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ORIGINAL ARTICLE

Persistent visual dysfunction following posterior reversible encephalopathy syndrome due to COVID-19: Case series and literature review

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Abstract

Background and purpose: The full spectrum of neurological sequelae in COVID-19 is beginning to emerge. SARS-CoV-2 has the potential to cause both direct and indirect brain vascular endothelial damage through infection and inflammation that may result in long-term neurological signs and symptoms. We sought to illuminate persistent neuro-ophthalmological deficits that may be seen following posterior reversible encephalopathy syndrome (PRES) due to COVID-19.

Methods: We identified three individuals with PRES due to COVID-19 in our hospital system. One patient was identified on presentation to our neuro-ophthalmology clinic. The other patients were identified through internal records search. These cases were compared to published reports of PRES in COVID-19 identified through systematic literature search of PubMed/LitCOVID.

Results: All three patients were hospitalized with severe COVID-19 and developed altered mental status with new onset seizures that led to the recognition of PRES through diagnostic imaging. During recovery, two patients had persistent visual dysfunction including visual field deficits. One patient also experienced hallucinatory palinopsia and visual hallucinations. Literature search identified 32 other cases of PRES in the context of COVID-19. Visual disturbances were described in 14 cases (40%), with only seven cases (50%) reporting full recovery by the time of publication.

Conclusions: As we learn about enduring neurological complications of COVID-19, it is possible that complications may be underrecognized and underreported. Understanding the range of complications can help in postcare evaluation and management changes in the critical care setting to potentially allow intervention before persistent deficits occur due to COVID-19.

KEYWORDS
case series, COVID-19, literature review, palinopsia, posterior reversible encephalopathy syndrome, PRES, visual field deficit

INTRODUCTION

A growing body of literature has documented the effects of SARS-CoV-2 infection on the central nervous system (CNS), which can range from mild anosmia and dysgeusia to encephalopathy, large vessel strokes, and other reported conditions [1]. Whereas some sequelae appear to be due to direct CNS infection, others may be an indirect effect of the infection-induced severe systemic inflammatory response [1]. Of concern, an increasing number of people with COVID-19, across the spectrum of disease severity, report persistent neurological symptoms weeks to months after the clearance

of infectious virus, including "brain fog," fatigue, headache, memory impairment, and concentration difficulty [2]. These individuals, who have been referred to as "long haulers" in the popular press, are currently estimated to represent 10% of patients recovering from COVID-19 [3].

The long-term consequences of SARS-CoV-2 infection on the CNS remain to be fully understood. In the next months to years of the pandemic, neurologists may begin to encounter patients experiencing neurological symptoms following COVID-19. It is vital to understand the range of post-COVID-19 neurological issues to provide the most appropriate treatments or referrals. Herein, we present a case series of two patients with persistent neuro-ophthalmological symptoms following posterior reversible encephalopathy syndrome (PRES) due to COVID-19. One patient presented to our clinic from within our health care system, whereas the other was discovered using an in-patient records search.

METHODS

Ethics statement

This study was conducted with approval by the institutional review board.

Institutional record search

Our institution's EPIC charting system was interrogated with a built-in, self-service reporting tool called SlicerDicer. Population data were first searched for patients with a confirmed diagnosis of "COVID-19" (International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM] U07.1). The search term "posterior reversible encephalopathy syndrome" (ICD-10-CM 167.83) was then added from the time period of 16 March 2020 (first confirmed cases of COVID-19 at our institution) to 23 February 2021.

Patient data

Patient data were extracted from chart review, including age, timing of diagnoses, brain imaging, COVID-19 hospital course, physical/occupational therapy documentation, follow-up appointment specialty, and progress notes. International case reporting (CARE) criteria were followed [4]. Imaging was reviewed by a fellowship-trained neuroradiologist (A.A.T.) to rule out other possible causes for the symptoms, such as stroke.

Literature review

The online database PubMed was searched with the query (posterior reversible encephalopathy syndrome) AND (COVID-19) from 1 January 2020 to 15 March 2021. All publications were publicly available through LitCOVID, an online datahub for tracking up-to-date information on COVID-19 scientific information. Publication abstracts were first reviewed for the presence of a case report or case series format describing COVID-19-associated PRES in adult patients. Publications were excluded if the main diagnoses in the abstract did not include PRES or COVID-19, if the cases occurred in pediatric patients, and if publications were reviews of the literature only. Included publications were retrieved from LitCOVID and reviewed for the presence of detailed clinical information on PRES occurring in a setting of COVID-19. Data extracted from these publications were age, sex, past medical history, visual and neurological symptoms related to PRES, PRES imaging findings, blood pressure (BP) measurements, and clinical outcomes. The clinical spectrum of COVID-19 was classified based on current definitions provided by the US National Institutes of Health [5].

Statistics

Descriptive statistics were employed. Graphs were created in Prism 8.

RESULTS

Institutional record search

From 16 March 2020 to 26 February 2020, our institution recorded 54,924 persons with confirmed COVID-19. Adding PRES to the search identified seven patients having both diagnoses. Chart review of these cases showed that only three of these cases were identified as having PRES during hospitalization for COVID-19, whereas the diagnoses were not temporally related in the other five cases. The two cases identified as having PRES in the context of COVID-19 are highlighted below because of persistent deficits, including one patient identified as having visual deficits noted during rehabilitation (Case 2 below). The third case of PRES due to COVID-19 did not experience any documented persistent neurological symptoms and is not reported here.

Case 1

A 69-year-old woman with a past medical history of hypertension and hyperlipidemia presented to an urgent care clinic with 5 days of cough and diarrhea. She had positive polymerase chain reaction (PCR) for SARS-CoV-2 RNA from a nasopharyngeal swab and had hypoxia requiring hospitalization. On hospital Day 4, she went into respiratory failure and was transferred to the intensive care unit (ICU) for mechanical ventilation. In addition to supportive care, she was treated with 2 days of azithromycin (1500 mg total), 4 days of hydroxychloroquine (1600 mg total), 7 days of ceftriaxone (7 g total),

and an 8-day hydrocortisone taper (650 mg total). Her respiratory status improved, but she remained minimally responsive despite weaning from paralytics and sedatives.

