



Case Report

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Headache can be the only symptom of COVID-19: A case series

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Abstract

Headache is the fourth most common cause among the total applications to emergency services; it constitutes 5% of the applications to hospitals every year. Five-fold increase was detected in the incidence of headache in the regions affected by coronavirus disease-2019 (COVID-19) pandemic. While the symptoms of respiratory systems have been frequently observed, the occurrence of symptoms and complications in peripheral and central nervous system has become increasingly prevalent in the cases of COVID-19 disease. In this case series, we highlight that the patients with isolated headache may be diagnosed with COVID-19 infection. Three female patients (forty, sixty and sixty-two years of old) were admitted to the emergency service with complaints of severe headache. Their headache did not respond to the paracetamol and the nonsteroidal anti-inflammatory drug (NSAID) they used prior to their application to the hospital. No pathologic finding was detected in cerebral imaging. All patients were diagnosed with COVID-19 by their clinical status and history. The headache was the isolated symptom of the COVID-19 in all the three cases. The possibility of COVID-19 infection must be considered in the evaluation of the patients admitted to hospital with complaints of headache, one of the most frequent reasons for hospital assistance requests.

Keywords: COVID-19, headache, neurologic manifestations, SARS-CoV-2

1. Introduction

Coronavirus disease-2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulted in 63, 965, 092 confirmed cases and 1,488,120 deaths all around the world as of December 3, 2020 (1). Respiratory system symptoms are frequently found in COVID-19 disease with complications in the peripheral and the central nervous systems are increasingly found (2). Headache is the fourth most common reason for total applications to emergency services; it represents 5% of the applications to hospital (3). Five-fold increase was detected in the incidence of headache in the regions affected by COVID-19 pandemic (4).

Only neurologic symptoms were found as the initial symptoms in some patients diagnosed with COVID-19 such as headache, anosmia, ageusia, languidness, unstable walking, cerebral hemorrhage, cerebral infarction, and other neurological diseases (5). These complications are possibly caused by direct viral injury, immunological mechanisms and by hypoxia (6). SARS-CoV-2 uses the transmembrane ACE2 receptor to enter the mammalian host cells. The ACE2 receptor was detected in various cells in humans including the airway lung epithelial cells, vascular endothelial, pericytes, and smooth muscle cells, and neuronal cells in the trigeminal ganglia, olfactory bulb, and other cortical and subcortical areas (7, 8). Headache is in close temporal relationship with the symptoms, and it is frequently accompanied by

phonophobia developed in patients with anosmia and ageusia (9). Headache was found as an early finding of COVID-19 infection. Additionally, it was observed that symptoms involving other systems or apparatus arise in the later stages of the disease, following the headache. Cases of isolated headache are less common than the cases where headache is combined to other symptoms (10).

In this case series, we aim to draw attention to the fact that the patients with isolated headache may be diagnosed with COVID-19 infection.

2. Case report

2.1. Case 1

A 62-year-old female patient applied to the emergency service with complaints of severe headache. She reported that she had had the headache continuously for three days and it became intolerable. She did not respond to the paracetamol and the nonsteroidal anti-inflammatory drug (NSAID) she used at home. She described the headache as the most severe one in her life. She had an intense pain in both sides of her head as if something were compressing her head. She had no cough, shortness of breath and fever history associated with COVID-19 for several days. She reported that she had not been in close contact with a person with COVID-19 infection to her knowledge. She stated that she had hypertension and type-2 diabetes as additional chronic diseases. On arrival, her

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temperature was 36.4°C, her pulse rate was 96 beats/min (regular rhythm), her blood pressure was 150/90 mmHg, and her oxygen saturation was 97% in room air. Her physical examinations including lung auscultation did not show any apparent abnormal findings. Neurological examination revealed alerted consciousness and normal eye movements. Her gait was normal. Muscle weakness or abnormal tendon reflexes of extremities was not observed. CRP:88 mg/L and D-Dimer: 96 µg/L was found in the blood tests; other results are given in Table 1. Emergency unenhanced cerebral computed tomography (CT) was normal. Magnetic resonance imaging (T1, T2, and fluid attenuated inversion recovery) and intracranial magnetic resonance angiography (arterial and venous) were normal. As the patient's severe headache continued, she was planned to be hospitalized in the neurology service for a follow-up. Considering the patient's elevated levels of CRP and D-Dimer values and the fact that headache is a potential symptom of COVID-19 infection, a SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) swab test was taken to rule out possible COVID-19 infection. The RT-PCR test result was found to be positive. Chest CT scanning was performed on the patient and ground-glass opacities were found in her right lung basal (Fig. 1). The patient was admitted to the pandemic service for a close follow-up and her COVID-19 treatment was started. Her headache intensity decreased in the following day after the admission and no additional symptom and finding were found in the follow-up. The finding that the intensity of the patient's headache further decreased and disappeared after the COVID-19 treatment, shows that the headache developed due to COVID-19 infection. The patient was discharged from the service with full recovery after she was followed up in the service for five days.

