CASE REPORT

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Peyronie's disease in a patient after COVID-19 infection: A case report

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Abstract

Coronavirus disease 2019 (COVID-19) is an emerging infectious disease caused by a novel coronavirus (SARS-CoV-2), which demonstrates the ability to invade endothelial cells and cause systemic inflammation. Many possible long-term sequelae of COVID-19 remain unidentified. We describe a case of a man who developed Peyronie's disease after a resolved COVID-19 infection. Erectile dysfunction was confirmed by the International Index of Erectile Function-15(IIEF) and Sexual Health Inventory for Men(SHIM) scores. A diagnosis was Peyronie's disease was confirmed on ultrasound. Furthermore, he was found to have low endothelial progenitor cells colony-forming units and low brachial artery flow-mediated vasodilation, both of that are indicative of endothelial dysfunction. This case suggests Peyronie's disease should be considered as a possible sequela of COVID-19 infection and providers should inquire about a history of COVID-19 infection in patients presenting with Peyronie's disease.

KEYWORDS
coronavirus, COVID-19, endothelial dysfunction, erectile dysfunction, Peyronie's disease

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an emerging infectious disease caused by a novel coronavirus (SARS-CoV-2), which causes systemic inflammation in some patients. Many possible long-term sequelae of COVID-19 remain unidentified. Herein, we describe a case of a man who developed Peyronie's disease after a resolved COVID-19 infection.

2 | CASE PRESENTATION

A 50-year-old man complained of painful erections with curvature onset approximately 10 days after recovering from COVID-19 infection, gradually worsening until presentation to urology clinic 80 days after resolution of COVID-19. He stated that his COVID-19 symptoms lasted around five days and included fever, myalgia (most prominent in his back and abdomen), cough, and fatigue. He denied any shortness of breath. His diagnosis was confirmed by an outpatient COVID-19 laboratory test. He took acetaminophen and ibuprofen at home and was never hospitalised or placed on oxygen. At the presentation to clinic, he noticed an upward penile curvature of ~45 degrees with erections that was new-onset. He localised the pain around his midshaft and rated the pain as 9/10 when erect. He did not have pain when the penis was flaccid. He denied any history of genital trauma. He had a history of testosterone replacement therapy intermittently for 8 years due to fatigue and low libido; he denied any testosterone replacement in the 2.5 years prior to presentation. He endorsed current low libido and fatigue. He also reported a family history of prostate cancer in his father at age 67. He brought in lab results, which were completed 29 days after resolution of his COVID-19 infection (Table 1). Written informed consent was provided prior to completion of any research-specific tests.

3 | TREATMENT AND EVALUATION

The patient was prescribed tadalafil 5-mg PO daily for painful erections. Penile duplex was conducted with a 0.05-cc intracavernosal injection of alprostadil, papaverine, and phentolamine (Trimix) to achieve 100% rigidity. A curvature of 40 degrees dorsal and 30 degrees to the left was noticed. Calcified plaques measuring 0.5×0.5 cm and 1.0×1.5 cm were seen on ultrasound (US). Normal systolic velocities (right = 33.6 cm/s, left = 31.4 cm/s), slightly elevated end-diastolic velocities (right = 5.76 cm/s, left = 5.76 cm/s), and possible venous leak were noted at 10 min (Figure 1). International index of erectile function-15 (IIEF-15) scores of 3, 1, 7, 0, and 2 were reported in corresponding domains indicating erectile dysfunction, orgasmic dysfunction, normal sexual desire, intercourse dissatisfaction, and overall dissatisfaction. Additionally, he scored 20 on the SHIM, indicating mild erectile dysfunction.