On hospital Day 12, she was noted to have seizurelike jerking of her left face, arm, and leg and a leftward gaze deviation. She received 6 mg of lorazepam without seizure recurrence. Brain magnetic resonance imaging (MRI) demonstrated nonenhancing, bilateral T2-weighted (T2)/fluid-attenuated inversion recovery (FLAIR) hyperintensities in the parietal and occipital cortex and subcortical white matter (Figure 1a). Diffusion-weighted imaging (DWI) showed no corresponding reduced diffusion (Figure 1b). The radiographic findings in combination with clinical correlations led to a diagnosis of PRES. A strict BP protocol was initiated with hydralazine; prior BPs had been noted of (84–180)/(55–90), with maximum BP at 180/90 prior to the seizure. Extubation occurred on hospital Day 13, followed by slow physical and cognitive recovery. Visual symptoms were noted immediately upon extubation, per the patient. She was gradually restarted on home BP medications and discharged after 27 days of hospitalization. Follow-up MRI 2 months after discharge demonstrated resolution of the parietal T2/FLAIR hyperintensities and DWI, and improvement in occipital signal changes with minimal residual subcortical edema (Figure 1c,d).

Six months after hospitalization, she sought follow-up care at our neuro-ophthalmology clinic for ongoing visual symptoms. Anamnesis since time of discharge noted significant continuation of visual symptoms of blurry vision, difficulty seeing on the left side, reading difficulties, visual hallucinations that were confined to her blind field, and recurrence of visual hallucinations that would reappear with change in gaze, in a palinopsialike fashion. Visual hallucinations were described as "seeing dogs and dog [footprints]," "lights," and "squiggly lines," with recurrence of the same visual hallucination with change in gaze, similar to palinopsia with real images. Visual acuity was normal (20/20 in both eyes), and visual field testing revealed a left homonymous hemianopia (Figure 1e). Fundoscopic examination was normal except for symmetric optic disc cupping and epiretinal membrane changes in the right eye. Her Montreal Cognitive Assessment score was 27/30 (points lost for Trails B and cube copy), and the remainder of her neurologic examination was normal. All signs and symptoms of visual dysfunction, including visual field loss, were still present at her 12-month follow-up appointment.

Case 2

A 55-year-old woman with a past medical history of diabetes mellitus and hypertension presented to our hospital system with a 4-day history of shortness of breath, nausea, vomiting, and diarrhea and was found to be RNA-positive by PCR for SARS-CoV-2 from a nasopharyngeal swab. She went into respiratory failure on hospital Day 3 and was transferred to the ICU for mechanical ventilation. In addition to supportive care, she received 6 days of hydroxychloroquine (2000 mg total), 6 days of methylprednisolone (760 mg total), 10 days of ceftriaxone (12 g total), and 10 days of azithromycin (5000 mg total). Her respiratory status improved, and she was extubated on hospital Day 9 but continued to experience profound bilateral upper and lower extremity weakness. On hospital Day 14, she complained of acute vision loss and vertigo and then had a witnessed seizure consisting of right arm and leg rhythmic clonic movements with initial preserved alertness and ability to speak followed by right gaze deviation and confusion. She was treated with 4 mg of lorazepam and 1500 mg of levetiracetam. Brain MRI revealed diffuse T2/FLAIR hyperintense edema of the occipital, parietal, and posterior frontal white matter consistent with PRES (Figure 2a,b), with a very minimal superior convexity subarachnoid hemorrhage and without corresponding diffusion restriction on DWI (Figure 1c). MRA and magnetic resonance venography of the head revealed no thromboses. BP during the seizure event was recorded at 178/88, with BPs of (130–160/70–90) in the 4 days prior to the seizure. She remained seizure-free on twice daily 1000 mg levetiracetam and was maintained on strict BP control with nicardipine. She made continued recovery and reported that she had visual hallucinations in association with these neurologic events. Occupational therapy examination evaluation noted a left-sided visual deficit with both eyes open. She was discharged after 21 days of hospitalization. She was referred for outpatient visual field but declined visual field testing and declined follow-up MRI. General optometric examination revealed normal visual acuity and no posterior fundus abnormalities.

Case 3

A 65-year-old man with a past medical history of hypertension, diabetes mellitus, and pyoderma gangrenosum on chronic immunosuppression with 20 mg prednisone, infliximab, and adalimumab presented to the hospital with worsening confusion in the context of a 4-day history of coldlike symptoms and fever. He was found to be SARS-CoV-2-positive. His respiratory status worsened progressively despite supportive care, requiring intubation on hospital Day 11 and treatment with 10 days of dexamethasone (66 mg total), 5 days of remdesivir (600 mg total), 6 days of ceftriaxone (6 g total), and 5 days of azithromycin (2500 mg total). His respiratory status slowly recovered, and he was extubated on hospital Day 39.

The same day as extubation, he was witnessed to have a bilateral tonic–clonic seizure lasting 2 min. A BP reading taken 6 min before the seizure was 115/89, with BPs of (90–140)/(70–100) throughout the course of that day, with a single transient BP of 163/119 at 12 h before the seizure. Stat computed tomographic (CT) imaging showed a new right-sided intraparenchymal hemorrhage (IPH) in the right parietal lobe, and MRI revealed symmetric T2/FLAIR white matter hyperintensities in the posterior frontal lobes and frontoparietal junctions consistent with PRES (Figure 3a), with corresponding diffusion restriction only at the site of the IPH on DWI (Figure 3b). He was started on 1000 mg levetiracetam twice daily, with no seizure reoccurrence. After a complicated recovery process, he was discharged on hospital Day 71. Within 1 month of discharge, however, he developed a

