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Case Report

Internal Medicine Section

Hypertension Secondary to COVID-19 Leading to Posterior Reversible Encephalopathy Syndrome in a 13-year-old Male

SARANYA SAI SATYA NELABHOTLA[1], PRADNYA DIGGIKAR[2], PRASHANT GOPAL[3]

ABSTRACT

Posterior Reversible Encephalopathy Syndrome (PRES) is a clinico-radiological condition defined by white matter vasogenic oedema predominantly affecting the posterior occipital and parietal lobes. A 13-year-old male presented with complaints of fever for four days. Upon evaluation, he turned out positive for COVID-19 with a Computed Tomography (CT) severity score of 5/25. Three days post admission (day 7 of illness), patient developed sudden onset of painless, diminution of vision in both eyes followed by two episodes of generalised tonic clonic seizures. Examination revealed a blood pressure of 180/110 mmHg. Characteristic Magnetic Resonance Imaging (MRI) findings led to a diagnosis of PRES. Patient was treated with antiepileptics, antihypertensives and intravenous mannitol and made a complete recovery. Early identification, treatment of symptomatology and correction of the underlying cause are all key aspects of management.

Keywords: Anticonvulsive agents, Coronavirus disease-2019, Convulsive generalised seizure disorder, Reversible cortical blindness, Vasogenic cerebral oedema

CASE REPORT

A13-year-old male with no significant medical history presented with complaints of fever for four days. Fever was continuous, high grade and relieved on taking over the counter medications. There was no history of cold, cough, breathlessness, palpitations, chest pain, pain in abdomen, headache or burning micturition. Patient was not vaccinated against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). His father and maternal uncle were both diagnosed with COVID-19 infection seven days earlier.

General examination revealed a Blood Pressure (BP) of 130/80 mmHg, Heart Rate of 96 beats per minute (bpm), respiratory rate of 16 cycles/minute, oxygen saturation of 97% at room air. All peripheral pulses were normal. Systemic examination revealed no abnormalities. Laboratory investigations revealed raised inflammatory markers and negative fever profile [Table/Fig-1].

Investigation	Value
Blood test	
Haemoglobin	11.0 gm%
Total leucocyte count	8700/mm^3 (54% neutrophils)
Platelets	3,18,800/mm^3
Total bilirubin	1.1 mg/dL
Lactate dehydrogenase	576 U/L
Urea	24 mg/dL
Creatinine	1.02 mg/dL
Serum sodium	136 mEq/L
Serum potassium (K^+)	4.8 mEq/L
Serum ferritin	526.7 ng/mL
Erythrocyte sedimentation rate	20 mm/hr
Dengue (NS1, IgM)	Negative
C-reactive protein	16.8 mg/L
Peripheral smear for malarial parasite	Negative
Urine culture	No growth
Sickling test	Negative
Procalcitonin	0.05 ng/mL
Urine analysis	
• Protein	Absent
• Glucose	Absent
• RBC	Absent
• Pus cells	1-2
Arterial Blood Gas (ABG)	
• pH	7.36
• pO_2	82
• pCO_2	36
• HCO_3	22.4
• Lactate	1.1
Others	
D-dimer	784 ng/mL
TSH	3.72 mIU/L
Antinuclear antibodies by indirect fluorescent antibody	Negative
Leptospira IgM	Negative
Blood culture	No growth
Serum cortisol	7 mcg/dL

[Table/Fig-1]: Laboratory investigations at presentation.

