Received: 30 March 2021 | Revised: 16 December 2021 | Accepted: 19 December 2021

DOI: 10.1002/mus.27482

CLINICAL RESEARCH SHORT REPORT

MUSCLE&NERVE WILEY

COVID-19 infection in patients with late-onset Pompe disease

Jennifer Avelar | Marie Wencel BS | Anastasia Chumakova MD | Tahseen Mozaffar MD, FAAN

Department of Neurology, University of California Irvine, Orange, California, USA

Correspondence
Tahseen Mozaffar, Department of Neurology, University of California Irvine, 200 South Manchester Avenue, Ste. 206, Orange, CA 92868.
Email: mozaffar@hs.uci.edu

Abstract

Introduction/Aims: Severe acute respiratory syndrome coronavirus-2 2019 (SARS-CoV2/COVID-19) is frequently more severe in individuals with pre-existing respiratory and cardiovascular conditions. The impact on patients with neuromuscular disorders is of concern, but remains largely unknown. Late-onset Pompe disease (LOPD) is a lysosomal-storage disorder characterized by progressive skeletal and respiratory muscle degeneration. Mortality is typically caused by respiratory failure. We examined the impact of COVID-19 on these patients.

Methods: This is a case series of four patients with LOPD who contracted COVID-19.

Results: All patients had a mild/moderate illness from COVID-19 and did not require hospitalization. Neurological worsening occurred in one, with no change in physical ability in the other three, and respiratory symptoms remained stable in all four.

Discussion: COVID-19 infection can result in a benign course in some patients with LOPD. However, individuals with LOPD remain at high risk and should receive COVID-19 vaccinations and exercise precautions to avoid exposure to COVID-19 infection.

KEYWORDS
COVID-19, fatigue, late-onset Pompe disease, pulmonary disease, SARS-CoV2

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 2019 (SARS-CoV2/COVID-19) is a virus responsible for the 2020 COVID-19 global pandemic.[1] The pandemic has lasted for nearly 2 years and has accounted for 269 million cases and 5.3 million deaths worldwide.[2] In the United States to date there have been 49.8 million cases and 796 349 deaths related to COVID-19, with a case-to-fatality ratio of 1.6%.[2] Symptoms are variable and can range from mild to severe. Hospitalization rates are very high for subjects with pre-existing medical illnesses, those who are immunocompromised, and those who are unvaccinated for the COVID virus. Due to the frequent impact of COVID the respiratory system, individuals with pre-existing respiratory and cardiovascular conditions frequently have more severe disease. The effect of COVID-19 on patients with neuromuscular disorders is of concern, but remains largely unknown.[3] We present a small series of individuals with genetically confirmed late-onset Pompe disease (LOPD), a lysosomal-storage disorder characterized by progressive skeletal and respiratory muscle degeneration, who contracted COVID-19. Pompe disease is caused by a deficiency of acid alpha-glucosidase, which results in the build-up of glycogen in the lysosomes. It is treated with enzyme replacement therapy.[4] LOPD results in significant disability, with most of the disability driven by progressive motor weakness and respiratory insufficiency. Because morbidity and mortality in LOPD are primarily driven by respiratory involvment,[5] we examined the impact of COVID-19 on these patients.

Abbreviations: FVC_e, erect forced vital capacity; LOPD, late-onset Pompe disease; SARS-CoV2/COVID-19, severe acute respiratory syndrome coronavirus-2 2019.

2 | CASE REPORTS

Details on each of the patients are presented in Tables 1 and 2. All patients were white males ranging in age from 37 to 71 years. All were genetically confirmed to have LOPD, with one allele carrying the common "Caucasian" leaky splice donor mutation and a second more aggressive mutation.