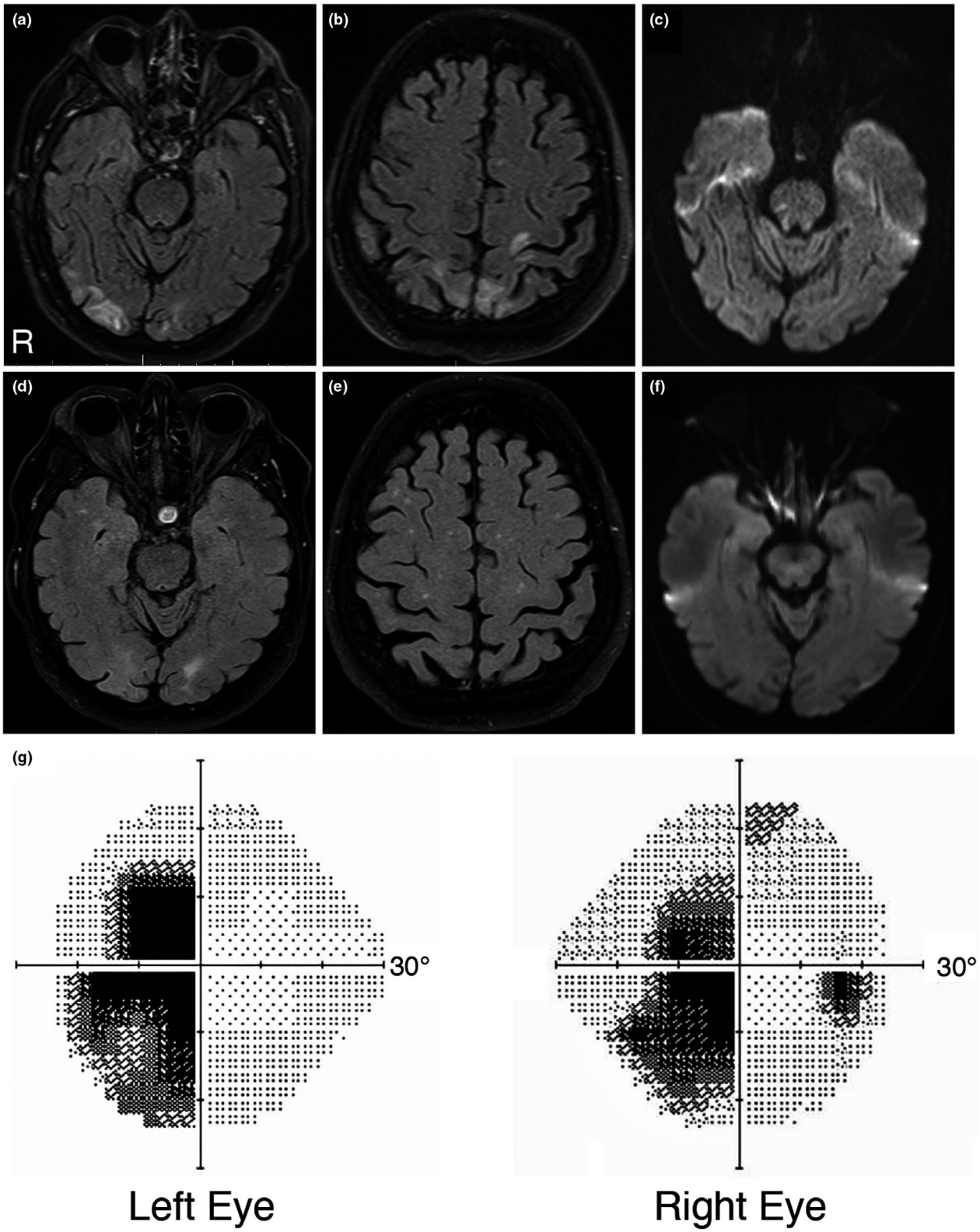

FIGURE 1 Brain magnetic resonance imaging (MRI) and visual field testing, Case 1. (a, b) T2-weighted imaging sequence with fluid attenuation and inversion recovery (T2/FLAIR) for MRI of the brain of Case 1 on day of seizure (hospital Day 12) showed extensive bilateral hyperintensities in (a) occipital and (b) parietal white matter. (c) Diffusion-weighted imaging (DWI) through the occipital level showed no evidence of corresponding reduced diffusion. (d, e) T2/FLAIR MRI sequences of the brain of Case 1 at 3-month follow-up after hospitalization showed significant improvement of (d) occipital signal changes and (e) resolution of parietal signal changes. Note the presence of an incidental Rathke's cleft cyst in images c and d and mild leukoaraiosis in image d. (f) DWI through the occipital level showed no evidence of corresponding reduced diffusion. (g) Results of Humphrey visual field for left eye (left) and right eye (right) testing at 6-month follow-up revealed a left homonymous hemianopia. R indicates the right side of the body

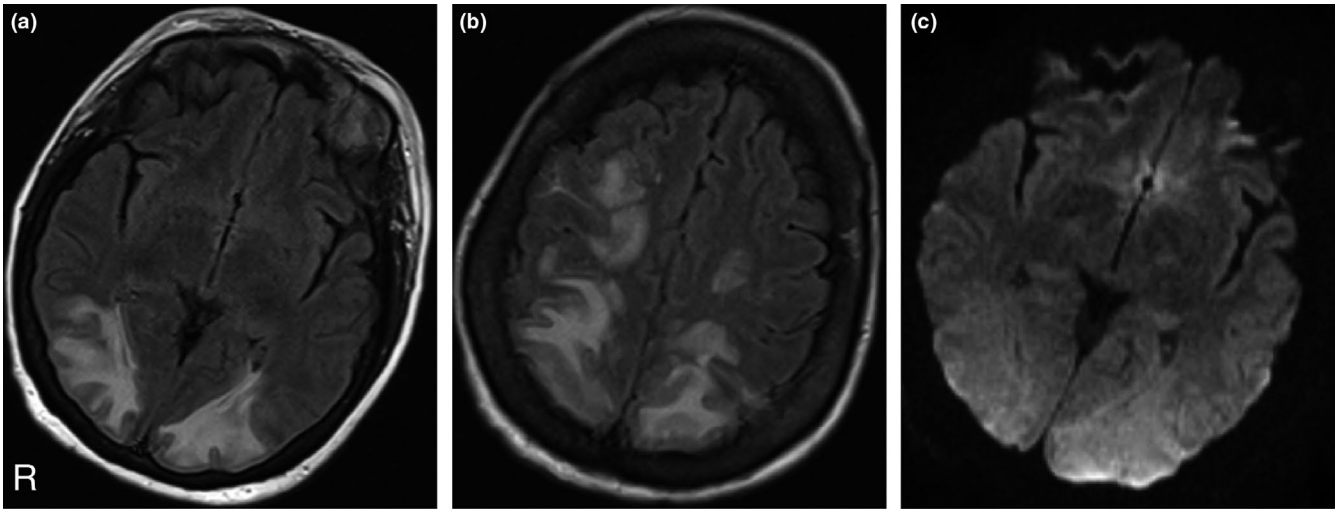

FIGURE 2 Brain magnetic resonance imaging (MRI), Case 2. (a, b) T2-weighted imaging sequence with fluid attenuation and inversion recovery (T2/FLAIR) for MRI of the brain of Case 2 on day of seizure (hospital Day 14) showed extensive bilateral hyperintensities in the white matter of the (a) occipital lobes and (b) frontoparietal lobes. (c) Diffusion weighted imaging (DWI) through the occipital level showed no evidence of corresponding reduced diffusion. R indicates the right side of the body

