharynx and tracheal aspirate were negative for SARS CoV-2 RT PCR. She was gradually weaned off the ventilator support and shifted to Bilevel Positive Airway Pressure (BiPAP) mode of NIV after 5 days of admission. Post extubation, on neurological examination she had tremulousness of tongue and horizontal nystagmus. Neuro-imaging showed a small hypo-dense area involving subcortical white matter in the right frontal lobe suggestive of infarct(Figure 3) and a small intra-cerebral hematoma in left frontal lobe with mild peri-lesional edema.

Her antibody titres for COVID were significantly raised with raised inflammatory markers. A diagnosis of MIS-C was made. She was started on IV dexamethasone (0.15mg/kg/dose 6 hourly) followed by oral steroids for one week. Child also had hypertension for period of two days the cause of which could not be ascertained. She gradually improved and was discharged after 17 days. A follow up at 4 month showed no neurological deficit.

Discussion:

We report a cohort of three patients with distinct neurological involvement due to SARS CoV-2 infection:One case each of acute cerebellitis, arterial ischemic stroke and encephalomyelitis. Evidence of infection was positive antibodies against SARS-CoV-2 in all. The IgG antibodies were measured in patients serum by using indirect chemiluminescence immunoassay(CLIA) technology for the quantitative determination of Anti-S1 and Anti –S2 specific IgG antibodies to SARS CoV-2, a value of more than 15AU/ml was considered positive. Recent studies have suggested that COVID serology has high sensitivity and specificity in COVID-19 detection[9,10]. A meta-analysis performed by Zhang et al to study the diagnostic efficacy of anti SARS- CoV-2 IgG/IgM test for COVID 19 reported pooled sensitivity and specificity of 0.85(95% CI 0.79-0.90) and 0.99 (95% CI 0.98-1.0)[9]. The diagnosis of MIS-C was made when all the criteria suggested by CDC or WHO were fulfilled [11,12]. In the current series all three patients had specific neurological complications, were seriously ill, had MIS-C and definite neuroimaging finding. It was

consistent with the reports showing association of specific neurological complications with seriously ill patients [13, 14].

In adults, cerebrovascular problems due to thrombotic complications are the most common neurological sequel followed by meningitis and encephalitis [15]. There is limited information about detailed neurological involvement by SARS COV-2 virus in children and no large case series or studies on the same are available till date. They are also underreported in preverbal and critically ill children. To study these complications, Panda et al conducted a systematic review and meta-analysis. They included all articles published from December 2019 to July 2020 in children < 18 years with confirmed neurological complications due to COVID-19. The review showed that amongst 41 children with COVID -19 associated definite neurological complications, encephalopathy was a predominant neurological manifestation (25 children) followed by meningeal signs (17 children) and seizures (12 children)[13]. Similarly encephalopathy was the most common finding in the present series. In the review by Panda et al neuroimaging findings were available only for few patients but most of them were normal [13]. In contrast to this Lindan et al described post infectious immune mediated acute disseminated encephalomyelitis as the most common neuroimaging abnormality followed by myelitis and neural enhancement in 38 children with neurological disease related to SARS CoV-2 infection[16].However we cannot assign such ranks to our findings due to small cohort with three different neuroimaging findings.

At the time of presentation one patient had no respiratory involvement, one presented with SARI (severe acute respiratory infection) and other with pharyngitis that later developed pneumonia. This is consistent with the study by Ahmad et al. They suggested that neurological symptoms may precede respiratory symptoms or may be the only symptom of COVID 19[14].

Till date only few cases of arterial ischemic stroke were reported in children whereas none of acute cerebellitis and acute hemorrhagic encephalopathy [13, 16-19]. To the best of our knowledge we here report the first case of acute cerebellitis associated with SARS CoV-2 in children. After the onset of COVID pandemic, only ten cases of cerebellar symptoms, associated with SARS COV-2 infection have been reported. All patients were adult males and only one had serious neurocognitive impairment. Abnormal neuroimaging (bilateral cerebellar edema) was present only in one patient. Seven patients were treated with combination of IVIG and steroids or either of them whereas three patients did not receive any specific therapy. There was mortality of one patient who had severe respiratory involvement. Rest recovered completely within a short duration. [20-26]. In contrast to these reported patients with cerebellar symptoms, our patient was an adolescent male who had serious neurological involvement with significant MRI changes. He was treated with IVIG and steroids. Though he responded gradually but recovered completely.

