Encephalopathy with progression to posterior reversible encephalopathy pattern in a patient with COVID-19: clinical, imaging findings and follow-up

Ali Kerro

SUMMARY
Neurological conditions are being more recognised in patients with COVID-19, with encephalopathy being the most prevalent problem. Posterior reversible encephalopathy is suspected to occur due to elevated blood pressure and overproduction of inflammatory markers, both of which have been reported in the setting of COVID-19 infection. Encephalopathy was the main presentation in this case, without respiratory dysfunction initially, and with imaging findings indicative of posterior reversible encephalopathy syndrome as an aetiology. Follow-up imaging showed resolution of the abnormal results with mental status returning to baseline upon discharge.

BACKGROUND
Posterior reversible encephalopathy syndrome (PRES) includes various neurological problems, predominantly headache, encephalopathy, visual symptoms and seizures. The condition is mostly reversible, with recovery expected to occur within days to weeks.1 Predominant involvement of regions supplied by posterior circulation, with the resolution of findings on repeat neuroimaging studies, is typical in most patients.1 2 Reversible vasogenic oedema due to endothelial injury and blood–brain barrier breakdown caused by loss of cerebral flow autoregulation is the leading theory behind this disorder, with suspected roles for systemic inflammatory markers such as tumour necrosis factor α, interleukin 1 and interferon γ.3 Cases of PRES in the settings of COVID-19 are being recognised and reported.4 5 This case presentation is about a patient with COVID-19 who presented with encephalopathy without respiratory symptoms or focal findings who developed PRES during hospitalisation.

CASE PRESENTATION
An 85-year-old, right-handed Caucasian man was brought to the hospital by ambulance for a reported odd behaviour. Per ambulance records, an automobile repair shop called them as the patient came asking for his car to be fixed but was acting unusual. Reportedly, he was oriented to self, place and time but was trying to use a remote controller as a phone. Patient vital signs were only remarkable for a blood pressure of 184/96 mm Hg. His heart rate and respiratory rate were within the normal range, and his oxygen saturation was at 97% on room air. His family member stated the patient lives and does all daily living activities independently, including driving and managing finances. The night before admission, he contacted his family to talk with them and did not seem to realise that it was at an inappropriate hour. He was last seen weeks before admission. The patient had a history of paroxysmal atrial fibrillation on apixaban, a history of well-controlled diabetes mellitus, chronic kidney disease stage 3, and a history of hypertension that appeared to be under control from his primary care provider records and was on losartan and furosemide. There was no report of similar presentation per family with no report of alcohol or illicit drug use. At the emergency room, the patient Glasgow Coma Scale was 14 (eyes 4, verbal 4, motor 6) as he was awake, not in pain or distress, tracking examiner and following simple commands. He knew the month and year as well as his name, age and date of birth. His speech was clear, and he was aware of being in a hospital but could not name the president. He had decreased attention and did not cooperate for aphasia testing. He was slightly impulsive, trying to pull out the lines and leads connected to him. No findings suggestive of gaze or face palsy were found, and motor strength testing was intact. His chest X-ray showed bilateral lower lobe opacities, and SARS-CoV-2 molecular assay testing came back positive.

The patient was admitted to the hospital to gradually lower his blood pressure as he was being treated for encephalopathy, possibly due to COVID-19 with...
hypertensive encephalopathy pattern. However, his impulsive behaviour limited the ability to administer continuous intravenous blood pressure medication. On the second night of admission, he became drowsy, not following commands, requiring tactile stimulation to open his eyes, and had decreased verbal

Figure 2  Initial MRI DWI sequence.

Figure 3  CT brain repeat with bilateral subcortical occipital lobe region hypodensity.

Figure 4  CT brain done around 24 hours after the abnormal CT finding.

Figure 5  Repeat MRI FLAIR sequence.
output. This deterioration prompted further investigation and neurology consultation.

INVESTIGATIONS

Initial laboratory values showed normal white cell count (7.46×10⁹/L; reference range 3.50–11.50×10⁹/L), low platelet counts (93×10⁹/L; reference range 150–400×10⁹/L), elevated serum creatinine (1.81 mg/dL; reference range 0.70–1.30 mg/dL), normal total bilirubin (1.0 mg/dL; reference range 0.2–1.0 mg/dL), elevated serum lactate (2.4 mmol/L; reference range 0.4–2.0 mmol/L), normal procalcitonin (0.16 ng/mL; reference range <0.10 ng/mL) and normal ammonia (<10 µmol/L; reference range 11–32 µmol/L). Troponin was elevated (0.250 ng/mL; reference range ≤0.045 ng/mL) which was similar on follow-up measures done within 24 hours of initial testing. Alcohol level was negative. His blood glucose and remaining electrolytes were within the normal range. At day 20 post hospitalisation, his repeat platelet counts, and serum creatinine were 93×10⁹/L and 1.09 mg/dL, respectively.

CT of the head obtained on arrival to the emergency department was negative for encephalomalacia, midline shift, hydrocephalus or other acute findings (figure 1).

A brain MRI was obtained approximately 8 hours prior to the patient’s mental status change showed negative Diffusion weighted imaging (DWI) and Apparent diffusion coefficient (ADC) sequences (figure 2). A full MRI was limited due to his lack of cooperation and the inability to sit still. Fluid attenuated inversion recovery (FLAIR) sequence was not obtained at that time.

A repeat CT of the head obtained within hours of exam deterioration showed new regions of decreased density in the right cerebellar hemisphere and bilateral subcortical occipital lobe regions (figure 3).