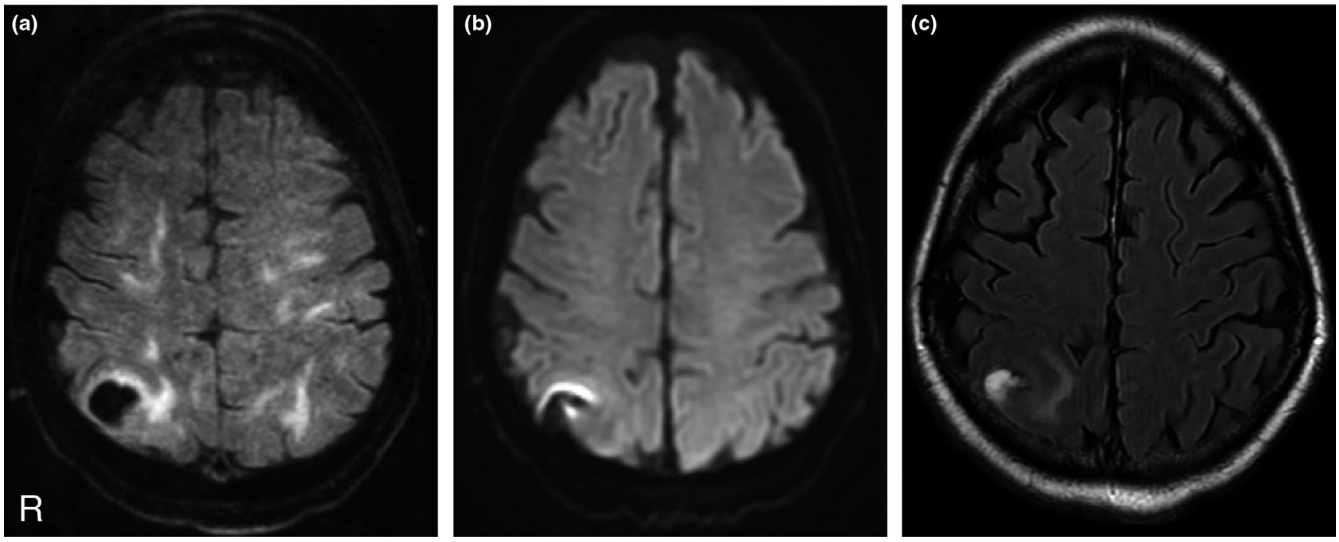

FIGURE 3 Brain magnetic resonance imaging (MRI), Case 3. (a) T2-weighted imaging sequence with fluid attenuation and inversion recovery (T2/FLAIR) for MRI on day after seizure (hospital Day 39) showing extensive bilateral hyperintensities in the white matter of the frontal and parietal lobes. Note the intraparenchymal hemorrhage (IPH) in the right parietal lobe. (b) Diffusion-weighted imaging through the frontoparietal level reduced diffusion in the area of the IPH only. (c) Resolution of white matter hyperintensities in the frontal and parietal lobes at 3-week follow-up with stable parietal hematoma with localized mass effect. R indicates the right side of the body

brain abscess due to *Streptococcus anginosus* at the site of the IPH that required repeated hospitalization for drainage and treatment. CT and MRI at this repeat hospitalization showed resolution of bilateral PRES findings (Figure 3c). Repeat neurological examination during and after hospitalizations did not detect any visual abnormalities.

Literature search

Database search recovered 37 unique articles describing PRES and COVID-19, of which five were excluded after abstract review. The remaining 32 articles underwent full text review; 22 articles met all inclusion criteria and contained detailed clinical information on 32 individuals with PRES and COVID-19 [6–27]. All cases reported MRI findings consistent with a diagnosis of PRES (Table 1).

The majority of cases of PRES occurred in the setting of critical COVID-19 illness requiring mechanical ventilation or severe COVID-19 requiring other forms of respiratory support (Figure 4a) [5]. Seven cases (20%) reported development of PRES with only mild or asymptomatic COVID-19 (Figure 4a) [5,10,12–14,16,26,27]. Of these, three individuals were older than 65 years, with medical risk factors for COVID-19 [1,10,12,16], and two were peripartum

(Table 1) [13,26]. BP was reported in nearly all cases and was often described as poorly controlled or fluctuating, but continuous monitoring information was difficult to glean from case descriptions. Notably, 10 cases (28%) reported systolic BP greater than 200 mmHg [10,21], diastolic BP greater than 100 mmHg [13,19,26], or mean arterial pressure greater than 100 mmHg [17,20,21].

Altered mental status (57%, *n* = 20) and seizures (54%, *n* = 19) were the most common neurological manifestations leading to a diagnosis of PRES (Figure 4b). Other neurological signs or symptoms described were visual disturbances (40%, *n* = 14), limb paresis (29%, *n* = 10), dysphasia/aphasia (14%, *n* = 5), other sensory deficits (6%, *n* = 2), vertigo (6%, *n* = 2), and headache (3%, *n* = 1). Some cases had more than one manifestation. Many cases had complete resolution of neurological issues by the time of publication, but approximately one third of individuals had residual problems including cognitive deficits, vision loss, and weakness (Figure 4b and Table 1). Death occurred in four (11%) cases (Figure 4b and Table 1) [6,18,23,25].

Neuro-ophthalmologic issues related to PRES were described in 14 (40%) of the case reports (Table 1). Signs and symptoms described included visual field defects at any level (57%, *n* = 8), cortical blindness (21%, *n* = 3), palinopsia (14%, *n* = 2), and other visual hallucinations (14%, *n* = 2; Figure 4c and Table 1). Whereas half of these cases reported complete resolution of the visual issue, the other half of case reports described ongoing visual problems at the time of publication (Figure 4c and Table 1).

DISCUSSION

We identified three patients in our health care system, one at presentation to neuro-ophthalmology and two through chart search, who developed PRES in the context of hospitalization for severe COVID-19. The three cases presented here had many features in common. All individuals experienced a protracted hospital course requiring ICU stay with mechanical ventilation due to COVID-19. Furthermore, all experienced new onset seizures after weaning of sedation or extubation that led to MRI that detected posterior circulation predominant T2/FLAIR hyperintensities within white matter and cortex of the parieto-occipital regions consistent with a diagnosis of PRES. Of these three cases, two experienced visual complications following development of PRES. Two patients had known persistent visual abnormalities at the time of hospital discharge, but only one had neurologic and neuro-ophthalmic follow-up to confirm that visual deficits were still present at 12 months. Of note, Cases 2 and 3 were not fully examined by our team, and, therefore, their long-term neurological outcomes are unknown.

Literature review supported our finding that visual manifestations of PRES in the context of COVID-19 may persist and include visual field defects, cortical blindness, visual hallucinations, with palinopsialike images. One case described previously had transient hallucinatory palinopsia due to PRES, also in the context of COVID-19, that was described as previously seen images recurring over 2 days (Table 1) [14]. Our (Case 1) patient's experience was different from this prior report, with palinopsia of prior release visual hallucinations and not of previously seen real images.

Literature review also identified that other persistent cognitive, motor, and sensory neurological sequelae were common following COVID-19-associated PRES. The development of both visual and other neurological manifestations of PRES could occur at any level of severity of COVID-19 illness from mild to critical. The individual risk factors for development of PRES sequelae associated with COVID-19 will require further investigation to determine whether they are different from the typical PRES-related risk factors (e.g., endotheliopathy and hypertension).

What is the mechanism of neurological injury? A key component to PRES development is endothelial injury secondary to immune activation [28]. As such, PRES is known to occur more commonly in patients with severely elevated BP, pregnancy, specific immunomodulatory medications, and increased systemic inflammation, such as in autoimmune diseases, sepsis, and organ transplants, among other predispositions [28]. With endothelial dysfunction and vascular autoregulation, rapid increases in BP may increase risk of damage to brain structures by further increasing vasogenic edema [29]. In the case of our patients, only one had a systolic BP near 180 mmHg, with most pressures in the high–normal range less than 150 mmHg, which are well below the upper limit of normal for cerebral perfusion autoregulation [28]. Lack of severe BP elevation was similarly a feature of most literature cases, and has been supported by one postmortem study [30]. Susceptibility to PRES during COVID-19 highlights the inflammatory nature of SARS-CoV-2 infection and implicates the previously described vascular endothelial injury that can occur in COVID-19. SARS-CoV-2 not only causes significant elevations in markers of inflammation (i.e., C-reactive protein, IL-6, ferritin, etc.), but may also directly infect the vasculature, which is known to express the viral receptor ACE-2 [12,17,23]. Of note, none of our patients had cerebrospinal fluid testing, so direct infection contributing to the development of PRES cannot be ruled out, although it is known to be rare. Given what we now understand about the vascular endothelial disease associated with COVID-19 and our current knowledge about non-COVID-19-related PRES, posterior vascular endotheliopathy combined with critical illness is the most likely explanation for the syndrome. The severe CNS vascular endothelial disease likely results in permanent ischemia to vulnerable posterior white matter and cortex, leaving patients with persistent deficits.

The observation that COVID-19 patients may develop PRES with persistent neurological complications has implications for pandemic patient care:

(i) Due to the complex nature of these cases and the difficulties in care of isolated patients, neurological complications may be underrecognized and underreported. As such, a lower index of suspicion may be warranted for CT imaging and electroencephalographic monitoring of severely ill COVID-19 patients or those in the peripartum period.
(ii) In the critical care setting, tight BP control may be warranted to prevent neurological complications, as even high–normal BPs may be associated with development of encephalopathy and PRES.

TABLE 1 Literature review of neurological outcomes of PRES due to COVID-19

Case	Age, years/sex/ PMH	Brief clinical summary	PRES symptoms and imaging	Neuro-ophthalmological outcome	Other neurological outcomes
1	48/M/obesity [12]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation, additional diagnosis of inflammatory cytokine release syndrome BP: Range 70/30 to 180/90 mmHg	PRES sx: AMS diagnosed at extubation Imaging: CT and MRI showing parieto-occipital vasogenic edema and small right-sided occipital hemorrhage	–	Improved by hospital Day 24; long-term outcome not reported
2	67/F/HTN, T2DM, CAD, gout, asthma [12]	COVID-19 course: Mild COVID-19 BP: Range 115/72 to 178/83 mmHg	PRES sx: AMS diagnosed at time of COVID-19 diagnosis Imaging: CT and MRI showing extensive bilateral parieto-occipital edema with hemorrhage, edema also noted in the right-sided frontal lobes, basal ganglia, and cerebellum	–	Improved at discharge (day not specified)
3	58/M/HLD [17]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Over 26 days, average MAP 106 mmHg and BP range 86–189/52–122 mmHg	PRES sx: AMS diagnosed following extubation Imaging: CT and MRI showing edema of bilateral occipital and temporal subcortical white matter	–	Recovered back to baseline by time of discharge on hospital Day 33
4	67/F/HTN, obesity, T2DM [17]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Over 25 days, average MAP 90 mmHg and BP range 79–193/44–97 mmHg	PRES sx: Altered mental status preventing extubation Imaging: MRI showing edema of right occipital subcortical white matter and left cerebellar hemisphere with petechial hemorrhages	–	Improved but not back to baseline at time of discharge on hospital Day 47
5	74/M/multiple myeloma [15]	COVID-19 course: Severe COVID-19 BP: SBP 140–150 mmHg at time of seizures up from baseline of 110–120 mmHg	PRES sx: Focal motor seizures and status epilepticus on Day 15 of hospitalization responsive only to verapamil; following verapamil developed cortical blindness and left upper limb palsy Imaging: MRI showing edema in frontal and occipital subcortical areas	Recovered after a few days	Recovered after a few days
6	64/F/HTN, GERD, HLD, OSA, afib [22]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 150/70 mmHg on admission, trend not described	PRES sx: Altered mental status and blurred vision following weaning of sedation Imaging: CT with bilateral edema in subcortical white matter of posterior frontal and temporoparieto-occipital lobes; follow-up MRI showed reduction of edema with bilateral occipital foci of subacute hemorrhages	Recovered at time of follow-up MRI 56 days after initial hospitalization	Recovered at time of follow-up MRI 56 days after initial hospitalization