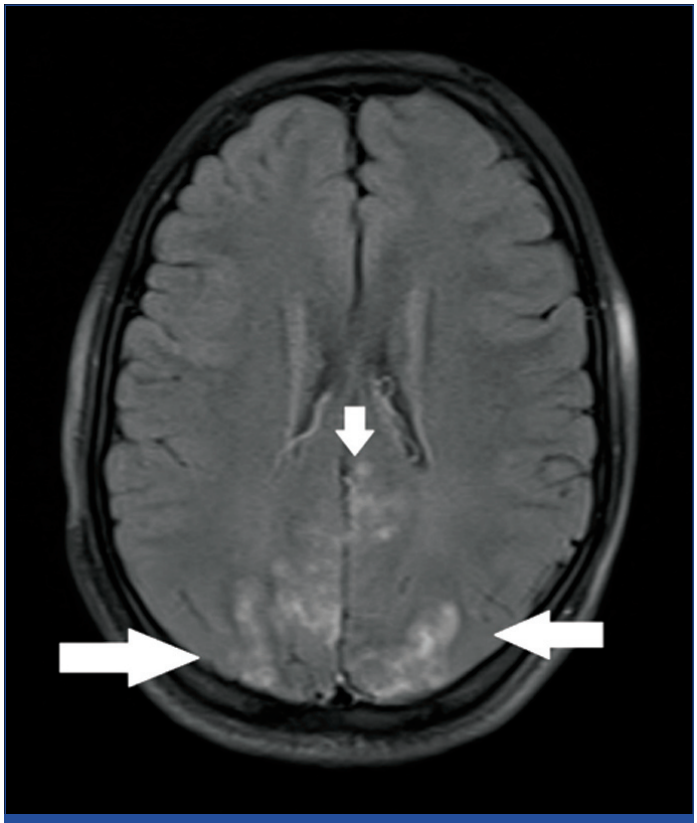
Test for COVID-19 Reverse Transcription-Polymerase Chain Reaction (RT-PCR) was positive. Patient was started on tab. paracetamol 500 mg and intravenous fluids. Steroids and antivirals were not started due to the mild nature of the disease. High-Resolution Computed Tomography (HRCT) thorax revealed bilateral peripheral basal consolidations with a Computed Tomography (CT) severity score of 5/25.

Patient was continued on symptomatic treatment and three days post admission, patient complained of painless sudden onset diminution of vision in both eyes associated with headache which was occipital and throbbing in nature. Patient was conscious, oriented and obeying commands. There was complete loss of vision in both eyes with no perception of light and projection of rays bilaterally. Ocular and fundus examination was normal. Pupil examination revealed normal accommodation and light reflexes.

Intraocular pressure was normal. Examination revealed a BP reading of 180/110 mmHg. Two hours later, patient developed two episodes of generalised tonic clonic seizures.Patient was unaware of these episodes and postictal confusion lasted for a few minutes with no bowel or bladder involvement. Kernig's and Brudzinski's were negative. Neurological examination revealed bilateral extensor plantar response. Cranial nerves, motor, sensory and deep tendon reflexes examination were normal.

An initial differential diagnosis of ischaemic stroke, cerebral haemorrhage, Cerebral Venous Sinus Thrombosis (CVST) and Posterior Reversible Encephalopathy Syndrome (PRES) was considered due to the abrupt onset of headache and bilateral vision loss with elevated blood pressure.

Cerebrospinal fluid analysis was normal. Neuroimaging {Magnetic Resonance Imaging (MRI) of brain with angiography and venography-plain and contrast} revealed T2-weighted Fluid Attenuated Inversion Recovery (T2/FLAIR) hyperintensities and corresponding T1WI hypointensities involving the cortical and subcortical white matter of bilateral parietal, occipital lobes and bilateral cerebellar hemispheres indicating vasogenic oedema suggestive of PRES [Table/Fig-2].



[Table/Fig-2]: Postcontrast T2/FLAIR image of MRI brain showing hyperintensities involving the cortical and subcortical white matter of bilateral parietal and occipital lobes.

Creatine kinase-MB (CK-MB) (112 IU/L) and cardiac Troponin-I (44 IU/L) were elevated. Electrocardiography (ECG) and 2D-echocardiography were normal. Plasma renin activity, aldosterone levels and plasma free nor metanephrine levels were normal. Renal artery doppler showed no abnormalities.

Based on the above findings, a diagnosis of PRES was made. A normal Cerebrospinal Fluid (CSF) picture and lack of an identifiable cause of hypertension led us to conclude that PRES was secondary to hypertension associated with COVID-19. Patient was started on injection mannitol, antiepileptics (inj levetiracetam 1 gm i.v. stat followed by 500 mg i.v. q12hr) and antihypertensives (tab. amlodipine 5 mg PO q12hr, tab. telmisartan 40 mg PO q24hr) anda target blood pressure of 130/80 mmHg was maintained. His vision started to improve on day 4 of admission and completely recovered by day five post admission. A contrast enhanced F-18 Fluorodeoxyglucose (FDG)-Positron Emission Tomography (PET) scan was done which showed mild to moderate hypometabolism in the region of the left sensorimotor cortex and mild hypometabolism in the left precuneus. Rest of the scan was normal.

Inj. mannitol (100 mL i.v. q8hr for 3 days followed by 100 mL i.v. q12hr for 1 day followed by 100 mL IV q24hr for 1 day) and antihypertensives (tab. telmisartan 40 mg q24hr for 5 days, tab. amlodipine 5 mg q12hr for 4 days followed by tab. amlodipine 5 mg q24hr for 5 days) were tapered and stopped by day 11 of admission. Patient was kept under observation for a total of 14 days at the end of which his BP was 130/80 mmHg. Visual acuity was 6/6 at the time of discharge. Patient was asymptomatic on follow-up three months postdischarge.

DISCUSSION

Posterior reversible encephalopathy syndrome is a clinico-radiological condition defined by white matter vasogenic oedema predominantly affecting the posterior occipital and parietal lobes. Hinchey J et al., originally described PRES in 1996 [1]. Seizures, loss of consciousness, headaches, visual problems, nausea/vomiting and focal neurological abnormalities are characteristics of this condition [2]. It has been reported in individuals ranging from 4-90 years, with the majority of cases affecting young to middle-aged adults [3].

Hypertension, preeclampsia/eclampsia, infections, renal dysfunction, autoimmune diseases such as systemic lupus erythematosus, systemic sclerosis, tumour lysis syndrome, Guillain-Barr syndrome, Acquired Immunodeficiency Syndrome (AIDS), thrombotic thrombocytopenic purpura, and immunosuppressive agents are among the most common causes of PRES, all of which cause cerebral vasogenic oedema, which appears to be the key pathogenic mechanism [4]. Stroke, meningoencephalitis, demyelinating diseases of the brain, and cerebral venous sinus thrombosis are all possible differential diagnoses [5].

Magnetic resonance imaging is the preferred imaging modality, which primarily shows bilateral subcortical hyperintense white matter regions, predominantly involving the parietal and occipital lobes. Hyperintensity on diffusion sequences with an elevated Apparent Diffusion Coefficient (ADC) is typically seen on MRI, indicating vasogenic oedema. In contrast, cytotoxic oedema caused by ischaemia is hyperintense and has low diffusion coefficient. The use of magnetic resonance angiography and venography helps rule out alternative diagnoses {Cerebral Venous Sinus Thrombosis (CVST) or stroke} [6].

Although the exact pathogenesis of PRES is unclear, it is thought to be due to rapid increase in blood pressure resulting in dysfunction of the autoregulatory mechanisms of cerebral blood vessels leading to vascular leakage and oedema. It is also suggested that the rapid rise in blood pressure could damage the blood-brain barrier, which explains involvement of the posterior circulation in PRES since it lacks sympathetic tone. However, in patients of PRES associated with other conditions like organ transplants, renal disease, and the use of immunosuppressive drugs with normal blood pressure, there may be certain endogenous or exogenous toxins that cause endothelial damages and vasogenicoedema [7].

Some cases of COVID-19 with PRES may develop macrophage activation syndrome (MAS) with fever and increased levels of tumour Necrosis Factor-alpha (TNF-α). TNF-α increases vascular permeability and upregulates vascular endothelial growth factor in the presence of hypoxemia causing endothelial injury and oedema [8].

The majority of PRES cases however, are associated with hypertension. In a study of six cases of PRES in COVID-19 patients by Colombo A et al., it was reported that CSF-PCR for SARS-CoV-2 genome was negative in all cases and that blood pressure fluctuations were the most relevant factor in PRES pathogenesis [9]. In a study of 15 COVID-19 patients with PRES by Hinchey J et al., 12 patients had abrupt increases in blood pressure [1].

Characteristic imaging findings and reversibility of symptoms were diagnostic of PRES. Since, other causes of hypertension were ruled out, and evidence of hypertension associated with COVID-19 is documented, the cause of PRES was determined to be due to hypertension secondary to COVID-19 infection. Elevated cardiac markers with normal electrocardiography and 2D-echocardiography were suggestive of myocardial injury.

The pathophysiology and consequences of COVID-19 are still poorly understood. COVID-19 patients without prior hypertension showed a rise in blood pressure during hospitalisation, and majority of the patients had higher systolic blood pressure. In a study of 190 COVID-19 patients, 8.42% patients had a rise in blood pressure during hospitalisation [10]. Another study on153 confirmed COVID-19 patients showed new onset hypertension in 18 patients [11].

The binding of SARS-CoV-2 to Angiotensin-Converting Enzyme 2 (ACE2), which inhibits angiotensin II breakdown and leads to increased blood pressure, is one possible mechanism. Another theory is that excessive Renin-Angiotensin-Aldosterone system (RAS) activation promotes inflammatory response and cytokine storm, which stimulates the Nicotinamide Adenine Dinucleotide Phosphate/Nicotinamide Adenine Dinucleotide Phosphate Hydrogen reduced form (NADP/NADPH) oxidase system and causes cell contraction and vasoconstriction [10].

