Case Report / Olgu Sunumu
doi: 10.5606/phhb.dergisi.2021.014

Opsoclonus-myoclonus syndrome as a post-infectious complication of COVID-19

COVID-19'un enfeksiyon sonrası bir komplikasyonu olarak opsoklonus myoklonus sendromu

Görkem Tutal Gürsoy, Fadime Erdoğan Küçükdağlı, İrem Sert, Tuğçe Saltoğlu, Yeşim Sücüllü Karadağ

Department of Neurology, Ankara City Hospital, Ankara, Turkey

ABSTRACT

Opsoclonus is the irregular, arrhythmic, and chaotic eye movements in all directions of gaze, and it is frequently accompanied by ataxia, encephalopathy, and myoclonus. Accordingly, the term "opsoclonus-myoclonus syndrome" (OMS) has been introduced. Opsoclonus-myoclonus syndrome is a rare and heterogeneous neurological condition caused by infections, malignancies, toxic and metabolic disorders. Immune mechanisms are associated with OMS. Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease has many neurological manifestations. Opsoclonus-myoclonus syndrome can manifest in consequence of this infectious disease as a parainfectious condition. In this article, we report two cases of OMS developed after SARS-CoV-2 infection.

Keywords: COVID-19, opsoclonus myoclonus, opsoclonus, SARS-CoV-2.

ÖZ

Opsoklonus bakış yönlerinin tümünde görülen irregüler, aritmik ve kaotik göz hareketleridir ve sıklıkla ataksi, ensefalopati ve myoklonus ile birlikte görülür. "Opsoklonus myoklonus sendromu" (OMS) terimi bu nedenle ileri sürülmüştür. Opsoklonus myoklonus sendromu; enfeksiyonlar, maligniteler, toksik ve metabolik bozuklukların neden olduğu nadir ve heterojen bir nörolojik durumdur. İmmün mekanizmalar OMS ile ilişkilendirilmektedir. Koronavirüs hastalığı 2019 (COVID-19)'a şiddetli akut solunum yolu sendromu koronavirüsü 2 (SARS-CoV-2) neden olur ve bu hastalığın birçok belirtisi vardır. Opsoklonus myoklonus sendromu, bu enfeksiyöz hastalığın sonucunda paraenfeksiyöz bir durum olarak ortaya çıkabilir. Bu makalede SARS-CoV-2 enfeksiyonu sonrası OMS gelişen iki olgu sunulmaktadır.

Anahtar Sözcükler: COVID-19, opsoklonus myoklonus, opsoklonus, SARS-CoV-2.

Correspondence: / İletişim adresi: Görkem Tutal Gürsoy, MD. Ankara Şehir Hastanesi, Nöroloji Kliniği, 06800 Çankaya, Ankara, Türkiye.
Tel: +90 538 - 326 17 79 e-mail *(e-posta):* gorkemtutal@gmail.com

Received / *Geliş tarihi:* December 08, 2021 Accepted: / *Kabul tarihi:* December 13, 2021

Citation:
Tutal Gürsoy G, Erdoğan Küçükdağlı F, Sert İ, Saltoğlu T, Sücüllü Karadağ Y. Opsoclonus-myoclonus syndrome as a post-infectious complication of coronavirus disease 2019. Parkinson Hast Harek Boz Derg 2021;24(1-2):5-8.

Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disease. The distinguishing feature of the disease is involuntary, arrhythmic multidirectional saccades and accompanying myoclonic jerks in the limbs and trunk. Often, cerebellar ataxia, tremor and encephalopathy coexist.[1] Opsoclonus-myoclonus syndrome is a rare and heterogeneous neurological condition caused by infections, malignancies, toxic and metabolic disorders. Humoral and cell-mediated immune mechanisms are both associated with OMS.[2] Immunopathogenesis is still poorly understood; however, neuronal surface antigens have been associated with OMS, and as a neuroinflammatory disorder, one could expect to see OMS after coronavirus disease 2019 (COVID-19) infection on a pandemic scale.[2] In this paper, we report two cases of opsoclonus myoclonus syndrome, presumably parainfectious in nature.

CASE REPORT

Case 1- A 59-year-old male was admitted to the emergency department with fever, cough, mild dyspnea, and anosmia. There was no leukocytosis or lymphopenia, and the sedimentation rate was mildly elevated. The chest computed tomography (CT) showed a multifocal ground-glass pattern compatible with COVID-19 pneumonia. The patient's nasopharyngeal swab test was positive for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by qualitative real-time reverse transcriptase-polymerase chain reaction assay. Favipiravir and hydroxychloroquine were started for treatment. On the fifth day of the treatment, the patient's speech worsened, and dizziness manifested. Two days later, the patient developed truncal ataxia and jerky movements in his face and limbs, mild somnolence, and abnormal eye movements called opsoclonus. Facial muscles, the trapezius muscle, and muscles of the upper and lower extremities were predominantly involved, and the findings were worsened with voluntary movements and augmented with action. They were stimulus sensitive and were treated with levetiracetam 500 mg bid. The patient's extraocular movements were jerky oscillatory movements in all directions. The patient was disoriented. There was no motor or sensory deficit, and the muscle tone, deep tendon reflexes, and plantar responses were normal. Brain magnetic resonance imaging and electroencephalogram were unremarkable. The cerebrospinal fluid (CSF) analysis revealed normal cell count, glucose, and protein, but the SARS-CoV-2 immunoglobulin (Ig)G and IgM index was higher than 10 (reference 0-0.99). Autoimmune and paraneoplastic antineuronal antibodies were negative. As the myoclonus was presumed an immune-mediated manifestation of the inflammatory phase of COVID-19, a 2 g/kg total dose of intravenous immunoglobulin and 2 mg/kg oral methylprednisolone treatment with dose tapering was started. After the treatment, the patient appeared to slightly improve as he could walk without support. The patient's eye movements and ataxia significantly improved three weeks after treatment. Levetiracetam was discontinued four weeks after treatment, and there were no further abnormal movements.

Case 2- A 66-year-old man with a history of hypertension was admitted to the hospital with a cough and fever. The patient's nasopharyngeal swab test was positive for SARS-CoV-2, and the chest CT scan confirmed COVID-19 pneumonia. On the 10th day, the patient's symptoms progressed, and the patient was transferred to the intensive care unit due to acute respiratory distress syndrome related to COVID-19. On the 14th day of the hospitalization, the patient's speech became incomprehensible and dysarthric, and his mental state was altered. Examination of eye movements revealed horizontal saccadic intrusions and transient ocular flutters. The patient developed facial jerks and generalized myoclonic jerks of the limbs. Myoclonic jerks were present in both rest and motion states, and they worsened with action. The myoclonus of the limbs was sensitive to touch and a loud acoustic stimulus. Finger-to-nose and heel-to-shin tests showed evidence of cerebellar pathology. There were no motor and sensory abnormalities, and deep tendon reflexes were normal. An extensive laboratory workup revealed elevated acute phase reactants. Magnetic resonance imaging and CSF analysis

revealed no abnormalities. The paraneoplastic panel on both CSF and blood were in the normal range. We administered 1000 mg/day intravenous methylprednisolone for three days and started 1.5 mg/kg oral methylprednisolone treatment with dose tapering. The steroid dose was tapered at 8 mg per week. After the one-month follow-up, neurological symptoms started to improve. The patient could stand up from the chair and walk without support. Myoclonic jerks had almost disappeared. The patient's ataxia was improved, but his speech was mildly dysarthric.

DISCUSSION

Coronavirus disease 2019 is a multi-organ viral infection associated with various aspects of neurological complications.[2] Severe acute respiratory syndrome coronavirus 2 binds to angiotensin-converting enzyme 2 (ACE2) receptors of airway epithelia, vascular endothelia, kidney cells, and small intestine cells. Although the virus's main target is the pulmonary system, it has been known to have diverse neurological complications among adult patients. The virus enters the brain via a hematogenous route by infected leukocytes or the olfactory system by the endothelial ACE2 receptors of the cerebral vessels.[3] Alteration of mental state, agitation, delirium, coma, headache, anosmia, ageusia, acute disseminated encephalopathies, acute necrotizing encephalopathies, ataxia, myalgia, and fatigue are among reported symptoms. Apart from the cytokine storm and hypercoagulable state, many parainfectious autoimmune complications such as Guillain-Barre syndrome have also been reported. Since OMS is a neuro-inflammatory disorder, one could expect it to manifest after this infection.