In adults cerebrovascular accidents (CVA) are more commonly seen neurological complication of SARS CoV-2. CVA is rarely seen in children. Only few case reports are available till date in pediatric age group [19, 27, 28]. Lauren et al performed a survey including 61 international sites with pediatric stroke expertise and found that 4.6% of all the patients who had stroke were found to be positive for SARSCoV-2 however most of them

had additional established risk factor [29]. No such risk factors suggestive of thrombophilia were found in our patient. The main presenting complaints in previous reports were headache, vomiting and weakness of extremities but in our patient with AIS (Arterial Ischemic Stroke) had no previous history and presented with seizures and severe respiratory distress.

In this series all patients were treated with intravenous dexamethasone and pulse methylprednisolone therapy while one patient with acute cerebellitis required intravenous immunoglobulin (IVIG). These patients responded gradually to the treatment. On follow up visits none had any neurological deficits. Recent studies have also shown that steroids, IVIG and supportive therapy are mainstay of management [30].

Various pathogenic mechanisms have been proposed but nothing confirmatory has been known so far. ACE2 receptors present on glial cells in brain and spinal neurons serve as a target receptor for attachment and internalization of virus followed by multiplication and damage. The virus enters the brain either through the circulatory or neuronal pathway. The cytokines disrupt the blood brain barrier during the cytokine storm through enabling the virus brain entry. Virus can also reach the brain through the nasal epithelium via olfactory neurons and olfactory bulb or through peripheral nervous system in a retrograde manner through neurons. Virus damages the cells either directly or through post infectious autoimmune process. The above two mechanisms can explain the occurrence of encephalitis, ADEM (autoimmune disseminated encephalomyelitis) etc. [31-33]. In our series, both patients with cerebellitis and encephalomyelitis had negative SARS CoV-2 RT PCR, positive serology, elevated inflammatory markers and responded to the immunosuppressive therapy, which favors an immune-mediated phenomenon.

Cerebrovascular complications have resulted from thrombotic events supported by various studies demonstrating a hypercoagulable state in COVID; the cause of which is multifactorial like endothelial dysfunction, inflammation, hypoxia etc [34, 35].

Binding to ACE-2 receptors may also cause abnormally elevated blood pressure which increases the risk of cerebral hemorrhage. In three of our patients who were seriously ill transient hypertension was present. In patient with acute cerebellitis it was attributed to raise intracranial tension but in other two patients it could be explained by either steroids or above-mentioned mechanism. Detailed studies can help to analyze the association of hypertension with SARS CoV-2 infection.

In conclusion, though the vaccine has been introduced in many countries across the globe, it is not yet recommended in children < 18 years of age [36]. Even after recommendation follow up studies are required to assess the neuro-protective efficacy. Poor immunization coverage especially in resource limited countries and emergence of new mutant strains are other potential challenges. Identifying a neurological disease associated with SARS CoV-2 in patients with mild or no respiratory involvement is often difficult. We hereby emphasize that any neurological symptom in a SARS CoV-2 infections needs to be investigated appropriately and reported in detail to create a better understanding of the disease spectrum. This will enable treating physician for timely diagnosis and management failure of which might leave patients with severe neurological sequelae. More detailed studies are required to

further comment on the association between hypertension and COVID 19 illness, till than careful blood pressure monitoring will help to detect hypertension and its complications

Learning points/Take Home messages:

- High index of suspicion is required to diagnose neurological disease following SARS CoV-2 infection and the pediatrician should be prepared to have a complete set of laboratory data focusing on CNS diseases.
- Patients may present with isolated neurological involvement without affecting the respiratory system.
- Blood pressure should be monitored in all patients with MIS-C till more detailed studies are available.
- We emphasize that early intervention with Intravenous Immunoglobulins and steroids is beneficial in MIS-C patients with neurological disease.

