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Pseudotumor Cerebri Syndrome With COVID-19: A Case Series

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Pseudotumor cerebri syndrome (PCS) either affects mostly overweight women of childbearing age as idiopathic intracranial hypertension (IIH) or can occur secondary to other medical conditions. Symptoms include headaches, transient visual obscurations (TVOs), pulse-synchronous tinnitus (PST), and vision loss (1). Diagnosis rests on increased intracranial pressure (ICP) without alternative explanation such as intracranial mass, meningitis, or cerebral venous sinus thrombosis (CVST) (1). COVID-19 is a global pandemic caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). We describe an association between PCS and COVID-19 in adult patients (2). Potential mechanisms include dysregulation of cerebrospinal fluid (CSF) dynamics in the setting of choroid plexus epithelium and meningeal infection (3), venous clotting (4), or quarantine-related lifestyle modifications promoting weight gain.

In this study, we report 8 patients (See **Supplemental Digital Content**, **Table 1**, http://links.lww.com/WNO/A536) who developed new or worsening PCS shortly after acquiring COVID-19 without meningoencephalitis or major CVST and mostly without significant recent weight gain.

Patient 1

A 22-year-old woman (body mass index [BMI] 35.2 kg/m^2) underwent resection of a pancreatic mass 8 months before presentation with a subsequent 40-pound weight loss. She developed headaches, blurred vision, diplopia, PST, and TVOs on the same day of onset of flu-like symptoms and was found to have papilledema Frisén Grade 5, with macular exudates OU. Lumbar puncture (LP) opening pressure was 50 cmH_2O (upper limit of normal: 25). Treatment included acetazolamide and a temporary lumbar drain, which improved her symptoms.

Patient 2

A 30-year-old woman with a history of episodic migraine lost 25 pounds over 4 months (BMI 27.5 kg/m^2) and underwent a brain MRI in 2019 demonstrating a partially empty sella. No papilledema was noted on routine ophthalmic examination. Two days after acquiring upper respiratory symptoms, she developed daily nonmigrainous headaches, PST, and vision changes. Fundoscopy revealed Frisén Grade 2 papilledema. MRI of the brain was unchanged, and an LP was declined. Her symptoms resolved without specific therapy.

Patient 3

A 34-year-old woman (BMI 28.3 kg/m^2) denied weight gain over the past 12 months. Two weeks after onset of subacute headaches (which led to COVID-19 testing despite no respiratory symptoms), she developed bilateral blurry vision and was noted to have bilateral Frisén Grade 4 papilledema with peripapillary hemorrhage. MRI of the brain demonstrated signs of increased ICP without CVST. LP opening pressure was 53 cmH_2O. Treatment included acetazolamide with improved symptoms.

Patient 4

A 36-year-old woman with a history of polycystic ovarian syndrome (BMI 28.2 kg/m^2) without weight gain over the past 6–12 months developed respiratory symptoms consistent with COVID-19. Despite a lack of weight gain over the past 6–12 months, and no known PCS triggers, she developed intermittent headaches with progressively blurred vision leading to recognition of Frisén Grade 2 papilledema. MRI/MRV of the brain revealed neuroimaging stigmata of PCS. LP opening pressure was 28 cm H_2O. Treatment included acetazolamide.

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Patient 5

A 25-year-old woman (BMI 40.7 kg/m^2) with a history of well-controlled IIH on acetazolamide with previously documented normal visual acuities and funduscopic examination developed fevers, chills, and a cough. After 1 week, despite a lack of medication noncompliance or weight gain over the past 6–12 months, she developed fulminant IIH with symptoms of worsening headaches, bilateral dimness of vision, and PST. Her ophthalmic examination showed acuities of 20/60 in the right eye and light perception in the left eye, dyschromatopsia in the left eye > right eye, a relative afferent pupillary defect in the left eye, and Frisén Grade 5 papilledema with pallor, vascular tortuosity in the left eye > right eye, and scattered peripheral retinal hemorrhages consistent with venous stasis retinopathy. Treatment included a large volume CSF tap with an opening pressure of 60 cm H_2O, high-dose acetazolamide, and an urgent ventriculoperitoneal shunt (VPS) with continued worsening. After 4 days, optic nerve sheath fenestration was performed, which led to improvement in symptoms.

