Post-acute COVID-19 syndrome: Prolonged effort intolerance after SARS-CoV-2 infection

Murat Duyan  
Antalya Egitim ve Arastirma Hastanesi

Ahmet Serbülent Savcıoğlu  
Antalya Egitim ve Arastirma Hastanesi

Ibrahim Ulas Ozturan (✉️ ozturan.iu@gmail.com)  
Mersin Toros State Hospital  https://orcid.org/0000-0002-1364-5292

Case Report

Keywords: SARS-CoV-2, COVID-19, post-acute COVID-19 syndrome

DOI: https://doi.org/10.21203/rs.3.rs-415122/v1

License: ☐ ️ This work is licensed under a Creative Commons Attribution 4.0 International License.  
Read Full License
Abstract

Many new complications have been arising after being infected with SARS-CoV-2. Post-acute COVID-19 syndrome is a new definition for patients with persistent symptoms and prolonged complications beyond 4 weeks of acute COVID-19. In this report, we present two cases of prolonged dyspnea and reduced effort capacity for 4 and 5 months, respectively. A 29-year-old male and 40-year-old female patients, found to be positive in rRT-PCR tests for SARS-CoV-2, had recurrent admission to the emergency department after having treated for COVID-19. Both of the patients were followed for 6 months. Although all potential cardiovascular, pulmonary and other system pathologies were ruled out, the prolonged dyspnea and reduced effort capacity started to improve after 4 months in the female and 5 months in the male patients. The patients were diagnosed with post-acute COVID-19 syndrome. It should be kept in mind that the post-acute COVID-19 syndrome may be a complication in patients with persistent symptoms after COVID-19.

Introduction

Since the beginning of the COVID-19 pandemic, many symptoms and complications have been reported to be associated with SARS-CoV-2 infection. Although most of the acute symptoms include fever (82%), cough (57%), fatigue (37%), and dyspnea (35%) [1], prolonged or delayed symptoms related to neurodegenerative or neuropsychiatric disorders have also been reported [2, 3].

Although the pulmonary and cardiovascular systems are among the most frequently affected systems in the COVID-19, it has been defined as a multi-organ disease with various manifestations [4]. Pulmonary signs or symptoms including cough, dyspnea, hypoxia or ground glass opacities in radiological studies are predominant findings in patients with pneumonia associated with COVID-19 [5]. Acute myocardial damage, myocarditis, pericarditis or heart failure are also reported disorders in COVID-19 patients with cardiovascular involvements [6].

Reduced effort capacity and dyspnea are common symptoms in COVID-19 patients with acute pulmonary and cardiovascular involvement. [7]. The reason of these symptoms can easily be detected with laboratory or radiology studies, and treatment can be planned according to underlying pathology. However, in some cases, even if the patients have had mild COVID-19, the symptoms such as exertional dyspnea and fatigue can continue for a long time after acute COVID-19 period [8].

The post-acute COVID-19 syndrome is a newly adopted definition which was described as prolonged or delayed symptoms or complications that are seen after 4 weeks of acute infection [4]. In this article, we report two cases of post-acute COVID-19 syndrome that were presented prolonged dyspnea and reduced effort capacity for 4 and 5 months.

Case Presentation
**Case 1:** Twenty-nine years old male patient who admitted to the emergency department (ED) with progressive fatigue, generalized muscle pain, decreased smell and taste sensation for 5 days. The patient had no remarkable past medical history. He had normal vital signs and physical exam revealed hyperemia in pharynx. The rRT-PCR tests taken from the nasopharyngeal swab were found to be positive for SARS-CoV2. Other laboratory tests results were within normal range. Electrocardiography (ECG) showed a normal sinus rhythm. No pneumonia was detected in the computerized tomography (CT) of the chest. Favipravir was administered orally with a loading dose of 1600 mg twice a day on day 1 and then 600 mg twice a day for another 4 days. The patients readmitted to the ED with dyspnea and decreased effort capacity after a month of the initial admission. He had a normal vital sign, laboratory tests and chest x-ray (CXR). The rRT-PCR test was negative. ECG and transthoracic echocardiography (TTE) showed no abnormal findings. Pulmonary embolism was excluded with a pulmonary CT-angiography. The patient was not be able to complete treadmill stress test due to increased shortness of breath and palpitation. Cardiac rhythm was sinus tachycardia. The patient was followed up monthly for 5 more months. Dyspnea and effort intolerance were gradually improved spontaneously in the fourth month and completely resolved in the fifth month of initial diagnosis.

**Case 2**

Forty-year-old female patient admitted to the ED with a history of fever, and fatigue for 3 days. The patient has no remarkable past medical history. Vital signs were normal except a temperature of 37.7 °C and heart rate of 105 beat per minute. Physical exam showed no abnormal findings except a regular tachycardia. ECG showed a sinus tachycardia. Laboratory tests showed a C-reactive protein of 14 mg/L (ref < 5 mg/L), for the rest were within normal limits. There was not a pneumonia in the CT of the chest. The rRT-PCR tests taken from the nasopharyngeal swab were found to be positive for SARS-CoV2. Favipravir was administered orally with a loading dose of 1600 mg twice a day on day 1 and then 600 mg twice a day for another 4 days for COVID-19. The patient readmitted to the ED with dyspnea and palpitation on minimal exertion after 3 weeks of initial admission. Vital signs and physical exam findings were normal. ECG showed a normal sinus rhythm. There were no abnormal findings in the laboratory tests including high-sensitive troponin, NT-pro-BNP and d-dimer. CXR was also normal. The patient was referred to the cardiology department for a further evaluation. TTE showed no abnormality, the patients became symptomatic again during the treadmill test. The patient was followed up monthly for 4 more months. Dyspnea and effort intolerance were gradually improved spontaneously in the fourth month of initial diagnosis.

