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Posterior Reversible Encephalopathy Syndrome: A Rare Complication in COVID-19

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Abstract

The coronavirus disease 2019 (COVID-19) has a broad spectrum of manifestations. Neurological complications are not uncommon in patients with COVID-19. We report the case of a middle-aged man who presented with a cough and fever. He had a decreased oxygen saturation and required supplementary oxygen therapy. During his stay, he developed an unexplained seizure. Computed tomography of the brain revealed vasogenic edema located posteriorly. Subsequently, magnetic resonance imaging demonstrated subcortical white-matter hyperdensities, in keeping with the diagnosis of posterior reversible encephalopathy syndrome, an exceedingly rare manifestation in COVID-19. This condition should be kept in mind when encountering unexplained neurological manifestations that developed in patients with COVID-19.

Categories: Emergency Medicine, Neurology, Radiology

Keywords: case report, encephalopathy, covid-19, posterior reversible encephalopathy syndrome (pres), seizure

Introduction

At the end of 2019, a novel coronavirus was identified as the pathogen responsible for a cluster of pneumonia cases in China. This coronavirus disease 2019 (COVID-19) spread rapidly worldwide and quickly reached a pandemic level. While COVID-19 predominantly involves the respiratory system, extra-pulmonary involvement is common. It is reported that more than 80% of hospitalized patients have neurologic symptoms during their disease course. Few cases of posterior reversible encephalopathy syndrome (PRES) have been reported in the setting of COVID-19. The majority of those cases occurred in critically ill patients receiving assisted mechanical ventilation. Herein, we report the case of a middle-aged man who developed a seizure in the setting of a moderate COVID-19 with no history of requiring mechanical ventilation. After thorough investigation, the patient was found to have PRES, an exceedingly rare complication of COVID-19.

Case Presentation

We present the case of a 43-year-old man who presented to the emergency department with a complaint of cough and fever for three days before presentation. His fever measured 38°C and did not improve with oral analgesic medications. The cough was associated with yellowish sputum. He did not report any history of shortness of breath, hemoptysis, or chest pain. His past medical history was remarkable for poorly controlled diabetes mellitus. He had no previous surgical history. He does not drink alcohol but had a 25-pack-year smoking history. He did not have any history of contact with ill persons. His family history was non-contributory.

On physical examination, the patient appeared tired but he was fully oriented. He had a heart rate of 105 bpm, a blood pressure of 136/84 mmHg, a respiratory rate of 21 bpm, and a temperature of 37.9°C. His oxygen saturation was 88% on room air. The patient was placed on a high-flow nasal cannula and maintained a normal oxygen saturation. Chest examination revealed a decreased air entry bilaterally with diffuse crackles. Cardiovascular and neurological examinations revealed normal findings.

Laboratory investigation revealed an elevated leukocyte count of 16,000/μL, C-reactive protein of 18 mg/L, erythrocyte sedimentation rate of 34 mm/hr., lactate dehydrogenase of 220 U/L, D-dimer level of 750 ng/ml, a ferritin level of 520 μg/L. Other laboratory investigations, including renal and liver function tests, revealed normal findings (Table 1). A chest X-ray demonstrated bilateral opacities throughout the lung fields with peripheral predominance. The patient underwent reverse-transcriptase polymerase chain reaction testing for the severe acute respiratory syndrome coronavirus 2, which yielded a positive result.

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Laboratory Investigation	Unit	Result	Reference Range
Hemoglobin	g/dL	14.2	13.0–18.0
White Blood Cell	1000/mL	16.0	4.0–11.0
Platelet	1000/mL	345	140–450
Erythrocyte Sedimentation Rate	mm/hr.	34	0–20
C-Reactive Protein	mg/dL	18	0.3–10.0
Total Bilirubin	mg/dL	1.0	0.2–1.2
Albumin	g/dL	4.0	3.4–5.0
Alkaline Phosphatase	U/L	65	46–116
Gamma-glutamyltransferase	U/L	34	15–85
Alanine Transferase	U/L	50	14–63
Aspartate Transferase	U/L	41	15–37
Lactate Dehydrogenase	U/L	220	140–280
Blood Urea Nitrogen	mg/dL	9	7–18
Creatinine	mg/dL	0.9	0.7–1.3
Sodium	mEq/L	139	136–145
Potassium	mEq/L	3.7	3.5–5.1
Chloride	mEq/L	101	98–107
Ferritin	µg/L	520	24–336
Procalcitonin	µg/L	0.04	0–0.05

TABLE 1: Summary of the results of laboratory findings

The patient was admitted for further evaluation and management of his COVID-19. He received empirical antibiotic therapy in the form of intravenous ceftiaxone 2 g once daily and intravenous dexamethasone therapy. Despite this, his oxygenation level deteriorated and required the use of bilevel positive airway pressure ventilation. Suddenly, the patient developed a tonic-clonic seizure that lasted two minutes. Subsequently, the patient underwent computed tomography (CT) scan of the brain and a bilateral subcortical hypodensity located posteriorly (Figure 1).