Patient 6

A 51-year-old woman with established PCS and chronic kidney disease (BMI 31.9 kg/m^2) with a 3-pound weight gain over the past 4 months developed worsening headaches over a few days with blurred vision, constricted visual fields, Frisén Grade 2 papilledema, and worsening renal failure requiring hemodialysis at the time of testing for COVID-19. Brain MRI/MRV was concerning for possible small cortical vein thrombosis and anticoagulation was initiated, but the large venous sinuses were patent. LP opening pressure was 26 cm H_2O. Treatment included switching acetazolamide to topiramate given worsening renal function and a VPS which improved her symptoms.

Patient 7

A 13-year-old postpubertal obese girl (BMI 38.5 kg/m^2) with a 20-pound weight gain over the prior 6 months developed flu-like symptoms. After 5 days, she developed "dimness" and blurry vision in the right eye only. Two weeks later, she developed nonmigrainous headaches that worsened in a recumbent position. Frisén Grade 2 bilateral papilledema was noted with reduced visual acuity to 20/25 OU. MRI/MRV was normal. LP opening pressure was 38 cm H_2O. Treatment included acetazolamide which improved her symptoms.

Patient 8

A 33-year-old woman with a history of IIH in 2014 (BMI 33.8 kg/m^2) with a 20-pound weight gain over the past 12 months developed a few days of fevers, pharyngitis, progressive headaches, TVOs, mild nasal field deficits in the left eye > right eye, with Frisén Grade 1 papilledema simultaneously, and without a history of acetazolamide or topiramate noncompliance. MRI/MRV showed an empty sella. LP opening pressure was 30 cm H_2O. Treatment consisted of increasing her acetazolamide and topiramate which led to improvement of symptoms.

We report a series of patients with new or worsening PCS in the setting of a recent COVID-19 infection, adding to the spectrum of COVID-19–related neurologic complications (2). Another series reported 6 patients with newly diagnosed PCS in the setting of COVID-19 infection, but only 2 patients had documented papilledema (4). One case of secondary intracranial hypertension has also been reported in a child with post–COVID-19 pediatric multisystem inflammatory syndrome who was found to have a new right abducens palsy, bilateral papilledema, and an opening pressure of 36 cm H_2O without pleocytosis but her initial presentation included fevers, rash, and elevated inflammatory markers (5).

The mechanism by which PCS developed or was exacerbated in this cohort may be unique to COVID-19 infection, as typical instigating factors, such as significant weight gain or exposure to vitamin A derivates or tetracyclines, were mostly absent. Notably, 2 patients lost significant weight preceding development of PCS. All patients in our cohort had positive RT-PCR testing for SARS-CoV2; CSF was not tested for SARS-CoV-2 because of the lack of a validated, readily available assay. CSF SARS-CoV-2 has only been detected in a few patients with neurological COVID-19 (2) and was negative when CSF testing was performed for refractory headaches (4). SARS-CoV-2 has tropism for the choroid plexus epithelium, meninges, and brain vasculature (cell types which express SARS-CoV-2 entry proteins ACE2 and TMPRSS2), suggesting a biologically plausible mechanism by which viral infection may dysregulate CSF hydrodynamics (3). COVID-19–infected CSF barrier cells display an altered proinflammatory transcription profile not seen in healthy controls or a comparator case with influenza (3). Alternatively, SARS-CoV2 infection could lead to hyperviscosity and hypercoagulability increasing venous pressure (4), although major CVST was ruled out with appropriate imaging.

In conclusion, PCS may develop or worsen in the setting of COVID-19 infection, even in the absence of classic triggers such as weight gain. Tropism of SARS-CoV2 to CSF–brain barrier tissues and resulting aberrant function provides a putative mechanism linking COVID-19 and PCS (3). Clinicians should be aware of the possibility of PCS developing in recent COVID-19 infection, especially with report of new headaches or other signs/symptoms of increased ICP such as TVOs, peripheral vision loss, papilledema, pulsatile tinnitus, or pseudoabducens palsy.

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