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## Clinical Observation

# Probable New Daily Persistent Headache After COVID-19 in Children and Adolescents

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## ABSTRACT

**Introduction:** Headache has been cited as both a primary symptom and a sequela of infection with the novel coronavirus. Cases of long coronavirus disease (COVID) headache have already been documented in adults, but literature on similar cases in children and adolescents is scant.

**Case Report:** We present three cases of persistent headache after infection with COVID-19 in pediatric patients presenting to a tertiary headache center.

**Conclusion:** Infection has been suggested as a trigger for chronic headaches, specifically those of the new daily persistent headache type. Although the association between new daily persistent headache and COVID-19 remains unclear, these cases highlight the importance of awareness of the neurological sequelae of novel coronavirus infection in children and adolescents.

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## Introduction

Although respiratory symptoms are the predominant symptoms of infection with coronavirus disease 2019 (COVID-19), systemic symptoms such as fever, myalgias, and headache also appear in both adult and pediatric patients. Headache has been described as both a symptom of current infection and one that persists after clearance of the virus.<sup>1,2</sup> However, there is little literature on persistent headache after COVID-19 infection in children and adolescents. Here, we describe the cases of three pediatric patients who presented with probable new daily persistent headache (NDPH) symptoms after contracting COVID-19.

## Case descriptions

The first patient was a 15-year-old girl who was diagnosed with COVID-19 by nasopharyngeal swab after seven days of headache,

extremity numbness, fatigue, and neck pain. Before diagnosis, her only comorbid condition was depression, treated with escitalopram. Neither did she have a prior personal or family history of headache disorder nor did she have a history of headache-related episodic syndromes. She experienced persistent headaches after resolution of COVID-19 symptoms that were described as a bitemporal pressure without radiation. The headaches were sometimes pounding in nature, were accompanied by neck tightness, and occurred almost daily. Treatment included a combination drug of acetaminophen, aspirin, and caffeine or ibuprofen for rescue medications, and lifestyle modifications such as sleep hygiene, adequate water intake, limiting screen time, and limiting caffeine products. This patient's headaches continued for almost seven months after diagnosis of COVID-19, and she is still receiving follow-up care.

The second patient was a 16-year-old male who presented for evaluation of approximately eight months of daily headache. Headache onset was in January 2021 with associated congestion. He tested positive for COVID-19 via nasal swab at the time of symptoms, after family contacts tested positive. Ultimately congestion improved with persistence of the headache. The headache was described as bilateral frontotemporal throbbing and pulling with associated light-headedness with position changes that persisted throughout the day with some improvement in the morning and worsening in the evening to an average of 7/10 pain

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intensity. Verapamil was ineffective in improving his symptoms. Acupuncture, chiropractic medicine, and massage therapy were also ineffective in improving his symptoms. Over-the-counter abortive therapies were minimally effective in symptom improvement. This patient had a history of dull constant frontal headache of 4/10 severity after a concussion with no associated episodic syndromes, which lasted approximately six months. The onset of his postconcussion headache was one year before the onset of this presenting headache. His headache history was otherwise negative. The patient's mother and sister both have migraines. After evaluation, verapamil was tapered off and a prednisone course was initiated. Reevaluation was scheduled for three months after the initial visit.

The third patient was a previously healthy 10-year-old girl with a COVID-19-positive sick contact. Her symptoms included anosmia, nasal congestion, rhinorrhea, headache, and decreased appetite. Two days after symptom onset, she was diagnosed with COVID-19 by nasopharyngeal swab. Two months later, she had complaints of a daily headache that had lasted for approximately two weeks. Her headaches occurred almost every afternoon and presented as a bilateral pressure behind the eyes. Each headache lasted about an hour and was associated with photophobia, dizziness, and occasionally, blurred vision. The headaches improved with lying down and were worsened with online activities, movement, and dehydration. The patient was treated with a combination drug of butbur, petasin, isopetasin, riboflavin, magnesium, and coenzyme Q10 as a preventative measure, and she used acetaminophen and ibuprofen for rescue medicines. She was also encouraged to keep a headache diary and make lifestyle modifications such as drinking water, avoiding frequent over-the-counter pain medications, and practicing good sleep hygiene. These headaches lasted for a duration of at least two months, although the patient could not recall the exact duration. At 5-month follow-up, the patient reported that her headaches were “resolved,” although on a follow-up phone call 14 months after headache onset, she endorsed continued intermittent tension-type headaches that she does not treat. Before this, she had no history of headache, episodic syndrome, or any other medical condition. The patient's mother did have a history of migraine and tension-type headaches.