TABLE 1 Patients' demographics, genetics, and baseline clinical status

Patient	Age (years)	Sex	Mutation	Use of NIV	Pre-COVID status
1	42	Male	c.-32-13T>G, c.1548G>A	Nightly	Diagnosed with Pompe 4 years earlier and started ERT 2 years earlier; mild axial and limb-girdle weakness, lordosis, and diaphragmatic insufficiency. No assistive devices used.
2	71	Male	c.32-13T>G, c.1951_1952delGGinSt	Nightly	Disease duration 20^{+} years, marked lordosis, axial muscle weakness, hip- > shoulder-girdle muscle weakness, and diaphragmatic insufficiency. Two walking sticks. ERT from 2006 to 2020 was discontinued 6 months after AAV-8 gene therapy. Immunosuppression until 12 months before COVID-19.
3	52	Male	c.32-13T>G, c.1781G>C	Nightly	Disease duration of 5 years; rigid spine and hip- > shoulder-girdle muscle weakness, lordosis, bilateral scapular winging, and diaphragmatic insufficiency; no assistive devices; on ERT. Currently in screening process for AAV-8 gene therapy.
4	37	Male	c.-32-13T>G, c.258dupC	Nightly	Disease duration of 6 years; on ERT for 5 years; axial muscle weakness and hip- > shoulder-girdle muscle weakness, with lordosis and diaphragmatic insufficiency; no assistive devices used. Currently in experimental drug trial for LOPD.

Abbreviations: AAV-8, adeno-associated virus serotype 8; ERT, enzyme replacement therapy; LOPD, late-onset Pompe disease.

TABLE 2 Patients' COVID-19 symptoms, assessments, treatments, and outcomes

Patient	COVID-19 symptoms	Duration (days)	FVC before COVID-19	FVC after COVID-19	O_2 saturation	Treatment	Follow-up	Outcome
1	Myalgia, fever, and mild dyspnea; patchy opacities on chest X ray; no loss of smell or taste	15	1.98 L (47%) sitting, 1.74 L (41%) supine	2.95 L (56%) sitting, 2.30 (43%) supine	88%-90%	Dexamethasone 6 mg/d for 10 d	3 mo	No ongoing COVID-19 symptoms
2	Coughing, congestion, fatigue, diarrhea, loss of appetite, and 10-lb weight loss; no fever or shortness of breath	16	3.25 L (77%) sitting, 2.26 L (53%) supine	3.36 L (78%) sitting	>94%	Acetaminophen as needed	3 mo	Pompe-related fatigue and general weakness worse
3	Chills, mild fever, body aches, and loss of smell	6	4.45 L (86%) sitting, 4.24 L (82%) supine	4.44 L (85%) sitting, 4.24 L (81%) supine	>94%	Acetaminophen, 325 mg every 6 h for 2 d	3 mo	No ongoing COVID-19 symptoms
4	Nasal congestion, hip pain myalgia, fatigue, diminished taste and smell, mild hallucinations, tactile hyperesthesia. Infiltrates on chest CT	6	4.09 L (76%) sitting, 3.53 L (67%) supine	No recent FVC done	Not reported	Monoclonal antibody, one infusion; prednisone for 10 d	4 wk	No ongoing COVID-19 symptoms

Abbreviations: COVID-19, coronavirus 2019; CT, computed tomography; d, days; FVC, forced vital capacity; L, liters; mo, months; NIV, noninvasive ventilation; %, percent predicted; wk, weeks.

All patients had been on nocturnal noninvasive ventilation due to diaphragmatic insufficiency, with erect forced vital capacity (FVC_e) measures ranging from 47% to 86%. Symptoms of COVID-19 infection included fever, fatigue, myalgia, diarrhea, cough, nasal congestion, anosmia, loss of appetite, chills, and dyspnea at rest and on exertion. Only one patient was found to have hypoxia, measured on repeated spot or continuous transcutaneous oxygen saturation measurements. Symptoms of the COVID-19 infection lasted from 6 to 16 days. All patients had confirmed PCR testing for SARS-CoV2/COVID-19. These patients have now been followed up for 1 to 3 months, and, except for one patient who reported persistent weakness and fatigue after COVID, symptoms of COVID-19 have recovered. Two patients were treated with high-dose corticosteroids and one was treated with COVID-19 monoclonal antibodies. The other two patients only received symptomatic acetaminophen treatments. Details of treatments given during COVID-19 are shown in Table 2. No change in FVC was seen after COVID-19 infection in the 3 patients with both pre- and post-COVID pulmonary function data available.