References:

1.Wang E, Brar K. COVID-19 in children: An epidemiology study from China. J Allergy Clin Immunol Pract 2020; 8:2118-2120.

2.Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. The Lancet 2020;395:1607-1608.

3.Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF et al. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383:334-346.

4.Cheung EW, Zachariah P, Gorelik M, Boneparth A, Kernie SG, Orange JS et al. Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City. JAMA 2020;324:294-296.

5.Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA 2020;324:259-269.

6.Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet 2020;395:1771-1778.

7.Licciardi F, Pruccoli G, Denina M, Parodi E, Taglietto M, Rosati S et al. SARS-CoV-2-induced Kawasaki-like hyperinflammatory syndrome: A novel COVID phenotype in children. Pediatrics 2020;146:e20201711. doi: 10.1542/peds.2020-1711. Epub 2020 May 21.

8.Hoang A, Chorath K, Moreira A, Evans M, Burmeister-Morton F, Burmeister F et al. COVID-19 in 7780 pediatric patients: a systematic review. E Clinical Medicine. 2020;24:100433. doi: https://doi.org/10.1016/j.eclinm.2020.10433.

9. Zhang ZL, Hou YL, Li DT, Li FZ. Diagnostic efficacy of anti-SARS-CoV-2 IgG/IgM test for COVID-19: A meta-analysis. J Med Virol 2021;93:366-374. doi: 10.1002/jmv.26211.

10. Böger B, Fachi MM, Vilhena RO, Cobre AF, Tonin FS, Pontarolo R. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. Am J Infect Control 2021 ;49:21-29.

11.Centers for Disease Control and Prevention Health Alert Network (HAN). Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19). https://emergency.cdc.gov/han/2020/han00432.asp (accessed on 11th April 2021)

12. World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19: Scientific Brief. 2020. https://www.who.int/publications-detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19 (accessed on 11th April 2021)

13.Panda PK, Sharawat IK, Panda P, Natarajan V, Bhakat R, Dawman L. Neurological complications of SARS-CoV-2 infection in children: a systematic review and meta-analysis. J Trop Pediatr 2020; fmaa 070.doi:10.1093/tropej/fmaa070.

14. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: A literature review. J Clin Neurosci 2020;77:8-12.

15. Taherifard E, Taherifard E. Neurological complications of COVID-19: a systematic review. Neurol Res 2020;42:905-912.

16. Lindan CE, Mankad K, Ram D, Kociolek LK, Silvera VM, Boddaert N et al. Neuroimaging manifestations in children with SARS-CoV-2 infection: a multinational, multicentre collaborative study. Lancet Child Adolesc Health 2021;5:167-177.

17. McAbee GN, Brosgol Y, Pavlakis S, Agha R, Gaffoor M. Encephalitis associated with COVID-19 infection in an 11-year-old child. Pediatr Neurol 2020;109:94.

18. Dugue R, Cay-Martínez KC, Thakur KT, Garcia JA, Chauhan LV, Williams SH et al. Neurologic manifestations in an infant with COVID-19. Neurology 2020;94:1100-1102.

19. Shen MY, Dugue R, Maldonado-Soto AR, Thakur KT, Zyskind I, Vargas WS. Acute ischemic stroke in a pediatric patient with known exposure to COVID-19 and positive serology. Pediatr Neurol 2021;116:39-40

20. Mukherjee D, Sarkar P, Dubey S, Ray BK, Pandit A, Lahiri D. Ataxia as a presenting manifestation of COVID-19: Report of a single case. medRxiv 2020.https://doi.org/10.1101/2020.05.24.20103648.

21.Fadakar N, Ghaemmaghami S, Masoompour SM, Yeganeh BS, Akbari A, Hooshmandi S et al. A first case of acute cerebellitis associated with coronavirus disease (COVID-19): a case report and literature review. Cerebellum. 2020;19:911-914.

22. Povlow A, Auerbach AJ. Acute cerebellar ataxia in COVID-19 infection: A case report. J Emerg Med 2021;60:73-76.

23. Shah PB, Desai SD. Opsoclonus myoclonus ataxia syndrome (OMAS) in the setting of COVID-19 infection. Neurology 2020.doi:10.1212/WNL.0000000000010978.

24.Sanguinetti S, Ramdhani RA. Opsoclonus Myoclonus Ataxia Syndrome related to the Novel Coronavirus (COVID-19). J Neuroophthalmol. 2020.

25. Dijkstra F, Van den Bossche T, Willekens B, Cras P, Crosiers D. Myoclonus and cerebellar ataxia following Coronavirus Disease 2019 (COVID-19). Mov Disord Clin Pract 2020;7:974-976

26. Foucard C, San-Galli A, Tarrano C, Chaumont H, Lannuzel A, Roze E. Acute cerebellar ataxia and myoclonus with or without opsoclonus: a parainfectious syndrome associated with COVID-19. Eur J Neurol 2021.doi:10.1111/ene.14726.

27.Gulko E, Overby P, Ali S, Mehta H, Al-Mufti F, Gomes W. Vessel wall enhancement and focal cerebral arteriopathy in a pediatric patient with acute infarct and COVID-19 infection. Am J Neuroradiol 2020;41:2348-2350.

28.Mirzaee SMM, Gonçalves FG, Mohammadifard M, Tavakoli SM, Vossough A. Focal cerebral arteriopathy in a pediatric patient with COVID-19. Radiology 2020;297:E274-275.doi:10.1148/radiol.2020202197.

29.Beslow LA, Linds AB, Fox CK, Kossorotoff M, Zuñiga Zambrano YC, Hernández-Chávez M et al. Pediatric ischemic stroke: An infrequent complication of SARS-CoV-2. Ann Neurol. 2020. doi: 10.1002/ana.25991.

30. Gupta S, Chopra N, Singh A, Gera R, Chellani H, Pandey R et al. Unusual clinical manifestations and outcome of multisystem inflammatory syndrome in children (MIS-C) in a tertiary care hospital of North India. Journal of Tropical Pediatrics 2021.https://doi.org/10.1093/tropej/fmaa127.

31. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol 2020;92:552-555.

32.Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host–virus interaction, and proposed neurotropic mechanisms. ACS Chem Neurosci 2020;11:995-998.

33.Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. Brain Behav Immun. 2020;87:18-22.

34.Klok FA, Kruip MJHA, Van der Meer NJM, Arbous MS, Gommers DA, Kant KM et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145-147.

35. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 ;395:1054-1062.

36. World Health Organization. (2021). Interim recommendations for use of the AZD1222 (ChAdOx1-S [recombinant]) vaccine against COVID19 developed by Oxford University and AstraZeneca: interim guidance, 10 February 2021. World Health Organization. https://apps.who.int/iris/handle/10665/339477.

Table 1 : Laboratory Features of Three Children with Neurological Involvement

	Case1: Acute cerebeliitis	Case 2: Encephalomyelitis	Case 3 : Arterial ischemic stroke
Hemoglobin(g/dl)	9.9	10.2	8
TLC(thousand/cmm)	$11.51X10^3$	$22X10^3$	$9.7X10^3$
DLC(polymorphs(P), lymphocytes(L) in %)	P88L9	P60L30	P85L11
Platelet counts(lacs/cmm)	1.32	1.2	1.49
Blood Urea(mg/dl)	24.9	32.8	18
Creatinine(mg/dl)	0.38	0.5	0.75
SGOT(IU/L)	30	56	45
SGPT(IU/L)	19	71	13
Albumin(g/dl)	2.1	2.5	2.9
CRP(mg/dl)	4.8	Positive(Qualitative)	18.3
ESR(mm/hr)	60	60	
S. Ferritin(ng/ml)	336	362.5	265.9
D-Dimer(FEU/L)	1.47	1.51	4.08
Coagulation Profile	ProthrombinTime:14.0 sec INR: 1.04	Prothrombin Time: 15.6 sec INR : 1.16	Prothrombin Time=19.9 INR=1.49
Urine R/M	RBC: 8-10/hpf	WNL	WNL
Culture	Blood c/s : sterile	Blood c/s : Sterile CSF c/s: Sterile Throat swab c/s: Sterile	Blood c/s: Sterile
COVID RT PCR	Negative	Negative	Negative
SARS Co V-2 Antiibody(AU/ml)	185	149.0	42.5
Others	Influenza A & B RT PCR : Negative Serology for HSV, RSV, EBV, JE, Rotavirus, Parvovirus B-19 were negative ANA: Negative Immunoglobulin profile: WNL	Malaria serology : Negative Typhidot IgM: Negative NS1Antigen : Negative Dengue serology ; negative Scrub typhus : Negative	ANA: Negative APLA: Negative Influenza PCR : Negative
ECG	WNL	WNL	WNL
Echocardiography	WNL	Mild pericardial effusion	WNL
CSF Analysis	-	HSV-I : Negative HSV II- Negative JE PCR : Negative CMV IgM : Negative	-
USG whole abdomen	Mesentric adenitis with minimal free fluid	Malrotated right kidney Mild gall bladder wall edema & pelvic ascites	
Neuroimaging	Figure1a and 1b	Figure 2a and 2b	Figure 3

Abbreviations : TLC: Total leucocyte count, DLC: Differential leucocyte count, CRP: C- Reactive Protein, ESR: Erythrocyte sedimentation rate, S.ferritin: serum ferritin, R/M: Routine microscopy, WNL: within normal limits, C/S: culture and sensitivity, CSF: cerebrospinal fluid, HSV: Herpes simplex virus, JE: Japanese encephalitis, EBV: Epstein bar virus, VZ: Varicella zoster virus, RSV: respiratory syncytial virus,ANA : Antinuclear antibody, APLA: antiphospholipid antibody, PCR: polymerase chain reaction, EEG: electroencephalogram, PS: peripheral smear, MP : malarial parasite, USG: Ultrasonography, CEMRI : Contrast enhanced magnetic resonance imaging.

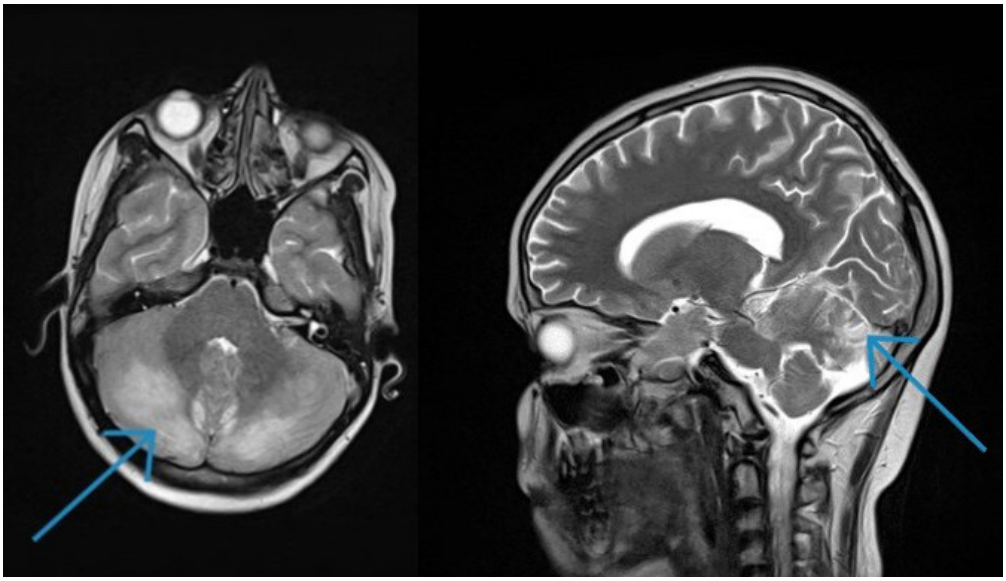

Figure 1a and 1b : Diffuse cerebellar swelling with T2/ FLAIR hyper intensity (arrows).These areas showed diffusion restriction on DW images and post contrast enhancement with mass effect suggestive of acute cerebellitis.