2.2. Case 2

A 41-year-old female patient applied to the hospital with complaints of sudden severe headache. She had a throbbing pain in both sides of her head. The pain was particularly focused in the frontoparietal area. She had no chronic disease and no history of headache previously. She did not respond to the paracetamol and NSAID medication she received during the day of her hospital visit. In the detailed medical history of the patient, it was found that she was too often present in crowded places, and she was at close distance with a person with COVID-19 infection. On arrival, her vital signs were normal. Her respiratory rate was at normal range and physical examinations including lung auscultation did not show any apparent abnormal findings. Neurological examination was normal. Laboratory test values are summarized in Table 1. No pathologic finding was detected in emergency unenhanced cerebral CT. In chest CT scanning of the patient, peripheral ground-glass opacities were found in all lobes and segments in both of her lungs (Fig. 1). The patient was also tested positive for SARS-CoV-2 RT-PCR. Her COVID-19 treatment was arranged as ambulatory treatment. The patient was called

on days 3 and 7 and she reported that she did not have additional symptoms or health complaints.

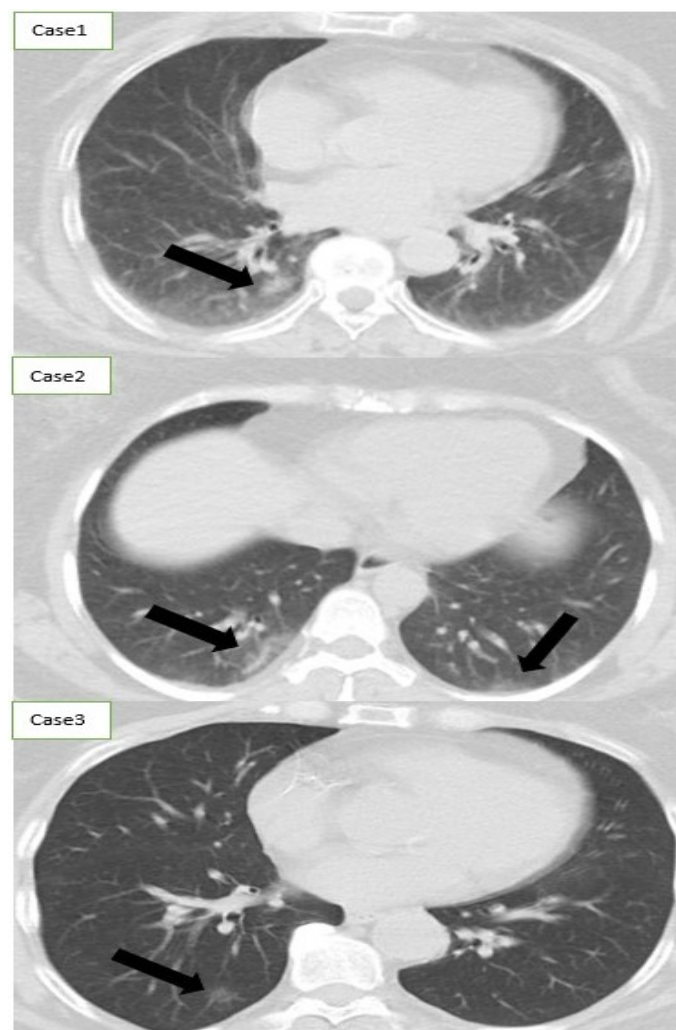


Fig 1. Chest CT images cases'

2.3. Case 3

A 60-year-old female patient had a severe headache for two days. She had a throbbing pain in both sides of her head. She reported that she also had complaints of headache and dizziness one month earlier; she applied to neurology clinic, but all test and examination results were normal. She did not have a history of migraine. She stated that she responded partially to paracetamol and NSAID medication in that period. She did not respond to any medical treatment for two days when she applied to the emergency service. She said that she entered in close contact with COVID-19 patients three days before the headache started. On arrival, her vital signs were normal. The physical examination was normal. Her neurological examination did not show pathological findings. Laboratory test values are summarized in Table 1. She was tested positive for SARS-CoV-2 RT-PCR in her nasopharyngeal swab sample. In chest CT scanning, ground-glass opacities were found in the periphery of the right lung (Fig. 1). Her COVID-19 treatment was arranged as ambulatory treatment. She was called on days 1, 3, and 7 and she said that she did not have any additional symptoms or health complaint.