**Discussion**

In this report, we presented two cases of post-acute COVID-19 syndrome that the symptoms prolonged for months after having mild COVID-19. In the studies that evaluated post-infection period of COVID-19, it was reported that the symptoms, especially weakness and dyspnea may continue for up to 3 months after COVID-19 [8–10]. However, in these studies, prolonged symptoms have been found to be related cardiac and pulmonary involvement of COVID-19 [9]. Conversely, none of the cardiac or pulmonary
involvement of COVID-19 could be detected in both of our cases. Moreover, symptoms had started to improve after 4 months of initial diagnosis. In another study, it was also showed that the symptoms, mostly fatigue and dyspnea, can continue after the COVID-19 infection with a mean duration of 79 days [8]. Although the severity of illness was not reported in the study, the duration of symptoms in our cases were longer than the average despite having a mild disease.

After some viral infections, it is known that a clinical course defined as chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) develops with prolonged fatigue symptoms. A similar one is the SARS infection caused by SARS-associated coronavirus that caused an epidemic in the past [11]. After the 2002 Canadian SARS epidemic, fatigue, muscle weakness and sleep disturbances were observed in patients for up to 3 years [11]. Similarly, the current pandemic can cause long-term post-viral symptoms with a similar pathogenesis. Some patients recovering from acute COVID-19 infection may experience long-term fatigue, generalized myalgia, and sleep disturbance [8–10]. These findings were also attributed to the post-exertional neuroimmune exhaustion [12].

It is foreseeable that the long-term complications of COVID-19 will be more prevalent in the near future. The diagnosis of post-acute COVID-19 syndrome can be common once the healthcare systems recognize and adopt the arising long-term effects of the COVID-19. However, the diagnosis of post-acute COVID-19 syndrome should only be made after ruling out many other life-threatening disorders.

**Conclusion**

The diagnosis of post-acute COVID-19 syndrome should be considered in patients with prolonged systemic symptoms beyond 4 weeks of acute COVID-19. Dyspnea and reduced effort capacity may prolong for months. However, the definitive diagnosis should only be made after the other complications were excluded.

**Declarations**

**Funding:** There was no funding to support this report.

**Conflicts of interest/Competing interests:** The authors have no commercial associations or sources of support that might pose a conflict of interest.

**Ethics approval:** IRB waived.

**Consent to participate:** Not applicable.

**Consent for publication:** Informed consent was obtained from the patients for this case report.

**Availability of data and material:** Not applicable.

**Code availability:** Not applicable.
Authors’ contributions: MD and ASS were the treating physicians. MD and ASS collected the data. MD, ASS and IUO conceptualized the report. IUO drafted manuscript. MD, ASS and IUO critically reviewed the manuscript. All of the authors approved the final version.

References

1. Hatmi, Z.N. A Systematic Review of Systematic Reviews on the COVID-19 Pandemic. *SN Compr. Clin. Med.* 2021; 3, 419–436. https://doi.org/10.1007/s42399-021-00749-y
2. Duyan, M., Ozturan, I.U. & Altas, M. Delayed Parosmia Following SARS-CoV-2 Infection: a Rare Late Complication of COVID-19. *SN Compr. Clin. Med.* (2021), ahead of print. DOI: https://doi.org/10.1007/s42399-021-00876-6
3. de Francisco Moure, J., Torres Ramón, I. & Almárcegui Lafita, C. Acute Polyneuropathy in an Outpatient Context During the SARS-CoV-2 Pandemic: A Brief Case Serie Report. *SN Compr. Clin. Med.* (2021), ahead of print. DOI: https://doi.org/10.1007/s42399-021-00855-x
4. Nalbandian, A., Sehgal, K., Gupta, A. *et al.* Post-acute COVID-19 syndrome. *Nat Med* (2021), ahead of print. DOI: https://doi.org/10.1038/s41591-021-01283-z
5. Bentivegna, E., Luciani, M., Spuntarelli, V. *et al.* Extremely Severe Case of COVID-19 Pneumonia Recovered Despite Bad Prognostic Indicators: a Didactic Report. *SN Compr. Clin. Med.* 2020; 2, 1204–1207. DOI: https://doi.org/10.1007/s42399-020-00383-0
6. Özturan, IU., Köse B., Özkân B., et al. Myopericarditis caused by severe acute respiratory syndrome coronavirus 2. *Clin Exp Emerg Med.* 2020;7(4), 326-329. DOI: https://doi.org/10.15441/ceem.20.109
7. Johnson KD, Harris C, Cain JK, Hummer C, Goyal H, Perisetti A. Pulmonary and Extra-Pulmonary Clinical Manifestations of COVID-19. *Front Med (Lausanne).* 2020;7, 526. DOI: https://doi.org/10.3389/fmed.2020.00526
8. Goërtz YMJ, Van Herck M, Delbressine JM, et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? *ERJ Open Res.* 2020; 6(4), 00542-2020. DOI: https://doi.org/10.1183/23120541.00542-2020
9. Carfì A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA.* 2020;Aug 11;324(6):603-605. DOI: https://doi.org/10.1001/jama.2020.12603
10. Halpin, SJ,Mclvor, C, Whyatt, G, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. *J Med Virol.* (2020); ahead of print. DOI: https://doi.org/10.1002/jmv.26368
11. Moldofsky H, Patcai J. Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC Neurol.* 2011;11:37. DOI: https://doi.org/10.1186/1471-2377-11-37
12. Perrin R, Riste L, Hann M, Walther A, Mukherjee A, Heald A. Into the looking glass: Post-viral syndrome post COVID-19. *Med Hypotheses.* 2020;144:110055. DOI:
