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COVID-19 Patient with Encephalitis as an Initial Clinical Presentation

İlk Klinik Prezentasyonu Ensefalit Olan COVID-19 Olgusu

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ABSTRACT

A growing number of extrapulmonary manifestations were described during COVID-19 pandemic. COVID-19 has both acute and long-term neurological complications affecting the central and peripheral nervous system. While acute encephalopathy was the most common clinically diagnosed neurological sign, the least common were meningitis and/or encephalitis. The patient was a 68-year-old previously healthy man who presented to the emergency department with symptoms of fever, headache, confusion, meaningless speech, and behavioral disorders. We present a COVID-19 patient with encephalitis as an initial clinical presentation who was treated with dexamethasone, IVIG and tocilizumab with a rapid neurological improvement. This report highlights COVID-19 encephalitis which is a rare form of the neurological involvement of COVID-19 and discusses diagnostic and therapeutic approaches.

Key Words: *COVID-19; Neurological complications; Encephalitis*

ÖZ

İlk Klinik Prezentasyonu Ensefalit Olan COVID-19 Olgusu

COVID-19 pandemisi süresince giderek artan sayıda akciğer dışı tutulumlar tanımlanmaktadır. COVID-19'un santral ve periferik sinir sistemini etkilenmesi sonucunda akut ve uzun dönem nörolojik komplikasyonlar gelişebilir. Akut ensefalopati en sık tanı koyulan klinik nörolojik bulgu iken, en nadir görülen, menenjit ve/veya ensefalittir. Altmış sekiz yaşında ek hastalığı olmayan erkek hasta; ateş, baş ağrısı, konfüzyon, anlamsız konuşma ve davranış değişiklikleri ile acil servise başvurmuştur. Deksametazon, intravenöz immünoglobulin (IVIG) ve tosilizumab ile tedavi edilen ve bu tedaviler ile hızlı nörolojik düzelme sağlanan, başlangıç klinik prezentasyonu COVID-19 ilişkili ensefalit olarak değerlendirilen bir vaka sunulmaktadır. Bu çalışmada COVID-19'un nadir nörolojik tutulumu olan COVID-19 ensefaliti ile tanısal ve terapötik yaklaşımlara dikkat çekilmiştir.

Anahtar Kelimeler: *COVID-19; Nörolojik komplikasyonlar; Ensefalit*

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INTRODUCTION

Typical manifestations of the coronavirus disease-2019 (COVID-19) include fever, cough, dyspnea, and fatigue[1,2]. Although respiratory symptoms were the hallmark of the disease, a growing number of extrapulmonary manifestations were described as the disease became a pandemic[3]. In a multi-cohort study, headache (38%) and anosmia/ageusia (28%) were the predominant self-reported symptoms whereas acute encephalopathy (50%) was the most common clinically diagnosed neurological sign followed by coma (17%). The least common neurological signs were meningitis and/or encephalitis (0.1%)[4]. Here, we present a COVID-19 patient with encephalitis as an initial clinical presentation.

CASE REPORT

A 68-year-old, previously healthy man was admitted to the emergency department with fever, headache, confusion, meaningless speech and behavioral disorders such as trying to eat soup with a fork or eat napkin for three days. He had two doses of inactivated COVID-19 vaccine, and he developed symptoms five months after the second dose. At admission, he did not have the usual COVID-19 symptoms. His temperature was 38ºC, pulse rate was 92 beats/min, blood pressure was 102/68 mmHg, and oxygen saturation was 90% on room air. Neurological examination revealed altered consciousness, limited orientation, and cooperation. Mild ataxic gait was observed. Meningeal irritation signs (including nuchal rigidity, Kernig sign and Brudzinski sign) were present. Laboratory tests revealed leukopenia [$2.97x10^9$/L, (4.5-11)], neutropenia [$1.36x10^9$/L, (1.8-7.7)], lymphopenia [$1.18x10^9$/L, (1.5-4)], thrombocytopenia [$135x10^9$/L (150-400)] and increased C-reactive peptide (CRP) [50.9 mg/L, (0-5)]. Biochemical parameters were normal. The chest tomography (CT) showed bilateral, peripherally and peribronchovascular ground glass opacities (Figure 1). Contrast enhanced cerebral diffusion weighted magnetic resonance imaging (MRI) revealed irregular lining of the lateral ventricles, bilaterally symmetrical hyperintensity in the periatrial and white matter of parietal lobes. (Figure 2). Ceftriaxone (2x2 gr IV), ampicillin (6x2 gr IV), acyclovir (3x10 mg/kg IV) treatment was started after lumbar puncture was performed

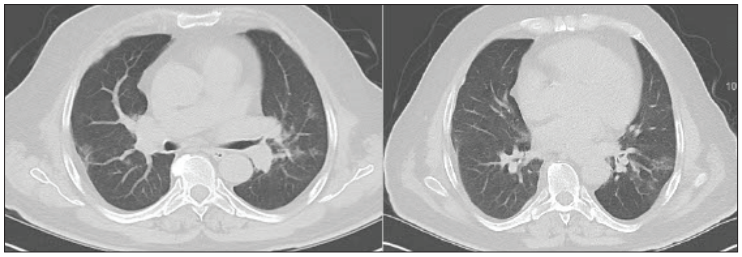


Figure 1. The chest CT imaging showing bilateral, peripheral and peribronchovascular ground glass opacities.

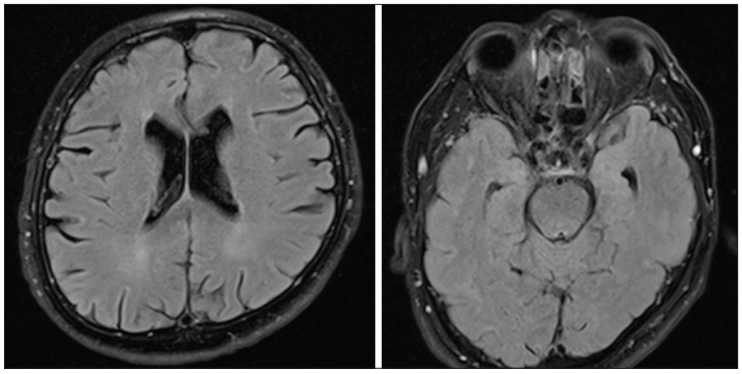


Figure 2. The brain MRI of the patient showing irregular lining of the lateral ventricles and hyperintensity in the parietal lobes.

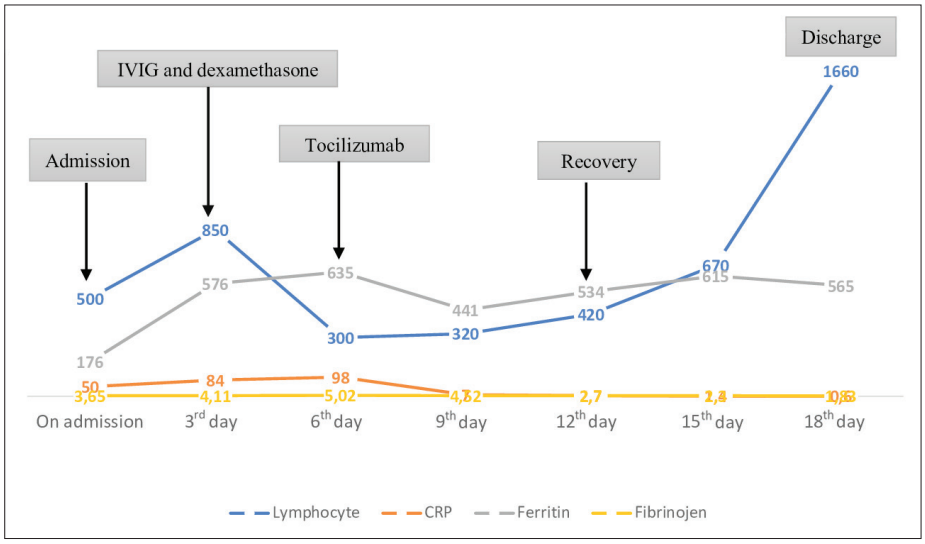


Figure 3. Levels of inflammatory parameters of the patient during hospitalization.