Angiotensin II has been shown to have direct or indirect effects on cardiomyocytes, some of which were linked to proinflammatory and prohypertrophic responses. Increased Angiotensin II activity could lead to cardiac inflammation, oxidative stress, and myocyte death, especially when the balance between ACE and ACE2 was altered in COVID-19 patients. This hypothesis explains why COVID-19 patient's blood pressure may rise in parallel with mild cardiac injury [12]. Studies have suggested that SARS-CoV-2 binds to ACE2 receptors, which are abundant in myocytes andcan result in direct injury to cardiomyocytes [13]. Though the exact mechanism is still unknown, it is becoming evident that RAS plays a major role in hypertension and COVID-19 infection.

CONCLUSION(S)

Early identification, treatment of symptomatology, and correction of the underlying cause are all important aspects of PRES management. As the term implies, proper treatment is expected to result in a complete recovery. However, there have been reports of long-term complications and fatalities. Recurrence of symptoms has been observed in a few cases.

REFERENCES

[1] Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. N Engl J Med. 1996;334(8):494-500.
[2] Kumari DS, Arumilli MNLN, Reddy LSK, Reddy DN, Motor R. Acute intermittent porphyria presenting with posterior reversible encephalopathy syndrome: A rare cause of abdominal pain and seizures. Indian J Crit Care Med. 2020;24(8):724-26.
[3] Legriel S, Pico F, Azoulay E. Understanding Posterior Reversible Encephalopathy Syndrome. In: Vincent, JL. (eds) Annual Update in Intensive Care and Emergency Medicine 2011. Annual Update in Intensive Care and Emergency Medicine. vol 1. Berlin, Heidelberg: Springer; 2011. https://doi.org/10.1007/978-3-642-18081-1_56.
[4] Bartynski WS. Posterior reversible encephalopathy syndrome, part 1: Fundamental imaging and clinical features. AJNR Am J Neuroradiol. 2008;29(6):1036-42.
[5] Admane SS, Yelne TS, Giri PJ. A Case of posterior reversible encephalopathy syndrome mimicking stroke. Indian J Crit Care Med. 2020;24(9):877-78.
[6] Hugonnet E, da Ines D, Boby H, Claise B, Petitcolin V, Lannareix V, et al. Posterior reversible encephalopathy syndrome (PRES): Features on CT and MR imaging. Diagnostic and Interventional Imaging. 2013;94(1):45-52.
[7] Alnass AJ, Alamer RA, Alamri HH, Alharthi AA, Assad MA, Sedran MK, et al. Posterior reversible encephalopathy syndrome: A rare complication in COVID-19. Cureus. 2021;13(10):e18426.
[8] Arslan G, Besci T, Karaca Ö, AylanGelen S. Posterior reversible encephalopathy syndrome related to COVID-19 in a child. Pediatrics International. 2022;64(1):e14908.
[9] Colombo A, Martinelli Boneschi F, Beretta S, Bresolin N, Versino M, Lorusso L, et al. Posterior reversible encephalopathy syndrome and COVID-19: A series of 6 cases from Lombardy, Italy. eNeurologicalSci. 2021;22:100306.
[10] Chen G, Li X, Gong Z, Xia H, Wang Y, Wang X, et al. Hypertension as a sequela in patients of SARS-CoV-2 infection. PLoS ONE. 2021;16(4):e0250815.
[11] Akpek M. Does COVID-19 cause hypertension? Angiology. 2022;73(7):682-87.
[12] Forrester SJ, Booz GW, Sigmund CD, Coffman TM, Kawai T, Rizzo V, et al. Angiotensin II signal transduction: An update on mechanisms of physiology and pathophysiology. Physiological Reviews. 2018;98(3):1627-738.
[13] Khan S, Rasool ST, Ahmed SI. Role of cardiac biomarkers in COVID-19: What recent investigations tell us? Current Problems in Cardiology. 2021;46(10):100842.

PARTICULARS OF CONTRIBUTORS:
1. Resident, Department of General Medicine, Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
2. Professor, Department of General Medicine, Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
3. Resident, Department of General Medicine, Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Prashant Gopal,
Resident, Department of General Medicine, Dr. D.Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
E-mail: drprashantgopal@gmail.com

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