## Discussion

NDPH was first described by Dr Walter Vanast in 1986 as a self-limiting and benign headache disorder.<sup>3</sup> The International Classification of Headache Disorders requires the headaches to be persistent, daily, and with a clearly remembered start.<sup>4</sup> The headaches can have either migraine-like or tension-type-like features, but must be present for at least three months.<sup>4</sup> The usual presentation involves bilateral, nonpulsating headaches that are not aggravated by routine physical activity.<sup>5</sup> The headaches may be accompanied by photophobia, phonophobia, nausea, or vomiting.<sup>5</sup> A number of patients also experience sleep disturbance, visual disturbance, and fatigue, among other comorbid symptoms.<sup>5</sup>

Within the pediatric population, NDPH occurs more frequently in females, and its start may correlate with stress from school or infection.<sup>6</sup> These headaches have classically been challenging to treat. These headaches are often refractory to treatment and/or unremitting. Treatment methods have included preventative drugs such as topiramate and amitriptyline; rescue drugs such as ibuprofen or acetaminophen; nonpharmacotherapy such as acupuncture, psychotherapy, and biofeedback; and lifestyle modifications such as regular sleep and diet, avoiding school absences, and limiting over-the-counter medications.<sup>5,6</sup> No pharmacologic treatment is one of the indicators of a poor prognosis for the condition. Approximately 50% of children and adolescents have either

complete resolution or reduced frequency of headache within a year of symptom onset.<sup>6</sup> Clinicians and researchers must take into account that headaches of this type are rare, occurring in approximately 0.1% of the population, but they are more prevalent in children and adolescents.<sup>5</sup>

In contrast, COVID-19 has become widespread, affecting millions of people since its identification in January 2020. Although infection and illness are common in adults, children are less likely to become severely ill than their adult counterparts. In children, the illness presents primarily with fever and cough. Other common symptoms include fatigue, myalgia, rhinorrhea, anosmia, and headache.<sup>1</sup> Studies suggest that headache is less likely to occur in children and adolescents than symptoms such as fever and cough, occurring in 10% to 20% of pediatric COVID-19 cases.<sup>7</sup> Despite this, there are already some accounts of adults with headache as a symptom of long COVID, a set of symptoms that patients may experience for months after their infection.<sup>2</sup> This headache may be accompanied by “brain fog,” poor cognition and memory, and worsening of migraines in patients with such history. The headache has been reported as occurring for up to six months after discharge from hospitalization for COVID-19.<sup>2</sup> An Italian study reported two cases of women with a diagnosis of probably NDPH after confirmed COVID infection. Both women were in their 40s and experienced persistent headache for at least 20 days after their headache onset.<sup>8</sup> There are no similar accounts documented in children.

## Conclusion

The distinction between long COVID headache and NDPH has yet to be explored. Headaches occurring as a manifestation of long COVID syndrome may have many pathophysiologic causes, including neuronal invasion of the virus, hypoxia-mediated damage, and cytokine storm.<sup>2</sup> The pathophysiology of NDPH remains unclear, although there are many widely recognized triggers. The link between infection and NDPH first became apparent when multiple patients with NDPH were found positive for Epstein-Barr virus.<sup>9</sup> Rozen also noted that there have been many historical cases of new persistent headache after pandemics.<sup>10</sup> Although these were noted before the classification of NDPH, Rozen also warned of the potential for NDPH to become a sequelae of COVID-19 infection based on this historical context and documentation of headache as a primary symptom of COVID-19.<sup>10</sup> It is still unclear how probable NDPH presentations occurring after COVID-19 will play out in patients; however, these three cases show a temporal association between the virus and headaches of NDPH character. Although it is possible that these patients had long COVID symptoms, or more general infection-triggered headaches, these cases align with the International Classification of Headache Disorders definition of NDPH. As such, they are probable cases of NDPH, especially when considered in the context of literature highlighting the association between viral illness and NDPH. In addition, these cases draw attention to the importance of awareness of the neurological sequelae of COVID-19 infection in the pediatric population.

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