3 | DISCUSSION

All four patients had pre-existing LOPD and pulmonary involvement and were in the category more likely to have complications from COVID-19 infection. Yet they only had mild/moderate manifestations and did not have additional pulmonary complications, hospitalization, or significant worsening of their neurological illnesses. Patient 1 had a pre-COVID FVC that was below 50%; similarly, patient 3, despite having an FVC around 75%, has had low inspiratory pressures, and was documented to have had extremely low diaphragmatic pressures on transdiaphragmatic manometry. Only two patients were treated with high-dose corticosteroids, and one was treated with the monoclonal antibodies directed against COVID-19. All patients had a benign course and two of our patients only required acetaminophen. It is possible that early institution of corticosteroids and treatment with monoclonal antibodies prevented further worsening of symptoms and disease in patients 1 and 4, but this is speculative. Unlike the first wave of COVID infections that occurred on the eastern seaboard of the United States, with a strain of COVID-19 virus that was reportedly more virulent and occurred at a time of rudimentary understanding of management of COVID-19 infection, the infections in California occurred later in the year at a time of improved understanding of disease management, and were associated with lower morbidity and mortality. This may have played a role in the apparent benign course in our patients.

As of December 10, 2021, there have been 269 million global cases of COVID-19, resulting in 5.3 million global deaths.[2] The majority of serious cases have been in the elderly or individuals with pre-existing illness, requiring prolonged intensive care unit stays and mechanical ventilation. More recently, most of the serious cases have been in individuals who were not vaccinated for COVID-19.

The four cases described herein demonstrate that a benign course may occur in some neuromuscular patients, who may not experience any persisting post-COVID symptoms. However, due to the variable nature of the virus, and continuous emergence of newer and more virulent mutant strains, individuals with LOPD remain at high risk and should receive COVID-19 vaccinations and exercise precautions to avoid exposure to COVID-19 infection.

ACKNOWLEDGMENTS

The authors acknowledge the patients for providing additional details on their COVID related illness.

CONFLICT OF INTEREST

T.M. has served in an advisory capacity for AbbVie, Alexion, Amicus, Argenx, Audentes, Modis, Momenta, Ra Pharmaceuticals, Sanofi-Genzyme, Sarepta, Spark Therapeutics, UCB, and Ultragenyx. He serves on the speaker's bureau for Sanofi-Genzyme and on the medical advisory boards for the Myositis Association, the Neuromuscular Disease Foundation, the Myasthenia Gravis Foundation of California, and the Myasthenia Gravis Foundation of America. He receives research funding from the Myositis Association; the Muscular Dystrophy Association; the National Institutes for Health (NIH); and from Alexion, Amicus, Argenx, Audentes, Bristol-Myers-Squibb, Cartesian Therapeutics, Grifols, Momenta, Ra Pharmaceuticals, Sanofi-Genzyme, Spark Therapeutics, UCB, and Valerion. He serves on the data safety monitoring board for Acceleron, Sarepta, and the NIH. The remaining authors declare no potential conflicts of interest.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Tahseen Mozaffar https://orcid.org/0000-0002-1230-0188

REFERENCES

1. Valencia DN. Brief review on COVID-19: the 2020 pandemic caused by SARS-CoV-2. *Cureus*. 2020;12:e7386.
2. Global Dashboard. 2020. https://coronavirus.jhu.edu. Accessed December 10, 2021.
3. Guidon AC, Amato AA. COVID-19 and neuromuscular disorders. *Neurology*. 2020;94:959-969.
4. van der Ploeg AT, Clemens PR, Corzo D, et al. A randomized study of alglucosidase alfa in late-onset Pompe's disease. *N Engl J Med*. 2010; 362:1396-1406.
5. Hagemans ML, Winkel LP, Van Doorn PA, et al. Clinical manifestation and natural course of late-onset Pompe's disease in 54 Dutch patients. *Brain*. 2005;128:671-677.

How to cite this article: Avelar J, Wencel M, Chumakova A, Mozaffar T. COVID-19 infection in patients with late-onset Pompe disease. *Muscle & Nerve*. 2022;65(3):334-336. doi:10.1002/mus.27482