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# A practical approach for the treatment of post-COVID symptoms

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## Abstract

For the past 3 years, our daily lives have been largely dictated by the coronavirus disease 2019 (COVID-19) pandemic. In many people, this infectious disease leads to long-lasting symptoms, which can vary greatly in form and intensity between individuals. This report describes the case of a young patient who had no health restrictions until she came into contact with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As part of a post-COVID syndrome, she not only temporarily lost her ability to work, but was also no longer able to manage her daily life independently. A crucial therapeutic approach, in this case, was the use of heparin-induced extracorporeal LDL/fibrinogen precipitation (H.E.L.P.) apheresis.

## Keywords

COVID 19 · Long COVID · H.E.L.P. apheresis · Hyperlipoproteinemia · Chronic condition

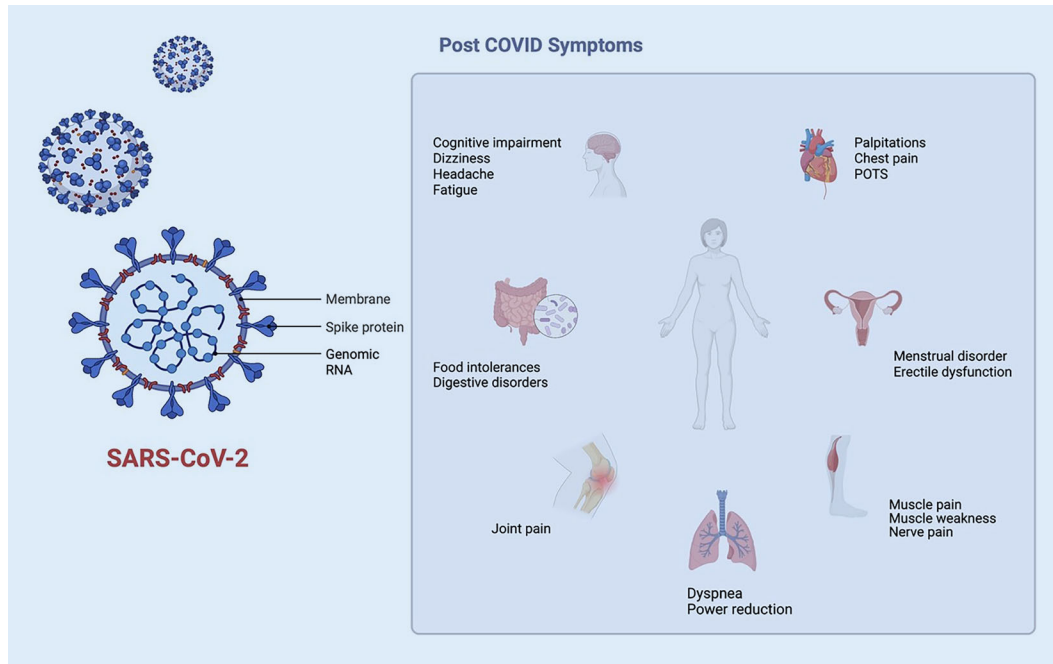
Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can be categorized into different disease stages based on viral load and symptoms [1]. Thereby, an acute phase of the disease, which can last up to 4–5 weeks, is distinguished from a chronic phase. The latter is known as the long-term effects of COVID-19 (long COVID, post-COVID) and is characterized by the persistence of symptoms such as fatigue, cognitive impairment, muscle pain and arthralgia, dyspnea, chest pain, and palpitations for weeks to months [1]. While most patients with COVID-19 fully recover within a few weeks, conservative estimates suggest that approximately 10% of people infected with SARS-CoV-2, and thus more than 65 million people worldwide, suffer from long COVID [2]. The risk of developing long COVID is higher in hospitalized than in non-hospitalized patients and is significantly reduced by prior vaccination [2]. Nevertheless, long COVID/post-COVID is most often a complication of

mild disease in non-hospitalized patients, as they represent the majority of COVID-19 patients [2].

The causes of long COVID/post-COVID are not yet fully understood but may be related to ongoing inflammation, autoimmune dysfunction, reactivation of underlying pathogens, microvascular blood clotting with endothelial dysfunction, or other factors [2, 3]. There is currently no single treatment for post-COVID syndrome, and management typically involves a multidisciplinary approach to address the range of symptoms and complications that patients may experience (■ Fig. 1; [3, 4]).

## Case presentation

A 38-year-old female patient (168 cm, 51 kg, body mass index [BMI] 18.1) presented to the Long Covid Outpatient Clinic in July 2022 with complex symptoms such as exercise-induced dyspnea, palpitations, thoracic burning, blood pressure dysregulations (often hypertensive), Raynaud's syndrome, muscle pain, and



**Fig. 1** ◀ Common symptoms of post-COVID. POTS postural orthostatic tachycardia syndrome. (Figure created in BioRENDER.com)

post-exertional malaise (PEM) in temporal relation after vaccination against SARS-CoV-2 and twofold infection. The patient was vaccinated in April 2021 and complained of joint pain, muscle twitching, drowsiness, muscle weakness, and chest pain 5 days later. In December 2020, the patient had already been infected with SARS-CoV-2 and had experienced a reactivation of herpes zoster, which had resulted in meningoencephalitis; this was treated with valganciclovir and the patient recovered in the same month.

In the following months after vaccination and recurrent SARS-CoV-2 infections, multiple symptoms were added, which occurred until the first presentation appointment. The patient reported an irregular menstruation cycle, upper abdominal pain, weight loss, and intermittent diarrhea, which partially responded to repeated cortisone boost therapies. In addition, the patient described visual and peripheral sensory disturbances as well as cognitive performance impairments, especially the ability to concentrate. At this time, the patient was unable to work. In June 2022, the patient suffered another SARS-CoV-2 infection, which was treated with remdesivir.

Relevant preexisting conditions of the patient were non-familial hypercholesterolemia and bronchial asthma.

A diagnosis of mild stenosis of the left arteria cerebri media (ACM) was made in April 2021. One year later, duplex sonography showed progression with moderate stenosis of the ACM on both sides. The carotids were bilateral without stenosis.

At the initial outpatient presentation, the patient was receiving rosuvastatin 5 mg, ezetimibe 10 mg, bempedoic acid 180 mg, acetylsalicylic acid 100 mg, B vitamins, vitamin D 2000 IE/day, glutathione liposomal, melatonin 1 mg, and quercetin. Lipid-lowering therapy was already in place for >12 months. Clinical examination revealed normotensive blood pressure (110/84 mm Hg). The patient is a non-smoker. The HbA1c value was 5.3%. Her electrocardiography showed a regular normofrequent sinus rhythm without higher-grade arrhythmias. Echocardiography revealed normal findings with normal cardiac output and good biventricular systolic function without valvular vitiation, while ergometry showed a limited exercise capacity with a regular heart rate and a normal blood pressure profile. There was no indication of an ischemic reaction. Laboratory chemical analyses initially showed no constellation of an acute infection (normal range of leukocytes, C-reactive protein [CRP], procalcitonin [PCT]). Thyroid hormones corresponded to a euthyroid metabolic

state. Iron deficiency without relevant anemia was found, and severe hypercholesterolemia was detected although the patient was under triple therapy. Vitamins B<sub>1</sub>, B<sub>12</sub>, and D were all within normal range, and folic acid levels were above normal. Furthermore, there was no evidence of infection or reactivation with cytomegalovirus (CMV), Epstein–Barr virus (EBV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), hepatitis A/B/C, varicella, *Borrelia burgdorferi*, or *Toxoplasma gondii*.

In the synopsis of the findings, we made the diagnosis of a post-COVID condition. Therefore, cholesterol-lowering therapy was continued. In addition, we recommended the therapeutic approaches described in the S1 guideline on long COVID/post-COVID [13] and recommended a low-histamine diet [14].

The first follow-up was performed after 5 weeks. The patient reported only a slight improvement in fatigue. In particular, the neurological, cardiac, and general complaints remained almost unchanged. The low-histamine diet was followed only irregularly. Long-term electrocardiography showed 5% bradycardia and isolated premature atrial and ventricular contractions without relevant pauses. Her cholesterol levels were still elevated on triple therapy. In view of the persistence of symp-

toms, the intensity of the complaints, and the lipoprotein parameters that could not be adequately treated with medication the decision for heparin-induced extracorporeal low-density lipoprotein (LDL)/fibrinogen precipitation (H.E.L.P.) apheresis therapy was made. The first apheresis was performed in early November 2022 and was completed without complications.

