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Bilateral papilledema with vision loss due to post–COVID-19–induced thiamine deficiency: illustrative case

Kern H. Guppy, MD, PhD,[1,2] Yekaterina K. Axelrod, MD,[1] and Han Kim, MD[3]

[1]Department of Neurosurgery, The Kaiser Permanente Medical Group, Sacramento, California; [2]Department of Neurological Surgery, University of California, San Francisco, San Francisco, California; and [3]Department of Ophthalmology, The Kaiser Permanente Medical Group, Stockton, California

BACKGROUND Bilateral papilledema with vision loss is considered a neurosurgical emergency due to high intracranial pressure. However, it may not be the only cause of papilledema. The authors reported an association among coronavirus disease 2019 (COVID-19), bilateral papilledema, blindness, and Wernicke's encephalopathy (WE).

OBSERVATIONS An 18-year-old woman presented to the neurosurgery service with rapid profound vision loss and bilateral papilledema. She had COVID-19 3 months earlier with subsequent loss of smell (anosmia) and taste (ageusia), which resulted in hyperemesis and a 43-lb weight loss. Examination revealed ataxia, horizontal nystagmus, and blindness. Magnetic resonance imaging and magnetic resonance venography of her brain were normal. Presumptive diagnosis of WE was made, and she was treated with intravenous thiamine with restoration of vision within 48 hours. Patient's thiamine level was less than half the normal value.

LESSONS Neurosurgeons should be aware of this unique correlation between papilledema and vision loss and its association with WE due to post–COVID-19 hyperemesis and weight loss from anosmia and ageusia.

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KEYWORDS COVID-19; vision loss; papilledema; Wernicke's encephalopathy; thiamine deficiency; hyperemesis

Bilateral papilledema with vision loss is usually a neurosurgical emergency due to optic disc swelling caused by high intracranial pressure. Although there are several causes of bilateral papilledema, idiopathic intracranial hypertension (IIH) is the most common in patients under the age of 50.[1] Clinical history and elevated opening pressure (OP) during lumbar puncture (LP) determined the diagnosis.

One of the rare presentations of bilateral papilledema can be seen in Wernicke's encephalopathy (WE) with a reported incidence of 4%.[2] Although WE has been typically found in poorly nourished persons with alcohol use disorder, it also has been diagnosed in patients who do not have the disorder.[3,4] More recently, WE has been associated with coronavirus disease 2019 (COVID-19) and was described in patients recovering from acute respiratory failure managed on mechanical ventilation,[5,6] noncritically ill patients with COVID-19,[7,8] and in one patient who previously had COVID-19.[9]

We present a unique case of a patient who had COVID-19 complicated by anosmia and ageusia who presented to the neurosurgery service with acute loss of vision, bilateral papilledema, nystagmus, and ataxia. The presumptive diagnosis of WE was made, and the patient was treated with thiamine replacement. She regained her vision within 48 hours. This is the first case report of a patient who had COVID-19 presenting with bilateral papilledema and vision loss due to thiamine deficiency with normal brain magnetic resonance imaging (MRI).

Illustrative Case

An 18-year-old woman with no significant past medical history except for COVID-19 infection 3 months prior presented to an outside hospital emergency department (ED) and stated she "was watching TV as usual, and suddenly noticed inability to see the

ABBREVIATIONS CN = cranial nerve; COVID-19 = coronavirus disease 2019; CSF = cerebrospinal fluid; ED = emergency department; FLAIR = fluid-attenuated inversion recovery; ICU = intensive care unit; IIH = idiopathic intracranial hypertension; IV = intravenous; LP = lumbar puncture; MRI = magnetic resonance imaging; OP = opening pressure; WE = Wernicke's encephalopathy.

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people on the screen." In the ED, her physical examination was significant for blunt affect, slow responses to conversation, and reddened lips. She had normal mentation. The patient was seen by an ophthalmologist in the ED; her pupils were equal and reactive to light with visual acuity in right eye (OD) 20/400; in left eye (OS) she was able to count fingers 3 ft away. Attempts to sustain horizontal or upward gaze resulted in slow nystagmus, and then eyes drifted to primary gaze. No primary position nystagmus was seen. Both fundi had diffusely blurred margins; the right fundus had grade III edema and large inferior disc hemorrhage, and the left had grade II edema without hemorrhage.

The patient was admitted to an outside hospital where MRI and magnetic resonance venography of the brain were performed. Both results were within normal limits. She received an LP with an initial OP of 35 cm H_2O (sitting position). Four tubes of cerebrospinal fluid (CSF) were taken for analysis (approximately volume of 12 mL). The clinical diagnosis of IIH was made and the patient was started on acetazolamide. Overnight, the patient's vision became worse: she only had light perception bilaterally. A repeat LP was performed (18 hours later) with an OP of 15 cm H_2O (lateral decubitus). The patient was transferred to our facility for tertiary neurosurgery care.