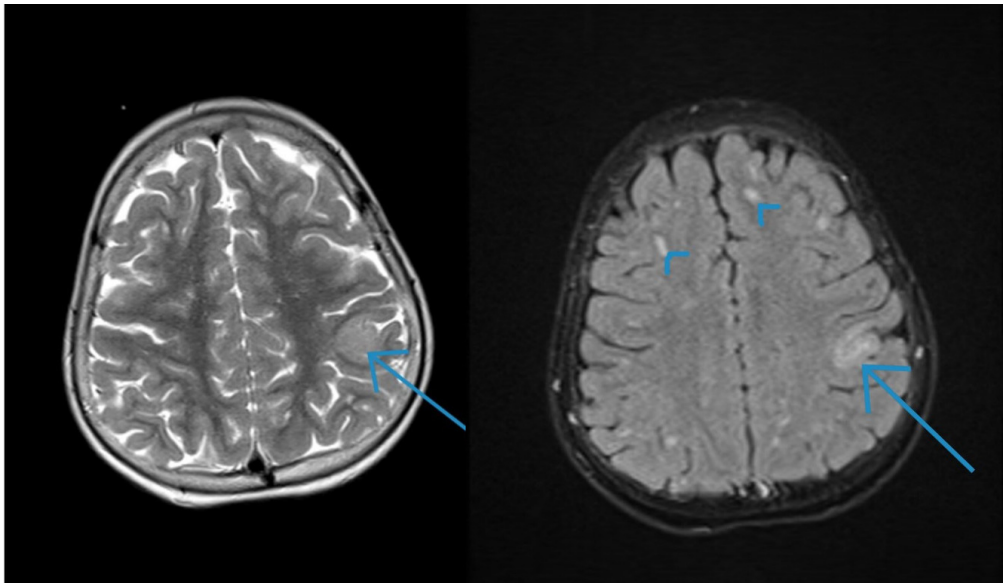

Figure 2a and 2b: Area of gyral swelling with hyper intensity in left frontal lobe on T2WI (arrow). Multiple smaller areas of hyper intensity are seen in the bilateral frontal and parietal lobes (arrowheads) On post contrast T1FS image, these show enhancements. Findings favored encephalomyelitis

112x65mm (300 x 300 DPI)

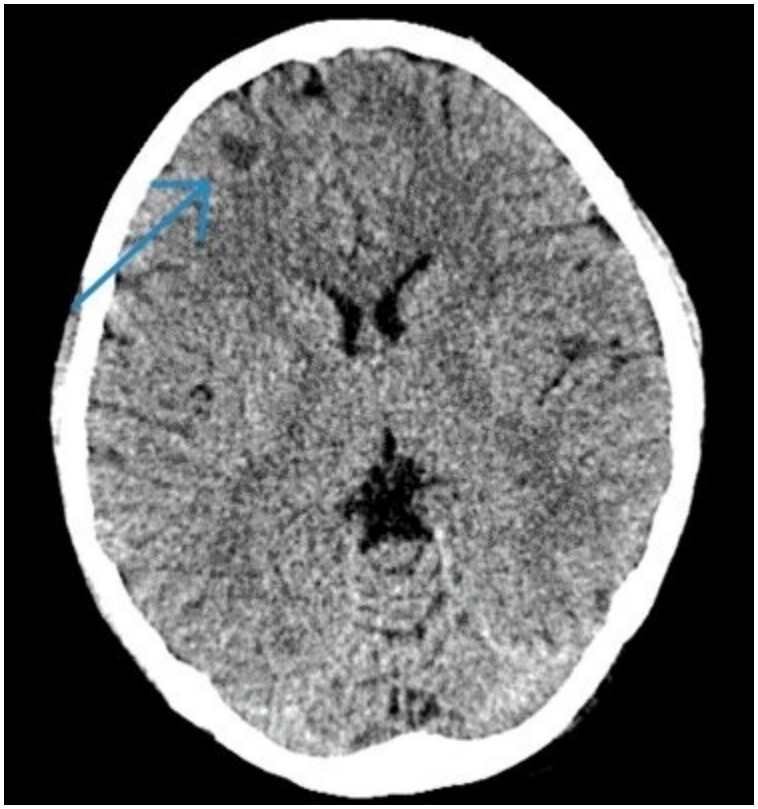

Figure 3 : Focal area of hypodensity (arrow) present in right frontal lobe suggesting ischemic change.

99x105mm (96 x 96 DPI)