We reported two patients with OMS infected with SARS-CoV-2. Opsoclonus-myoclonus syndrome is characterized by the combination of opsoclonus and arrhythmic-action myoclonus, and these symptoms are usually accompanied by axial ataxia.[2] Although the two most common causes of OMS are paraneoplastic and idiopathic, infections, toxic and metabolic disorders are also responsible.[4] In a series of 114 patients by Armangue et al.,[2] 39% of the OMS cases were paraneoplastic, and 61% were of idiopathic origin. One of the largest series of OMS established that after toxic, metabolic, and structural causes of OMS are ruled out, the most important indicator of paraneoplastic OMS is the patient's age.[2] Ovarian teratoma and lung, breast, and gynecological cancers can be all responsible for OMS. Suspicions of these tumors lead to clinicians using extensive panels of paraneoplastic antibodies. In younger adults, particularly those younger than 40 years, the more likely cause of OMS is idiopathic or parainfectious. Influenza, varicella, human herpesvirus 6, human immunodeficiency virus, enteroviruses, Epstein-Barr virus, cytomegalovirus, coxsackievirus, West Nile virus, *Borrelia, Salmonella, Mycoplasma pneumoniae*, and post-streptococcal syndrome are reported to be related to OMS. Saini et al.[5] reported that post-infectious opsoclonus is frequently seen in older individuals without a history of paraneoplastic OMS. Similarly, Guillain-Barre syndrome, also an immune-mediated neurological condition, was reported following a COVID-19 infection. The spike protein of SARS-CoV-2 has been hypothesized to be a trigger for autoimmune disorders.[6] First-line immunotherapies, such as intravenous immunoglobulin, steroids, or plasma exchange, are associated with a good outcome. Symptomatic therapies can also be utilized for myoclonic jerks.

Both of our patients displayed opsoclonus, generalized action myoclonus, and ataxia after a SARS-CoV-2 infection. The first patient had no relevant disease except COVID-19, and the neurological symptoms began with the cytokine storm. Autoimmune antibodies were all negative in the plasma and CSF. The main clue for SARS-CoV-2 related OMS is the positive SARS-CoV-2 IgG and IgM antibody index in the CSF (>10, reference 0-0.99). Although CSF analysis would be ideal for the patients, we could not find any data on positive CSF tested SARS-CoV-2 in the literature. The second patient also had cerebellar signs accompanying OMS. Both patients were administered immunotherapies with symptomatic treatment,

and the outcomes were excellent. The clinical profile of our patients' OMS suggests an immune-mediated pathogenesis.

In conclusion, OMS is the manifestation of various disorders and is one of the significant neurological conditions observed after COVID-19.[6] Immun-mediated syndromes are treatable if recognized. Further research will contribute to identifying immunological mechanisms in OMS, increasing our knowledge on the prevalence of neurological symptoms in patients with COVID-19, and clarifying the relationship between SARS-CoV-2 infection and the post-COVID-19 myoclonic syndrome.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Wong AM, Musallam S, Tomlinson RD, Shannon P, Sharpe JA. Opsoclonus in three dimensions: oculographic, neuropathologic and modelling correlates. J Neurol Sci 2001;189:71-81.
2. Armangué T, Sabater L, Torres-Vega E, Martínez-Hernández E, Ariño H, Petit-Pedrol M, et al. Clinical and immunological features of opsoclonus-myoclonus syndrome in the era of neuronal cell surface antibodies. JAMA Neurol 2016;73:417-24.
3. Brouwer MC, Ascione T, Pagliano P. Neurologic aspects of covid-19: A concise review. Infez Med 2020;28(suppl 1):42-5.
4. Klaas JP, Ahlskog JE, Pittock SJ, Matsumoto JY, Aksamit AJ, Bartleson JD, et al. Adult-onset opsoclonus-myoclonus syndrome. Arch Neurol 2012;69:1598-607.
5. Saini L, Dhawan SR, Madaan P, Suthar R, Saini AG, Sahu JK, et al. Infection-associated opsoclonus: A retrospective case record analysis and review of literature. J Child Neurol 2020;35:480-4.
6. Wiegand SE, Mitchell WG, Santoro JD. Immunotherapy responsive SARS-CoV-2 infection exacerbating opsoclonus myoclonus syndrome. Mult Scler Relat Disord 2021;50:102855.