Table 1. Laboratory test values of cases*

Parameters	Case-1	Case-2	Case-3
Leucocytes (x10 ⁹ /l; normal range 4.5-10.5)	5.0	6.1	5.8
Hemoglobin (g/dl; normal range 12-17.4)	13.9	12.9	12
Platelets (x10 ⁹ /l; normal range 142-424)	165	270	358
Lymphocytes (x10 ⁹ /l; normal range 0.6-3.4)	1.2	2.2	2.1
Neutrophils (x10 ⁹ /l; normal range 2-6.9)	3.4	3.3	3.2
Na ⁺ (mmol; 136-146)	133	137	140
K ⁺ (mmol; 3.5-5.1)	4.1	4.4	5.1
Cl ⁻ (mmol; 101-109)	96	106	103
Glucose (mg/dl; normal range 74-106)	262	105	93
Serum creatinine (mg/dl; normal range 0.67-1.17)	0.9	0.5	0.6
Urea (mg/dl; normal range 17-43)	43	23	24
Aspartate aminotransferase (U/l; 5-50)	35	21	25
Alanine aminotransferase (U/l; 5-50)	23	15	17
C-reactive protein (mg/l; 0-5)	88	0.9	6.5
D-Dimer (µg/L; normal range; 0-0.55)	96	0.2	0.4
Troponin (ng/ml; normal range 0-0.16)	0.03	0.01	0.01

3. Discussion

While COVID-19 symptoms are mainly related to the respiratory system, the symptoms and complications in the central and peripheral nervous system including headache are increasingly reported. All the patients in this study applied to the emergency service with complaints of isolated headache. All the three patients had bilateral and severe headache. While two out of the three patients had a headache of migraine phenotype, one patient defined the pain as tension. The two patients did not have any diagnosed disease related to headache before and it was the most severe headache that the two patients had in their life. One patient occasionally had headache and dizziness before. All neurological and sensory examinations were normal in neurology polyclinic check one month earlier; no pathology was found in the examinations. The headache related to COVID-19 is generally found bilaterally (11). Headache like migraine was described with respect to various viral infections in previous studies (12, 13). In a study on 73 cases, it was found that the pain reported by the patients who had migraine previously is mostly considered to be the migraine phenotype during COVID-19 disease (9). Tension type headache was found more commonly in a study on the evaluation of neurological symptoms of the patients admitted to hospital due to COVID-19 (14).

No COVID-19 infection related disease or symptom in systems, including the respiratory system, were found in the follow-up of all the three patients in the study. As being one of the initial symptoms and early manifestation of the disease, headache seems not to be necessarily associated with the disease severity during the progression of the disease including lung involvement and vascular complications (7). Headache prevalence was found 10.9% in the metanalysis involving 21 studies on 6486 patients (15). Incidence of headache was found to be higher in the two studies on evaluation of neurological symptoms in the patients with

COVID-19 (27% (11) and 43% (14)). As the symptoms related to respiratory system come into prominence with the highest hospitalization rate in the studies on COVID-19, the symptoms of headache may be underestimated. All the three patients applied to the hospital with the complaints of headache had higher intensity, rapid course, and resistance to usual analgesic medication. It indicates that the symptoms related to COVID-19 headache are probably related to peripheral infection mechanisms. It is rather improbable to link the isolated and early emergence of headache in the cases applying to hospital with complaints of isolated headache to the indirect effects of the virus by means of the circulating inflammatory mediators causing cytokine storm, viremia, endothelial and vascular invasion, metabolic disorder, or hypoxic damage (7). All the three cases were in good condition in terms COVID-19 infection. This points out the significance of headache for diagnosis of mild COVID-19 cases. Headache can be an isolated symptom of COVID-19 disease. The possibility of COVID-19 infection must be taken into consideration in evaluation of the patients with the complaints of headache, a common reason for the application to hospital.

Conflict of interest

We declare that there is no conflict of interests.

Acknowledgments

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