At our facility, additional history revealed multiple hospital visits over the past 3 months for nausea, vomiting, and inability to tolerate oral intake. Ever since her diagnosis of COVID-19, she had lost her senses of smell and taste ("everything tasted gross"). She had only been eating popsicles and lost 43 lb (24% of her body weight) in the last 3 months. The patient's mother also related unsteadiness in the patient's gait that required help for the past several weeks. The patient denied history of headaches.

Another LP was performed, leading to the placement of a lumbar drain for a trial of CSF diversion due to a presumption of IIH; however, the OP was still low at 12 cm H_2O (lateral decubitus). The lumbar drain was draining CSF at a rate of 10 to 12 mL/hr, but the patient's vision continued to get worse. Because of conflicting information regarding the possibility of IIT and a suspicion of WE, thiamine level was obtained, and the lumbar drain was clamped. The patient was empirically started on intravenous (IV) thiamine 200 mg every 12 hours. Within 48 hours, her vision improved: OD 20/50; OS 20/40 (measured by Snellen chart 4 ft away) with minimal residual nystagmus. She continued to have some ataxia. The blunt affect had improved. The lumbar drain was removed, and the acetazolamide was discontinued. The patient was observed for 3 more days in the hospital and then discharged. Her thiamine level was 34 nmol/L (normal 70–180 nmol/L). Six months later, the patient had no evidence of papilledema or optic disc hemorrhages and had a thiamine level of 184 nmol/L.

Discussion

Observations

COVID-19 has affected millions of people worldwide, but its adverse post–COVID-19 health outcomes and potential long COVID-19–related effects are still evolving. Such adverse outcomes affect almost all organ systems.[10] Neurological manifestations were seen in approximately 36.4% of patients,[11] with ageusia and anosmia being the most common (35.8%–51% and 38.5%–53%, respectively).[12,13] The pathological basis is still unresolved but is believed to be due to neurotropic infection of the gustatory or olfactory systems.[14] The average duration of symptoms range from short term (average 8 days)[15] to several months.[16] Complications from anosmia and ageusia resulting in hyperemesis have not been well documented in the literature. Complications from hyperemesis, however, have been reported in pregnant women during their first trimester. When severe, hyperemesis gravidarum, as it is called, has been associated with thiamine deficiency resulting in WE.[3,4]

The classic triad of WE, initially described in malnourished persons with alcohol use disorder, includes confusion, ataxia, and nystagmus; however, only a small percentage of patients experience all three symptoms.[17,18] Bilateral papilledema, although infrequent, has been reported in patients with WE.[2,19,20] De Wardener and Lennox, in their study of patients in a Singapore prisoner-of-war camp, found that 2 of 52 (4%) patients with WE had papilledema.[2] In 1989, Mumford[21] described a 24-year-old woman who presented in her 16th week of pregnancy, having had symptoms of vomiting for 8 weeks, with ataxia, vertical and horizontal nystagmus, inability to abduct both eyes with marked bilateral papilledema with capillary dilation, and peripapillary flame hemorrhages. The patient eventually became comatose. She was treated with high-dose IV thiamine; improvement in symptoms occurred within 6 hours of treatment.

It is postulated that optic disc edema in these patients represents a thiamine-induced mitochondrial dysfunction that results in obstruction of axoplasmic flow.[20] Disc hyperemia and retinal hemorrhages can also result from the obstruction. Reports have also shown that resolution of the disc edema occurs and visual function is restored if WE is treated in a timely manner; therefore, visual function is often preserved.[21,22]

The association between COVID-19 and WE has been reported in several studies.[5–9] Branco de Oliveira et al. presented a retrospective case series involving 15 patients in the intensive care unit (ICU) with COVID-19 infections who developed WE and their response to treatment with IV thiamine. All patients had encephalopathy, with 67% displaying at least one other sign of the classic WE triad (ophthalmoparesis and ataxia). These patients developed WE from their lengthy stay in the ICU with poor nutritional status.[5,6] There have been four other cases of patients infected with COVID-19 who were not in the ICU who developed WE (Table 1).[7–9] All reported poor nutrition from emesis; all had brain MRI that indicated WE;[7–9] three had active COVID-19 infections[7,8] and one had post–COVID-19 status;[9] two had normal thiamine levels;[7] and three had cranial nerve (CN) involvement.[7,8] None of the patients had papilledema.