Two weeks after the first apheresis, laboratory chemical analysis showed hypercholesterolemia again. Incidental findings included normochromic and normocytic anemia. Rosuvastatin had been paused by the patient in the meantime due to muscle pain, which is why a drug change to, e.g., simvastatin was recommended. After apheresis, the patient reported an improvement in visual disturbances as well as peripheral blood flow with an overall decrease in Raynaud's symptoms. The next apheresis was performed at intervals of 2–4 weeks and resulted in further improvement in the patient's symptoms, which lasted for about 10 days after apheresis. The patient reported that especially her vision and hearing had become better, and her sleep more restful. Additionally, Raynaud's symptoms and livedo had regressed, while muscular pain and chest pain on exertion had also subsided. Currently, the apheresis is being continued. At present, the patient is able to work 30% of the time. Her cognitive performance is still limited in everyday working life.

Subjectively, the patient states that she has experienced a significant improvement in her symptoms and benefits from lipid apheresis in her daily life.

## Discussion

Treatment of people with long COVID or post-COVID requires a multidisciplinary approach including symptomatic therapy, physiotherapeutic exercise, psychiatric support, and concomitant drug therapy [3]. A potential benefit of pharmacological therapies is still being addressed in multiple studies. There is currently limited data on the use of statin therapy in the management of long COVID, which refers to persistent symptoms or complications that continue beyond the acute phase of COVID-19. However, statin therapy is a well-established treatment for reducing

the risk of cardiovascular disease, and some studies suggest that it may have a beneficial effect on certain aspects of COVID-19 [5].

Moreover, the use of renin–angiotensin system (RAS)-modulating drugs is widely discussed and is now considered to be at least without negative effects on acute SARS-CoV-2 infection [6]. Since RAS dysregulation can also be associated with many of the symptoms of chronic COVID disease, the investigation of the effects of RAS inhibitors on long COVID is also gaining importance [7]. However, pioneering studies are currently lacking.

In addition, the occurrence of mast cell activation in patients with long COVID has been described and a possible benefit from the use of antihistamines has been hypothesized [9]. In smaller studies, the use of antihistamines was already able to improve the symptoms of long COVID [8, 9]. Whether patients benefit additionally from a low-histamine diet should be considered on an individual basis.

Beyond pharmacological therapy, H.E.L.P. apheresis is gaining increasing importance [10]. Based on its successful use on patients with hyperlipidemia, arteriosclerosis, coronary heart disease, neurological and rheumatological diseases as well as in cases of acute bacterial and viral infections, its use in long COVID or post-COVID seems promising [10]. Apheresis is a medical treatment that was initially developed for the removal of lipids in severe dyslipidemias [11]. It involves removing blood from a patient, separating and removing certain components, and returning the remaining blood components to the patient. In this way, the blood viscosity and microcirculation are improved [12].

## Conclusion

The treatment of patients with long COVID continues to be a clinical challenge and multimodal therapeutic approaches are often used. Although in the present case heparin-induced extracorporeal LDL/fibrinogen precipitation (H.E.L.P.) apheresis was successful, further studies of this therapeutic procedure will be necessary to confirm its effectiveness in post-COVID treatments.

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## Declarations

**Conflict of interest.** J. Heitmann, J. Kreutz, S. Aldudak, E. Schieffer, B. Schieffer and A.-C. Schäfer declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case. Additional written informed consent was obtained from all individual participants or their legal representatives for whom identifying information is included in this article.

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## Praktischer Ansatz zur Behandlung von Post-COVID-Symptomen

Die letzten 3 Jahre wurde unser Alltag maßgeblich durch die COVID-19-Pandemie (Coronavirus Disease 2019) diktiert. Bei einer großen Zahl an Menschen führt diese Infektionserkrankung zu langanhaltenden Beschwerden, welche interindividuell sehr stark in ihrer Form und Intensität variieren können. Im vorliegenden Fallbericht wird über eine junge Patientin berichtet, die bis zum Kontakt mit SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) keine gesundheitlichen Einschränkungen auswies und im Rahmen eines Post-COVID-Syndroms nicht nur ihre Arbeitsfähigkeit temporär verloren hat, sondern auch ihren Alltag nicht mehr selbstständig bewältigen konnte. Ein entscheidender Therapieansatz war in diesem Fall der Einsatz der H.E.L.P.-Apherese (heparininduzierte extrakorporale LDL-Präzipitation).

### Schlüsselwörter

COVID 19 · Long-COVID · H.E.L.P.-Apherese · Hyperlipoproteinämie · Chronische Erkrankung