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The unusual course of a migraine attack during COVID-19 infection — Case studies of three patients

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**ABSTRACT**

The effect of the coronavirus disease 2019 (COVID-19) on the nervous system remains undefined. Some studies have shown that headache is one of the most common symptoms and often the first neurological symptom in patients with confirmed infection. There are only a few reports concerning the effects of COVID-19 on the course of migraine.

This article investigates three female patients with prolonged history of migraine, in which atypical phenomenology and course of migraine attacks were observed during COVID-19 infection.

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**Introduction**

The coronavirus disease (COVID-19) which emerged in Wuhan, China in November 2019 has become a global pandemic [1]. Although understanding of this disease entity and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus itself which causes it is growing, the mechanism of the development of neurological symptoms in COVID-19 is still unknown [2]. It seems that the emergence of neurological symptoms occurs through three possible mechanisms: direct involvement of the nervous system, immune-mediated post-inflammatory complications, and a mechanism secondary to lung damage and systemic disease [3,4].

Although the main symptoms of COVID-19 are fever, cough and shortness of breath, one of the most frequently observed symptoms preceding or occurring during and after SARS-CoV2 infection is headache [5,6]. Most often, this is phenotypically similar to tension type headache and is described as a pressing or distressing pain, bilateral and difficult to treat. There are few reports concerning the effects of COVID-19 on the course of migraine [7].

This article presents three patients suffering from migraine over many years, in which atypical phenomenology and course of migraine attacks were observed during COVID-19 infection.

**Case reports**

**Case 1**

This 45-year-old female had experienced episodic migraines, without aura or photophobia, since she was 26 years old. Consistently, her migraine attacks occurred about twice a month with a good response to triptans or paracetamol. In September 2020, the first visual aura appeared in both left visual fields along with olfactory hypersensitivity. She experienced a geometric shape within the peripheral visual field that continued to enlarge proximally; ultimately leading to severely obscured vision. The visual disturbance was grey and dark green in colour and gradually dissipated, lasting about 35 min. Subsequently, she experienced the most severe migraine headache in her life with simultaneous photophobia which did not respond to typical pain medication. Brain MRI and angio-MRI were performed and showed no abnormalities. After 2 days, the headache disappeared and then the patient lost her sense of smell. She developed a fever and severe muscle pain. A PCR (polymerase chain reaction) test for COVID-19 was positive, confirming infection. After the infection, aura with or without migraine headache did not occur again.

**Case 2**

This 24-year-old female had suffered from episodic migraines without aura or photophobia since she was 16 years old. Her migraine attacks appear approximately once a month with a good response to nonsteroidal anti-inflammatory drugs and paracetamol. In September 2020 there was a sudden, paroxysmal stinging

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and burning sensation in her ears with transient hearing impairment. The symptoms were accompanied by a visual aura in both right visual fields that lasted 20 min. The patient described these two as white spots and disco lights that lasted for a few minutes and then a colourful, curved, enlarging rainbow appeared in the outer field of vision, which eventually covered the entire field of vision in that eye (Fig. 1). After the visual aura had subsided, very severe migraine pain with photophobia and nausea occurred, which provoked status migrainosus. The patient required hospitalisation and a brain MRI was performed which showed no abnormalities. Two days after the migraine condition stabilised, the patient lost her sense of smell and developed a dry cough. A PCR test for COVID-19 was positive. After the infection, the migraine with aura or aura without headache did not occur again.

Case 3

This 52-year-old patient presented with a history of suffering from chronic migraine without aura from when she was 45 years old. She is treated prophylactically with topiramate. Her migraine headache occurs approximately nine days a month, no visual auras have ever occurred. In August 2020, she experienced anosmia, muscle aches, fever and a dry cough. A PCR test for COVID-19 was positive. During the infection, she developed a visual aura without headache three times within a week. The patient described this as flashes of light and various movements of images in the visual field, she described these as coloured lines bending inward and jumping grey zigzags. The entire field of vision was not covered. The visual symptoms disappeared after approximately 15–30 min.

Discussion

The effect of COVID-19 on the nervous system and the mechanisms of neurologically related symptoms present in patients with COVID-19 remain undefined. Several possible routes for the spread of the SARS-CoV-2 virus in the human body are currently postulated: use of the bloodstream with subsequent neuronal dissemination, infection of endothelial cells within the blood-brain barrier or blood-cerebrospinal fluid barrier, use of trans-synaptic pathways after infection of the endings of nerves (forward or retrograde transport) mainly in the olfactory bulb, crossing the blood-brain barrier as a result of infection of leukocytes or through the use of the glymphatic system [8–10]. However, it seems that the most likely receptor mechanism is the use of angiotensin-converting enzyme type 2 (ACE2) to break the blood-brain barrier. ACE2 expression outside the lung tissue has been confirmed in neu-
by increasing activity, especially in the occipital lobes – it may be responsible for CSD and successive appearance of aura. The mechanism of this phenomenon remains unknown. These observations require confirmation in larger groups of patients and with the use of functional imaging techniques. To the best of our knowledge, this is the first report in the world literature regarding the association of migraine aura with COVID-19.

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Competing interests

None declared.

Ethical approval

Approval for this research was given by the Commission of Ethics at the Wroclaw Medical University.

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