(Continues)

TABLE 1 (Continued)

Case	Age, years/sex/ PMH	Brief clinical summary	PRES symptoms and imaging	Neuro-ophthalmological outcome	Other neurological outcomes
7	69/F/CAD [10]	COVID-19 course: Mild COVID-19 BP: 200/116 on admission, trend not described	PRES sx: Seizures, mutism, delirium, asthenia Imaging: MRI showing edema of temporal and occipital lobes; follow-up MRI 8 days later showed improvement in edema	–	Improved after 3 days with continued attention difficulties, simultagnosia
8	64/M/none reported [21]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Max MAP 128 mmHg and peak SBP of 187 mmHg	PRES sx: Encephalopathy, aphasia, focal nonconvulsive status epilepticus on EEG Imaging: MRI showing edema of bilateral occipital white matter and left-sided thalamus and internal capsule	Ongoing right homonymous hemianopia at time of discharge (day not specified)	Improved but ongoing attention difficulties at time of discharge (day not specified)
9	73/M/none reported [21]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Max MAP of 135 mmHg and max SBP of 212 mmHg	PRES sx: Encephalopathy, left gaze preference, subclinical focal seizures on EEG Imaging: MRI showing edema of bilateral occipital gray and white matter	–	Recovered at time of discharge (day not specified)
10	65/F/HTN, T2DM [21]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Max MAP of 138 mmHg and max SBP of 190 mmHg	PRES sx: Altered mental status following extubation Imaging: MRI showing edema of bilateral occipital suboccipital white matter	–	Improved with continuing mild cognitive deficits and temporal disorientation at time of discharge (day not specified)
11	74/F/T2DM, HLD, hypothyroidism [21]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Max MAP of 150 mmHg and max SBP of 237 mmHg	PRES sx: Persistent confusion and agitation throughout course, new onset right arm weakness (day not specified) Imaging: MRI showing edema in the bilateral parieto-occipital lobes	–	Improved with continued disorientation to place at time of discharge (day not specified)
12	27/F/none reported [6]	COVID-19 course: Severe COVID-19 requiring ICU level care, respiratory status not described, fulminant liver failure BP: Not reported	PRES sx: Encephalopathy, dizziness, vertigo during ICU care Imaging: MRI showing edema in bilateral occipital subcortical white matter	–	Death during Week 2 of hospitalization
13	63/F/HTN [9]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Reported as normal	PRES sx: Convulsive status epilepticus beginning on hospital Day 30 after initial extubation; was reintubated for seizure treatment, then noted to have left lateral hemianopsia and mild left hemiparesis following re-extubation on hospital Day 41 Imaging: MRI showing diffuse bilateral white matter lesions most prevalent in posterior regions	Ongoing left lateral hemianopsia at 180-day follow-up appointment	Hemiparesis recovered at 180-day follow-up appointment

(Continues)

TABLE 1 (Continued)

Case	Age, years/sex/ PMH	Brief clinical summary	PRES symptoms and imaging	Neuro-ophthalmological outcome	Other neurological outcomes
14	59/M/none [23]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: One-day max BP 173/96 mmHg, trend described as labile	PRES sx: Encephalopathy with weaning of sedation (day not specified) Imaging: MRI showing diffuse, bilateral, posterior predominant edema of the subcortical white matter	–	Death on Day 14 of admission
15	66/F/none [18]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Maximum reported SBP of 160 mmHg	PRES sx: AMS, and epileptiform discharges and focal slowing on EEG (timeline unclear) Imaging: CT showing edema in bilateral temporo-occipital white matter	–	Death (timeline unclear)
16	46/M/T2DM, HTN [20]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Difficult to control HTN with average MAP 120–130 mmHg	PRES sx: AMS, agitation, disorientation, and lower extremity weakness at extubation on hospital Day 18 Imaging: MRI showing edema of bilateral frontal and occipital lobe subcortical white matter; MRI 15 days after discharge showed resolution of edema	–	Ongoing lower extremity weakness at discharge on hospital Day 34 with resolution of AMS
17	33/F/none [14]	COVID-19 course: Mild COVID-19 BP: Not reported	PRES sx: Hallucinatory palinopsia Imaging: MRI showing edema in bilateral parieto-occipital regions and bilateral frontal, parietal, and temporal gray–white junctions	Recovered after 5 days	–
18	35/F/pregnant 40 weeks 6 days, hypothyroidism [13]	COVID-19 course: Asymptomatic COVID-19 BP: Described as >160/100 mmHg	PRES sx: Bilateral tonic–clonic seizures at presentation resulting in emergency C-section; sudden blindness 4 h after C-section Imaging: Negative CT and CT angiography, no MRI available	Recovered after 48 h	–
19	24/F/pregnant (no details given) [19]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Diastolic BP to ≤110	PRES sx: Delirium, disorientation, agitation, aphasia, decreased movement of right lower limb after extubation (day not specified) Imaging: MRI showing diffuse, edema of bilateral parietal and frontal cortex and subcortical white matter	–	Improved but not fully recovered with continued "mental clouding" several days after discharge on hospital Day 18

(Continues)

TABLE 1 (Continued)