The first two cases (Table 1) were reported by Pascual-Goñi et al.[7] The first patient was a 60-year-old woman hospitalized for COVID-19 with diplopia and a right-sided abducens palsy. Her MRI showed symmetrical hyperintensities in the mammillary bodies and hypothalamus typical of WE. The second patient was a 35-year-old woman with a 3-week history of vomiting with COVID-19 infection who had developed diplopia and bilateral abducens palsy, altered mental state, and encephalopathy. She also had MRI findings of symmetrical hyperintensities in the mamillary bodies and hypothalamus and demonstrated unusual involvement of the limbic system not typical of WE.[7] The third case involved a 24-year-old man with COVID-19 infection who presented with right-sided facial droop, mild left-sided extremity tingling and weakness, and the sensation of falling to the left when walking.[8] The patient had nausea and vomiting for a week prior to his diagnosis of COVID-19, with the only respiratory symptom being a dry cough. His brain MRI showed T2 fluid-attenuated inversion recovery (FLAIR) hyperintensity in the splenium of the corpus collosum, mammillary bodies, periaqueductal gray matter, tectum, and ventral and dorsal medulla, which was a pattern typically seen in WE.[23] This was the first COVID-19 case with CN VII palsy and WE. Finally, the fourth case involved a 36-year-old man diagnosed with COVID-19 infection 6 weeks earlier who presented with subacute onset of painless bilateral

TABLE 1. Comparison of our case report with four case reports of patients with COVID-19 and WE

Authors & Year	Age (yrs), Sex	Symptoms	Cranial Nerve Affected	Papilledema	Brain MRI	COVID-19 Status	OP	Thiamine Level (nmol/L)*	Conclusions
Pascual-Goñi et al., 2020[7]	60, F	Diplopia	Rt CN VI palsy	No	WE	Active	NA	Normal	Patient presenting w/ CN finding & MRI findings of involvement of hypothalamus & mesencephalic tegmentum, features of WE, but w/ normal thiamine level
Pascual-Goñi et al., 2020[7]	35, F	Diplopia, paresthesia, emesis, encephalopathy	Bilat CN VI palsy	No	WE	Active	NA	Normal	Similar to above; however, brain MRI also included limbic system not typical of WE
Alexandri et al., 2022[8]	24, M	Rt-sided facial droop, mild lt-sided tingling, weakness, ataxia, emesis × 1 wk	Rt CN VII palsy	No	WE	Active	NA	NA	Patient had at least 1 wk of poor nutrition & emesis, which may have contributed to his susceptibility
Shepherd et al., 2022[9]	36, M	Bilat blindness, nausea, diarrhea, odynophagia, thrush	No	No	WE	Post	Normal	NA	Patient Dx w/ thrush; lost 20% of body weight (52 lb); no light perception; authors believe vision loss was from brain cortex; unlike other WE, no optic nerve edema found; this case represents poor nutritional intake & vomiting secondary to COVID-19, resulting in WE & blindness
Present study, 2022	18, F	Vision loss, ataxia, nystagmus hyperemesis, weight loss	No	Yes, bilat	No	Post	High × 1, normal × 2	34 nmol/L	Unique from other cases w/ bilat papilledema; no MRI findings of WE; 1st case of post–COVID-19 w/ anosmia & ageusia resulting in hyperemesis & weight loss w/ thiamine deficiency

Dx = diagnosed; NA = not applicable.
* Normal level: 70–180 nmol/L.

blindness.[9] He had multiple hospitalizations for severe nausea, diarrhea, and odynophagia, with the eventual diagnosis of oral thrush that limited his oral intake. He had unintentional weight loss since his COVID-19 diagnosis (52 lb, or 20% of body weight). His brain MRI showed FLAIR hyperintensity of the medial thalami, mammillary bodies and periaqueductal gray matter, and associated enhancement with restricted diffusion of the medial thalamus bilaterally consistent with WE. The patient was treated with IV thiamine and within 5 hours his vision improved. It should be noted in this case an LP was performed with a normal OP.

Finally, the association between elevated OP and papilledema in WE is elusive. Our patient had elevated OP initially and subsequent punctures yielded normal OP while her vision was deteriorating. Interestingly, Mumford described a comatose patient with WE who had bilateral papilledema and OP of 19 cm H_2O.[21] The association between papilledema and normal OP is not a unique finding in ophthalmology. Half of patients with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes) syndrome presented with bilateral papilledema with normal OP.[24] We believe that bilateral papilledema in the setting of WE after COVID-19 may also be associated with normal OP. However, more data are needed to fully support such a conclusion.

Lessons

The cases in the literature showing an association between COVID-19 and WE involve malnutrition resulting in thiamine efficiency. None of the patients had papilledema. Our report is the first case of a patient who had COVID-19 and had bilateral papilledema and blindness without typical MRI findings of WE with documented thiamine deficiency. The diagnosis was based on clinical presentation of hyperemesis, weight loss, ataxia, nystagmus, and bilateral papilledema. This case illustrates that the finding of papilledema and vision loss does not always require neurosurgical intervention and that patients who have had COVID-19 and have papilledema, vision loss, and hyperemesis should be evaluated for thiamine deficiency.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Guppy, Axelrod. Acquisition of data: all authors. Analysis and interpretation of data: Guppy. Drafting the article: Guppy, Axelrod. Critically revising the article: all authors. Reviewed submitted version of manuscript: Guppy, Kim. Approved the final version of the manuscript on behalf of all authors: Guppy. Study supervision: Guppy, Axelrod.

Correspondence

Kern H. Guppy: University of California, San Francisco, CA. kguppy@yahoo.com.