These findings were confirmed with repeat head CT 24 hours after (figure 4). 1 hour electroencephalogram testing obtained after his exam deterioration showed theta range generalised slowing around 6 Hz without epileptiform discharges or focal slowing. A repeat brain MRI with and without contrast was delayed to limit over sedation and was done on day 12 post admission, which was normal without FLAIR abnormality or contrast enhancement (figure 5).

TREATMENT

His blood pressure continued to be elevated throughout the first 2 days of admission. Given the CT head findings, he was sent to the intensive care unit and was started on nicardipine continuous infusion for blood pressure goals of <140/90. The patient gradually became more awake but with decreased verbal output and would communicate only through a yes/no pattern. The patient required restraints at that time due to hyper motor delirium features. He was started on low dose valproic acid on day 4 of admission and tapered in a month. Nicardipine was no longer required by day 4, and he was restarted on his home blood pressure medication. A lumbar puncture was planned but was held as it was opted not to do invasive procedures that would require sedation since he gradually improved.

Throughout his hospitalisation, the patient did not show respiratory symptoms, and thus current treatment assigned for COVID-19, such as steroids or remdisivir, was not used.

OUTCOME AND FOLLOW-UP

The patient continued to show improvement and became more oriented on hospital day 19. He recognised his family members voices through phone conversation and would give consistently correct answers regarding basic orientation questions. He did require physical therapy given generalised weakness that is suspected to be due to prolonged hospital stay/deconditioning pattern. He was discharged to a skilled nursing facility 22 days from his initial presentation to the hospital. His family member stated the patient is back to baseline from a cognitive perspective during a phone interview with the patient and family member 15 days post discharge. Prior to discharge, he would experience fatigue and exertional dyspnoea easily from getting out of bed. At the time of the phone interview, the patient would use a walker to ambulate and shower by himself, which was an improvement as he could not do so when discharged from the hospital with fatigue continuing to improve.

DISCUSSION

Neurologic manifestations have been seen in patients with COVID-19 infections and can reach up to 82% of patients at any time during the disease course, with encephalopathy being most common.6 Delirium pattern appears to be a common feature in the elderly with COVID-19 and was reported to be a primary problem in about 16% of delirium with COVID-19 infection.7 The patient did present with elevated blood pressure and signs of acute kidney injury, which can also cause PRES in isolation without concomitant COVID-19 infection. Non-adherence to medication was felt unlikely given primary care records of patient adherence, confirmation from the family who visited the patient’s perspective

I remember driving down the road, it was a fair road, and I think I might have hit the outside of the curve and overcorrected, and I went into the ravine. I remember a lot of policemen and a lot of ambulance people who wanted to assist me and get me to the hospital. Basically, that is about all that I remember and then recall being stuck in the hospital. Truthfully, I did not like the experience of being in a hospital. My mind kept wandering, and I did not fathom why I was there and thought I was well. I did not think I was weak, but they told me I was, and when they told me I was not like a bull, I realized not a strong as I thought. I thought I was as strong as a bull, but I realized I was like a calf. I came to this realization maybe about a week or more after starting to know where I was. About two weeks after or so, I realized when I exercise too much, I was losing control of my breathing. I would lose the ability to breathe good whenever I try to walk. I am currently tired all the time.

I was happy when my nephews told me they were taking me out of the hospital, and happy good thoughts came to my head. I do not know if COVID was an issue, but my nephews seemed to think it was partially an issue.

Learning points

► A wide variety of neurological manifestations have been reported to occur with COVID-19.
► Posterior reversible encephalopathy is further recognised to occur in the setting of COVID-19 infection.
► Given the suspected effect of COVID-19 on blood pressure and cerebral autoregulation, a high level of vigilance towards avoiding elevated blood pressure for these patients may be considered.
his household, and patient confirmation on his phone interview post discharge. COVID-19 is suspected of causing cerebral auto-regulation and endothelial dysfunction, which result in blood pressure elevation through binding to the ACE two receptors.8 Most cases reported with COVID-19 and PRES have respiratory distress as their main cause of presentation to the hospital with only rare PRES presentation like behaviour without respiratory involvement.4 5 Avoidance of further workups, such as early repeat MRI and lumbar puncture, does pose a limitation to this case. However, further investigations were withheld given the patient’s progression towards improvement and preference to avoid anaesthesia and over sedation to obtain these workups not to lose patient exam.

The patient’s spontaneous resolution with an absence of signal changes on repeat MRI studies argues against the presence of vascular/inflammatory causes of initial patient CT and points further towards PRES as suspected pathology.

Contributors AK: sole author.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES
1. Lee VH, Wijdicks EFM, Manno EM, et al. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Arch Neurol 2008;65:205.
2. Shankar I, Banfield J. Posterior reversible encephalopathy syndrome: a review. Can Assoc Radiol J 2016;1–7.
3. Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol 2015;14:914–25.
4. Parauda SC, Gao V, Gewirtz AN, et al. Posterior reversible encephalopathy syndrome in patients with COVID-19. J Neurol Sci 2020;416:117019.
5. Anand P, Lau KH, Chung DI, et al. Posterior reversible encephalopathy syndrome in patients with coronavirus disease 2019: two cases and a review of the literature. J Stroke Cerebrovasc Dis 2020;29:105212.
6. Cardona GC, Loraine D, Pájaro Q, Moscote Salazar. J Neurol Sci 2020;412:116824.
7. Kennedy M, Helfand BK, Gou RY, et al. Delirium in older patients with COVID-19 presenting to the emergency department. JAMA Netw Open 2020;3:e2029540.
8. Zhang H, Penninger JM, Li Y, et al. Angiotensin-Converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med 2020;46:386–90.