Case	Age, years/sex/ PMH	Brief clinical summary	PRES symptoms and imaging	Neuro-ophthalmological outcome	Other neurological outcomes
20	25/F/primigravida [26]	COVID-19 course: Mild COVID-19 BP: Max 190/120 mmHg	PRES sx: Headache, bilateral tonic–clonic seizure clusters requiring mechanical ventilation 1 day after COVID-19 symptom onset Imaging: MRI showing edema of bilateral occipital lobes with small bilateral hemorrhages	–	Improved at discharge on hospital Day 12, long-term outcome unclear
21	61/F/none [7]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 152–187/79–98 mmHg	PRES sx: AMS after weaning of sedation on hospital Day 15, seizures on hospital Day 18 Imaging: MRI showing edema of bilateral parietal and occipital lobes	–	Improved at discharge on hospital Day 48, long-term outcome unclear
22	52/F/HIV [7]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 140–180/70–97 mmHg	PRES sx: Focal and bilateral tonic–clonic seizures on hospital Day 34 Imaging: MRI showing edema of bilateral parietal, occipital, frontal, and temporal white matter	–	Improved by hospital Day 43, long-term outcome unclear
23	55/M/not reported [8]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Reported as poorly controlled	PRES sx: Seizures following extubation with right homonymous hemianopsia, hypotonic tetraparesis, and critical illness polyneuropathy at discharge (timeline unclear) Imaging: MRI showing edema in bilateral occipital cortex and subcortical white matter	Ongoing at time of discharge (day not specified)	Ongoing hypotonic tetraparesis and critical illness polyneuropathy at time of discharge (day not specified)
24	63/F/not reported [8]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Reported as poorly controlled	PRES sx: Seizures and status epilepticus 2 days after extubation and visual field defect (timeline unclear) Imaging: MRI showing edema in bilateral occipital subcortical white matter; MRI at follow-up reported as improved	Recovered at time of follow-up MRI (day not specified)	Recovered at time of follow-up MRI (day not specified)
25	64/M/not reported [8]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Reported as poorly controlled	PRES sx: Seizures followed by nonconvulsive status epilepticus after extubation, tetraparesis, visual field defect (timeline unclear) Imaging: MRI described as having white matter alterations in both hemispheres that were recovered on follow-up MRI	Recovered (day not specified)	Recovered (day not specified)

(Continues)

TABLE 1 (Continued)

Case	Age, years/sex/ PMH	Brief clinical summary	PRES symptoms and imaging	Neuro-ophthalmological outcome	Other neurological outcomes
26	68/M/not reported [8]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: Reported as poorly controlled	PRES sx: Right visual deficit, difficulty walking, and reduced muscle tone after extubation (timeline unclear) Imaging: MRI showing edema in bilateral occipital lobe	Improving but not fully recovered (timeline unclear)	Unclear outcome
27	57/F/not reported [8]	COVID-19 course: Severe COVID-19 requiring hospitalization and low-flow oxygen therapy BP: Reported as poorly controlled	PRES sx: Focal and convulsive seizures on hospital Day 9 and then global aphasia, disinhibition, left hemianopsia, and visual hallucinations days after the seizures (timeline unclear) Imaging: MRI showing edema in bilateral occipital lobe	Recovered (day not specified)	Recovered (day not specified)
28	54/F/none [11]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: With seizure 190/90 mmHg, range 121–165/62–69 mmHg	PRES sx: Bilateral tonic–clonic seizures on hospital Day 21, found to have cortical blindness with Anton syndrome, receptive dysphasia, and limb apraxia after extubation on hospital Day 31 Imaging: MRI showing edema of bilateral occipital cortex	Ongoing profound sight impairment after 8 weeks of follow-up	Recovered (timeline unclear)
29	55/M/HTN, obesity, CKD, OSA, HLD [27]	COVID-19 course: Mild COVID-19 BP: 171/85 mmHg, MAP 116 mmHg on presentation	PRES sx: Lethargy, confusion, disorientation on Day 7 of COVID-19 symptoms Imaging: MRI showing edema in bilateral periventricular, occipital, and frontal white matter	–	Recovered at discharge on hospital Day 3
30	85/M/HTN, T2DM, afib, CKD [16]	COVID-19 course: Asymptomatic COVID-19 BP: 184/96 mmHg on presentation	PRES sx: Disorientation, decreased attention, impulsivity on presentation with deterioration of mental status over 2 days following admission Imaging: Normal CT at presentation, CT following deterioration on Day 2 showed new edema of bilateral subcortical occipital lobes and the right cerebellar hemisphere, normal MRI on hospital Day 12	–	Recovered 37 days after initial presentation

(Continues)

TABLE 1 (Continued)

Case	Age, years/sex/ PMH	Brief clinical summary	PRES symptoms and imaging	Neuro-ophthalmological outcome	Other neurological outcomes
31	43/F/sickle cell disease [24]	COVID-19 course: COVID-19+, unclear symptomatology BP: SBP 80–160 mmHg	PRES sx: Lethargy, myoclonic jerks, and convulsive seizures within 1 day of presentation Imaging: MRI showing diffuse white matter edema; MRI recovered at 4-month follow-up	–	Recovered 4 days after presentation
32	70/M/HTN, asthma, CAD [25]	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 140–160/90–100 mmHg with intermittent elevations	PRES sx: Progressive delirium following extubation on hospital Day 17 Imaging: MRI showing edema of bilateral occipital lobes	–	Death 27 days after presentation due to aspiration pneumonia
33	69/F/HTN, HLD (Hixon et al.)	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 84–180/55–90 mmHg, max 180/90 prior to seizure	PRES sx: Minimally responsive despite weaning sedation and paralytics while on ventilator, seizures on hospital Day 12; visual deficits, hallucinatory palinopsia, and cognitive deficits noted at extubation on hospital Day 13; homonymous hemianopsia diagnosed at 6-month follow-up with neuro-ophthalmologist Imaging: MRI showing edema in bilateral parietal and occipital cortex; MRI at 2-month follow-up showed resolution of edema	Ongoing hallucinatory palinopsia and left homonymous hemianopsia	Recovered at discharge on hospital Day 27
34	55/F/HTN, DM (Hixon et al.)	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 130–160/70–90 mmHg prior to seizure, 178/88 mmHg during seizure	PRES sx: Global limb weakness after extubation on Day 9; acute vision loss, vertigo, and seizure on hospital Day 14 Imaging: MRI showing edema in bilateral parietal, occipital, and posterior frontal white matter with small subarachnoid hemorrhage	Unclear outcome	Unclear outcome
35	65/M/HTN, DM, pyoderma (Hixon et al.)	COVID-19 course: Critical COVID-19 requiring mechanical ventilation BP: 90–140/70–100 mmHg the day of the seizure, 115/89 mmHg just prior to the seizure	PRES sx: Bilateral tonic–clonic seizure after extubation on hospital Day 39 Imaging: MRI showing edema in bilateral posterior frontal lobes and frontoparietal junctions, right-sided intraparenchymal hemorrhage in right parietal lobe; MRI at follow-up showed resolution of edema	–	Recovered (timeline unclear)

Abbreviations: afib, atrial fibrillation; AMS, altered mental status; BP, blood pressure; CAD, coronary artery disease; CKD, chronic kidney disease; CT, computed tomography; DM, diabetes mellitus; EEG, electroencephalogram; F, female; GERD, gastroesophageal reflux disorder; HIV, human immunodeficiency virus; HLD, hyperlipidemia; HTN, hypertension; ICU, intensive care unit; M, male; MAP, mean arterial pressure; MRI, magnetic resonance imaging; OSA, obstructive sleep apnea; PMH, past medical history; PRES, posterior reversible encephalopathy syndrome; SBP, systolic BP; sx, symptoms; T2DM, type 2 DM.

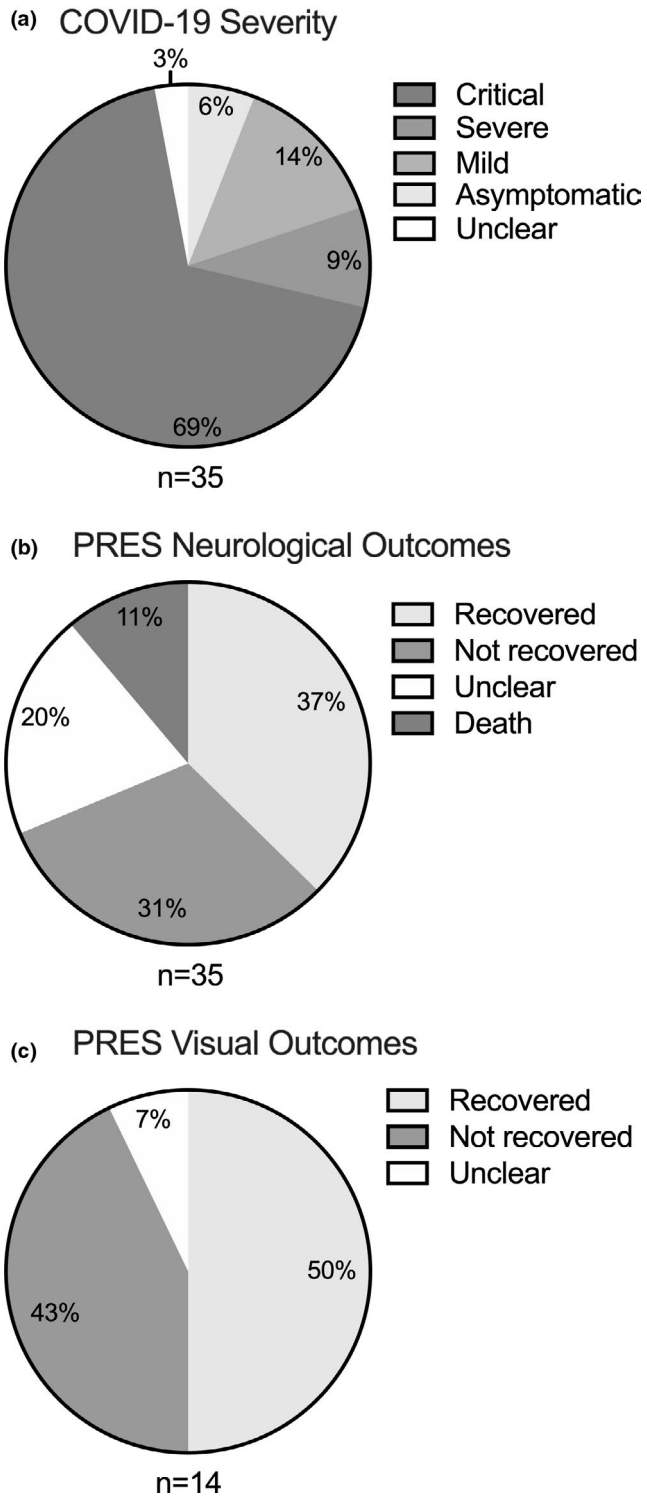

FIGURE 4 Summary of literature review cases. Literature review resulted in inclusion of 35 cases of posterior reversible encephalopathy syndrome (PRES) due to COVID-19 across 22 publications. (a) Level of illness with COVID-19 was described as critical in 69% (*n* = 24/35), severe in 9% (*n* = 3/35), mild in 14% (*n* = 5/35), and asymptomatic in 6% (*n* = 2/35), and was not clearly described in 3% (*n* = 1/35). (b) PRES patients reported neurological manifestations that included altered mental status, seizures, visual disturbances, limb paresis, other sensory disturbances, vertigo, and headaches. Outcomes of PRES neurological manifestations were described as full recovery in 37% (*n* = 13/35), not full recovery in 31% (*n* = 11/35), and unclear recovery in 20% (*n* = 7). Death occurred in 11% (*n* = 4) of cases. (c) Visual problems were described in 40% (*n* = 14/35) of cases. Separating out the visual problems from the other neurological data revealed that full recovery was described in 50% (*n* = 7/14), whereas 43% (*n* = 6/14) were not recovered by the time of the case report, and 7% (*n* = 1/14) had unclear outcomes.

(iii) All persons recovering from COVID-19 should be carefully evaluated for neurological deficits. Individuals not recovering may warrant MRI to examine for brain structural injuries.

(iv) Long-term neurological symptoms related to COVID-19 could be related to viral or inflammatory-related endothelial dysfunction and merit detailed scientific investigation to uncover further risk factors and disease mechanisms.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

Ashesh A. Thaker: Formal analysis (equal), writing–review & editing (supporting). **Victoria S. Pelak:** Conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), methodology (equal), resources (equal), supervision (equal), writing–original draft (equal), writing–review & editing (equal). **Alison M. Hixon:** Conceptualization (equal), data curation (equal), formal analysis (equal), investigation (equal), methodology (equal), writing–original draft (equal), writing–review & editing (equal).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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