Trigeminal Neuralgia as the Only Neurological Manifestation of COVID-19: A Rare Case

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ABSTRACT Trigeminal neuralgia is a neuropathic disease characterized by severe pain that reduces the patient’s quality of life. This case report presents a Coronavirus Disease 2019 (COVID-19) positive case whose only neurological symptom is trigeminal neuralgia. A 59-year-old male patient with complaints of weakness, joint pain, cough, and respiratory failure was diagnosed with COVID-19. The patient was started on COVID-19 treatment and quarantined. Severe pain occurred on the right side of the patient’s face on the third day of the onset of COVID-19-related complaints. There was severe pain in the distribution region of the maxillary and mandibular nerves, occurring 10-20 times a day and lasting 1-2 minutes. The patient was diagnosed with trigeminal neuralgia, and carbamazepine was started. Within three days, a significant decrease was observed in the complaint of pain. It should be kept in mind that SARS-CoV-2 may cause trigeminal neuralgia by activating the trigeminal nerve.

Keywords: COVID-19; headache; SARS-CoV-2; trigeminal nerve diseases; trigeminal neuralgia

Trigeminal neuralgia (TN) is a neuropathic disease characterized by severe pain that reduces the patient’s quality of life. It can be seen unilaterally or bilaterally. The maxillary and mandibular branches of the trigeminal nerve are most commonly involved, while the ophthalmic branch may be affected more rarely. The incidence of TN is about 4.5 per 100,000.

Approximately 36% of Coronavirus Disease 2019 (COVID-19) patients have had neurological signs and symptoms. In addition to the symptoms of fever, cough, and respiratory distress, different neurological symptoms such as loss of smell or taste, muscle pain, paralysis, headache, loss of consciousness, dizziness, and seizures can be seen in patients. Headache is reported in approximately 11-34% of hospitalized patients, although few studies characterize pain. Trigeminal and glossopharyngeal neuralgias have been reported rarely in these patients.

We aimed to present a COVID-19-positive case whose only neurological symptom was trigeminal neuralgia.

CASE REPORT

COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020. The first case in Turkey was reported on the same date. About one year after the first case was reported in Turkey, a 59-year-old male patient with no history of systemic disease developed complaints of fatigue, joint pain, mild cough, and respiratory failure. Real-time PCR (Polymerase Chain Reaction) test was performed...
with the preliminary diagnosis of COVID-19 in the patient who did not have any vaccine for COVID-19, and thorax CT imaging was performed. In thorax CT, peripheral ground-glass infiltration was observed in both lungs, interpreted as COVID-19. The PCR test was positive. In line with the guidelines of the Ministry of Health, the patient was started on Favipiravir treatment and quarantined for 14 days. On the third day of the appearance of COVID-19-related complaints, the patient developed very severe facial and headaches. The patient presented to the emergency service with the criticism of very intense and sharp pain (VAS: 9-10) on the right side of his face, in the distribution region of the maxillary and mandibular nerve, which occurs 10-20 times a day on average and lasts for 1-2 minutes. Pain complaints of the patient, who were administered paracetamol, tramadol, and meperidine as analgesics, did not resolve. The patient, who was tachypneic and dyspneic, was admitted to the Intensive Care Unit (ICU).

In her neurological examination, there was short-term paroxysmal pain triggered by eating and talking in the distribution of the trigeminal nerve's maxillary (V2) and mandibular (V3) branches. No autonomic symptoms associated with vesicular lesions or sensory loss were detected in the areas of pain. The laboratory examination, WBC:12.6x10³ µL⁻¹, CRP: 71.8 mg L⁻¹, procalcitonin 1.2 µgL⁻¹, ferritin >2000 ng mL⁻¹ and D-dimer: 106 ug mL⁻¹. No pathology was detected in brain tomography imaging. Due to the typical characteristics, localization, and triggering of pain by specific actions, the patient was diagnosed with TN secondary to COVID-19, and carbamazepine (Tegretol, Novartis, Türkiye) 200 mg 2x1 treatment was started. Three days after starting carbamazepine treatment, the patient's complaints of pain decreased significantly (VAS:2-3). Respiratory failure came to the fore with the decrease in the complaint of pain. The patient, who was followed up in the ICU for 13 days and was treated with high-flow oxygen and non-invasive mechanical ventilation, was transferred to the service. The patient, who was followed up in the inpatient service for six days, had no complaints of TN. It was planned to continue carbamazepine treatment for another 20 days, and the patient was discharged. Carbamazepine was discontinued in the patient who did not have pain in the controls, and there was no recurrence in 1 year.

Written and verbal consent was obtained from the patient for the case report.

**DISCUSSION**

Our patient, who was followed up in quarantine on the third day of complaints of joint pain, cough, and respiratory failure due to COVID-19, developed very severe facial and headaches. There was unbearable pain on the right side of the face, which increased with jaw movements in the distribution region of the maxillary and mandibular nerves. Severe pain, seen 10-20 times daily and observed in short attacks, was evaluated as TN secondary to COVID-19. TN is an episodic chronic pain condition that typically affects the right side of the face in middle-aged and older patients. It may develop without an apparent cause or occur secondary to another pathology. Trigeminal neuropathies accompanied by sensory loss and longer duration of pain, SUNCT (Short lasting Unilateral Neuralgiform headache with Conjunctival injection and Tearing), and SUNA (short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms) should be considered in the differential diagnosis. Our case was also middle-aged and had severe pain in the classical nerve distribution on the right side of the face. Findings in differential diagnosis were not observed.

While the idiopathic subtype is present in half of the patients in the etiology of TN, neurovascular compression of the trigeminal root is present in classical TN. Our patient had no history of trigeminal root compression. It has been reported that the angiotensin-converting enzyme type-2 (ACE-2) located at the trigeminal nerve terminals of SARS-CoV-2 can directly enter the trigeminal and facial nerve by binding to its surface receptors. Thus, it was stated that it may cause TN and facial neuralgia. Another hypothesis is that the hyperinflammatory state associated with COVID-19 causes head and facial pain by activating the trigeminal-vascular system with cytokine storm.

Molina-Gil et al. reported a case of TN in the right-sided V1 distribution on the third day of
COVID-19 infection.\textsuperscript{9} It was emphasized that the patient did not benefit from pregabalin and diazepam treatment, and the pain was relieved by improving the symptoms due to COVID-19. Our case developed TN in right-sided V2 and V3 distribution three days after the onset of symptoms related to COVID-19 and did not respond to classical analgesics.

Bohania et al. reported four cases of cranial neuropathy secondary to COVID-19.\textsuperscript{10} While facial paralysis developed in two patients after COVID-19, TN developed in the V2 and V3 distribution in the other two patients. It has been reported to be successfully treated with carbamazepine. They stated that the pathophysiology of COVID-19-associated cranial neuropathies may be immune-mediated or that SARS-CoV-2 can directly enter the trigeminal and facial nerve via ACE-2 receptors of neuronal and glial cells.

Ricciardi et al. reported four cases of TN secondary to COVID-19 treated with carbamazepine.\textsuperscript{11} The authors emphasized that the hyperinflammatory state associated with COVID-19 may be mainly induced by hypercytokinemia. They also stated that the high level of inflammatory markers such as CRP and D-dimer might indicate the entry of the virus into the central nervous system due to extensive endothelial damage. Another study reported higher D-dimer levels in severe COVID-19 patients with neurological symptoms.\textsuperscript{12} Consistent with the literature, high levels of CRP and D-dimer were also found in our case.

There are also cases of TN seen after the first dose of the Pfizer/BioNtech (USA, EU) vaccine for COVID-19 in the literature.\textsuperscript{13}

In conclusion, it should be kept in mind that TN may be the only neurological manifestation of COVID-19. Although there are various opinions on the pathophysiology of TN secondary to COVID-19, the mechanism still needs to be determined. Carbamazepine is effective in treatment.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

\textbf{Idea/Concept:} Kadir Arslan, Hale Çetin Arslan; \textbf{Design:} Kadir Arslan; \textbf{Control/Supervision:} Kadir Arslan, Hale Çetin Arslan; \textbf{Data Collection and/or Processing:} Kadir Arslan, Hale Çetin Arslan; \textbf{Analysis and/or Interpretation:} Kadir Arslan, Hale Çetin Arslan; \textbf{Literature Review:} Kadir Arslan; \textbf{Writing the Article:} Kadir Arslan; \textbf{Critical Review:} Kadir Arslan, Hale Çetin Arslan.
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