on the patient with suspected central nervous system infection based on clinical presentation. Nasopharyngeal swab on admission was positive for the delta variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Favipiravir, acetylsalicylic acid, prophylactic enoxaparin sodium were added to the treatment. Cerebrospinal fluid (CSF) examination was clear with a leukocyte count of 25/mm^3, predominantly lymphocytes. The glucose level in the CSF was 60 mg/dL (simultaneous blood glucose was 113 mg/dL), and the protein level was 15.2 mg/dL. No growth was detected on CSF culture plates and the multiplex PCR for microbial detection in CSF was negative. SARS-CoV-2 PCR of the CSF specimen was negative. He was transferred to the intensive care unit (ICU) due to deterioration of neurological and respiratory symptoms. His oxygen saturation was 86% on room air supported with 5 L/min oxygen mask; he had progression of confusion, cognitive fluctuation, and positive Kernig's and Brudzinski's signs were detected on the 3rd day of hospitalization. Serum inflammatory markers also progressed (Figure 3). Since he did not have any laboratory evidence of bacterial or other viral central nervous system (CNS) infections ceftriaxone, ampicillin, and acyclovir were stopped on the 4th day of the treatment and he was started high dose dexamethasone (12 mg/day) and intravenous immunoglobulin (IVIG-0.4 gr/kg/day) with the diagnosis of COVID-19-associated encephalitis. Three days later, his neurological examination was partially improved, but his oxygen requirement increased to 8 L/min with oxygen mask, and tocilizumab (400 mg) was added to therapy. The patient showed dramatic neurological and respiratory improvement and was discharged to ward on the 10th day of ICU. Laboratory parameters were also improved. The patient no longer needed oxygen and was discharged with recovery on the 17th day of hospitalization. He was SARS-CoV-2 PCR (-) after four weeks of his first positive test without any neurological deficits.

DISCUSSION

COVID-19 has both acute and long-term neurological complications affecting the central and peripheral nervous system. The mechanism of these manifestations is not clearly understood. Some evidence supports direct viral invasion since angiotensin converting enzyme 2 (ACE2) receptors are expressed in brain tissue and postmortem examinations in patients with neurological manifestations revealed SARS-CoV-2 in brain tissue. Some other reports suggest that hyperactivation of immune system or molecular mimicry with autoantibodies might be the reason for some of the neurological manifestations[5,6].

Our patient was a severe COVID-19 case requiring intensive care support without mechanical ventilation. He presented with neurological symptoms suggesting encephalitis on admission, and later developed respiratory failure. He was a probable COVID-19 encephalitis case since SARS-CoV-2 PCR was positive in respiratory samples with compatible radiological abnormalities and no other explanatory pathogen was found[5]. In the CSF sample, there was mild pleocytosis, whereas other viral and bacteriological screenings and SARS-CoV-2 PCR were negative. EEG could not be performed. The absence of SARS-CoV-2 positivity in CSF does not exclude viral invasion. Also encephalitis cases with SARS- CoV-2 PCR positivity in the CSF are rare in the literature[7].

In a meta-analysis of 138 encephalitis patients, the time from the COVID-19 diagnosis to the development of encephalitis was reported as 14.5 days on average[8]. Our patient initially presented with predominating encephalitis features, but respiratory involvement, manifested by decreased oxygen saturation and ground glass opacities on chest CT, was also present. In the ENCOVID multicenter study, there were 20 COVID-19 cases with concomitant encephalitis with respiratory infection, similar to our patient. Almost half of the patients with COVID-19-associated encephalitis had normal MRI findings while some of them had cortical and subcortical hyperintensities[7]. Cerebral MRI findings of COVID-19 encephalitis are heterogenous; diffuse hyperintensities in white matter could be detected. This patient's cerebral MRI revealed hyperintensity in the parietal lobes.

The treatment modalities of COVID-19 encephalitis are still being studied. Intravenous steroids, IVIG, monoclonal antibodies, plasmapheresis have been tried in different case reports and yielded positive patient outcomes. We used dexamethasone, IVIG and tocilizumab which led to rapid neurological and respiratory improvement in our patient.

This report highlights COVID-19 encephalitis, which is a rare form of the neurological involvement of COVID-19, and discusses diagnostic and therapeutic approaches. During the pandemic, it is crucial to consider SARS-CoV-2 infection in the differential diagnosis when patients present with neurological manifestations. This consideration helps to avoid delays or misdiagnosis and ensures appropriate management and timely intervention.

CONFLICT of INTEREST

No conflict of interest declared.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: All of authors

Analysis/Interpretation: All of authors

Data Collection or Processing: All of authors

Writing: EMS, FY

Review and Correction: All of authors

Final Approval: All of authors

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