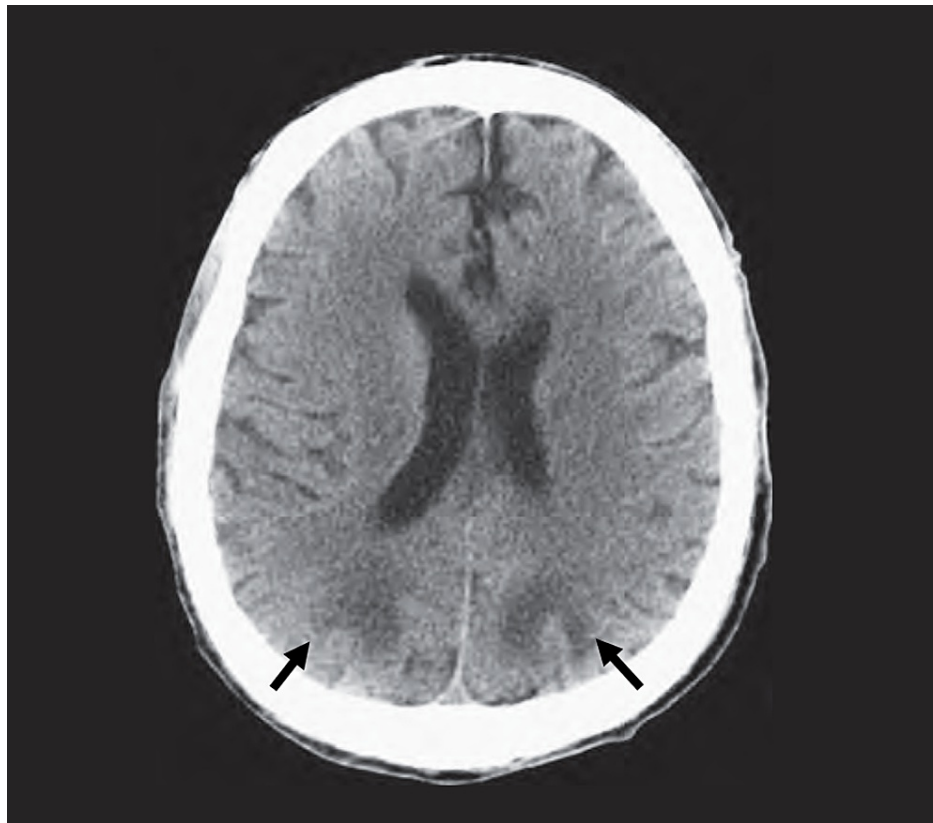


FIGURE 1: Computed tomography axial image of the brain demonstrating a bilateral subcortical hypodensity located posteriorly (arrows).

For further characterization of this lesion, the patient underwent magnetic resonance imaging (MRI) which revealed an increased signal in the subcortical area posteriorly (Figure 2). Considering the aforementioned clinical and radiological findings, the diagnosis of a PRES was established. The patient received supportive measures during his stay and his oxygen requirement decreased gradually. He was discharged in good clinical status.

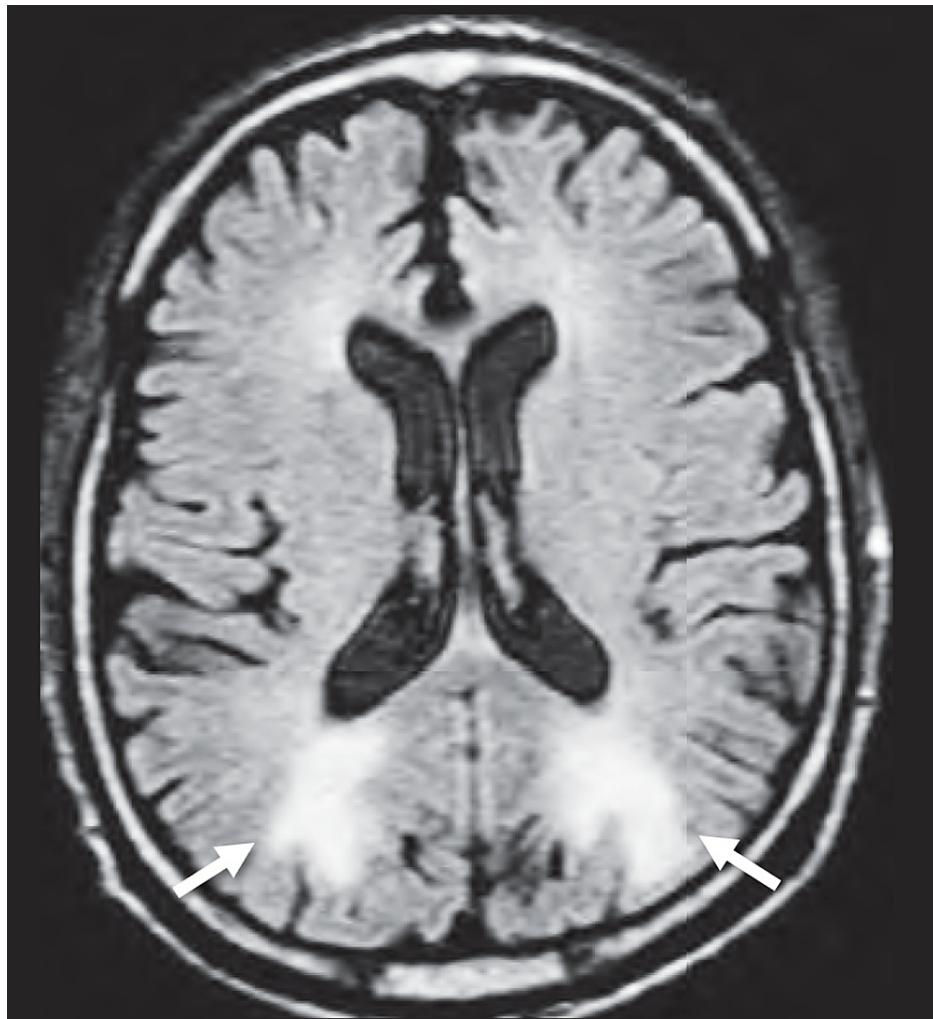


FIGURE 2: Magnetic resonance image of the brain demonstrating revealed an increased signal in the subcortical area posteriorly (arrows).

Discussion

We report the case of a middle-aged man with COVID-19 who developed PRES. This syndrome was first described by Hinchey in 1996 [1]. Previously reported cases of PRES were described in the setting of abnormal blood pressure during the event such as pre-eclampsia, renal disease, auto-immune diseases, and certain medications [2]. This condition may affect patients of any age and gender but it is more prevalent among women [3].

Imaging plays a crucial role in making the diagnosis of PRES because of its non-specific symptoms. PRES may present in a wide spectrum of clinical manifestations. Its presentation ranges from headache to seizure and altered level of consciousness [4]. On imaging, PRES demonstrates a bilateral symmetrical vasogenic edema involving the parietal and occipital lobes. While findings on CT could suggest the diagnosis of PRES, MRI remains the gold standard to diagnose this condition with high accuracy. Further, MRI is useful to exclude other clinical entities that share similar radiological features to PRES. Such conditions may include demyelination disorders, vasculitis, metabolic diseases, and venous thrombosis. It should be remembered that atypical features may occur such as involving the non-posterior lobes in PRES [3].

The exact pathogenesis of PRES remains unclear. It is thought to be related to a marked increase in blood pressure [5]. The acute elevation in the blood pressure results in overcoming the autoregulatory mechanisms of cerebral blood vessels leading to vascular leakage and brain edema. Furthermore, it is suggested that the rapid rise in blood pressure could damage the blood-brain barrier. This explains the predominant involvement of the posterior circulation in PRES since it lacks a sympathetic tone [1]. However, this theory provides insufficient explanation because a remarkable proportion of patients do not have abnormal blood pressure during the event, as in the present case. PRES has been associated with some medical conditions such as organ transplants, renal disease, and the use of immunosuppressive drugs [2]. However, none of

these risk factors were present in our patient. It is assumed that patients with PRES may have certain endogenous or exogenous toxins that cause endothelial damages and vasogenic edema.

Recent studies suggest that the PRES is increasingly being reported in COVID-19. For instance, Lallana et al. [6] reported eight cases of PRES in patients with COVID-19 requiring intensive care admission and mechanical ventilation. It was noted that half of those patients received immunomodulatory therapy suggesting its role in the pathogenesis of PRES in COVID-19. Additionally, Colombo et al. [7] reported six cases of PRES in COVID-19 from Italy. Similarly, five out of those cases occurred in patients with assisted ventilation. Hence, our study provides additional evidence that the PRES can occur in patients who were not on mechanical ventilators. None of the patients with PRES syndrome was found to have evidence of the viral genome in the cerebrospinal fluid. In our patient, analysis of the cerebrospinal fluid was not performed.

Careful monitoring and active treatment of hypertension in the setting of PRES are crucial [8]. Anti-convulsant medications may be used as adjunct therapy. Additionally, magnesium supplementation should be used in case of hypomagnesemia which is a common finding in PRES. The outcome of PRES is usually favorable if recognized early. However, complications can occur if the diagnosis was missed. These complications include ischemic stroke, status epilepticus, and possible herniation.

Conclusions

We present a rare case of PRES in a patient with COVID-19. The case suggests that patients with COVID-19 who are not assisted by mechanical ventilators can develop PRES. Hence, physicians should consider the diagnosis of PRES in patients with COVID-19 who develop unexplained neurological manifestations, including seizures. Given the non-specific symptoms of PRES, imaging studies should be performed in the appropriate clinical settings to make the diagnosis accurately.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. University Institutional Review Board issued approval Not Applicable. Case reports are waived by the institutional review board in our institution. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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