Endothelial progenitor cells (EPCs) are a unique type of stem cell, which is involved with the repair of vascular endothelium throughout the body. Patients with higher levels of circulating EPCs are thought to have higher capacity for cardiovascular self-regeneration. EPCs can be tested by collecting a blood sample and growing the cells in culture according to an established 5-day standard protocol, generating a quantifiable amount of EPC-colon forming units (EPC-CFUs) (Hill et al., 2003). Brachial artery flow-mediated vasodilation (FMD) is another measure of systemic endothelial function, which utilises ultrasound to assess changes in brachial artery diameter after blood pressure cuff arterial occlusion (Corretti et al., 2002). Patients with FMD values less than 7% are considered to have endothelial dysfunction. EPCs and FMD were compared against a positive and negative control group to contextualise the endothelial function results. Negative control group ('No PD') contained 27 patients with cardiovascular disease (such as diabetes or cardiomyopathy) and had IIEF scores >24 (indicative of normal erectile function). Positive control group consisted of nine healthy controls who had no significant medical history. This patient's EPC-CFUs were zero. Additionally, his FMD was impaired at 2.35% (normal value >7%) (Table 2, Figure 2).

4 | CONCLUSIONS

This case represents a patient with confirmed Peyronie's disease after the resolution of COVID-19 infection. His IIEF and SHIM scores were both indicative of erectile dysfunction. His low EPC and FMD% are suggestive of endothelial dysfunction. To our knowledge, this is the first case of Peyronie's disease reported after COVID-19 infection. Peyronie's disease should be considered as a possible sequela of COVID-19 infection due to widespread endothelial dysfunction.

5 | DISCUSSION

COVID-19 is often considered to be a vascular disease due to the prothrombotic state it produces in many patients; the mechanism behind this involves direct endothelial invasion, which decreases the antithrombic activity of the normal epithelium (Bonaventura et al., 2021). Cell cultures demonstrate that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) receptor for cell entry and transmembrane protease serine 2 (TMPRSS2) receptor for viral spike

TABLE 1 Lab results completed 29 days after resolution of COVID-19 infection brought in by patient upon initial presentation to urology clinic

Lab Results	
Testosterone	205 ng/dl
Prostate-specific antigen	0.2 ng/ml
Cholesterol	297 mg/dl
Triglycerides	194 mg/dl
Low density lipoprotein	207 mg/dl
Glycated haemoglobin	5.8%

TABLE 2 Peyronie's disease (PD) patient's mean endothelial progenitor cells-colon forming units (EPC-CFUs) and brachial artery flow-mediated vasodilation (FMD) compared to positive (healthy) and negative ('No PD') control groups

Group	Sample Size	EPC-CFUs	FMD%
PD Subject	1	0	2.35
Negative Control	27	2.61 ± 2.56	4.73 ± 2.28
Positive Control	9	21.56 ± 10.41	7.23 ± 1.38

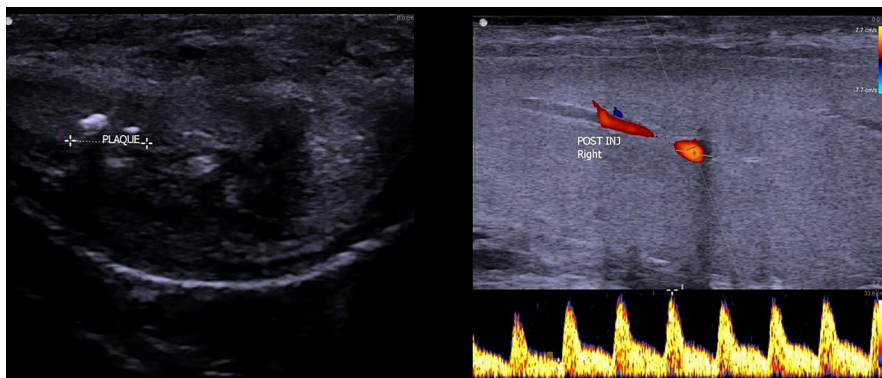*Note:* The PD patient's EPC-CFU and FMD measurements are indicative of endothelial dysfunction.

FIGURE 1 Penile ultrasonography demonstrating a calcified plaque (left). Doppler ultrasonography of right cavernous artery (right)
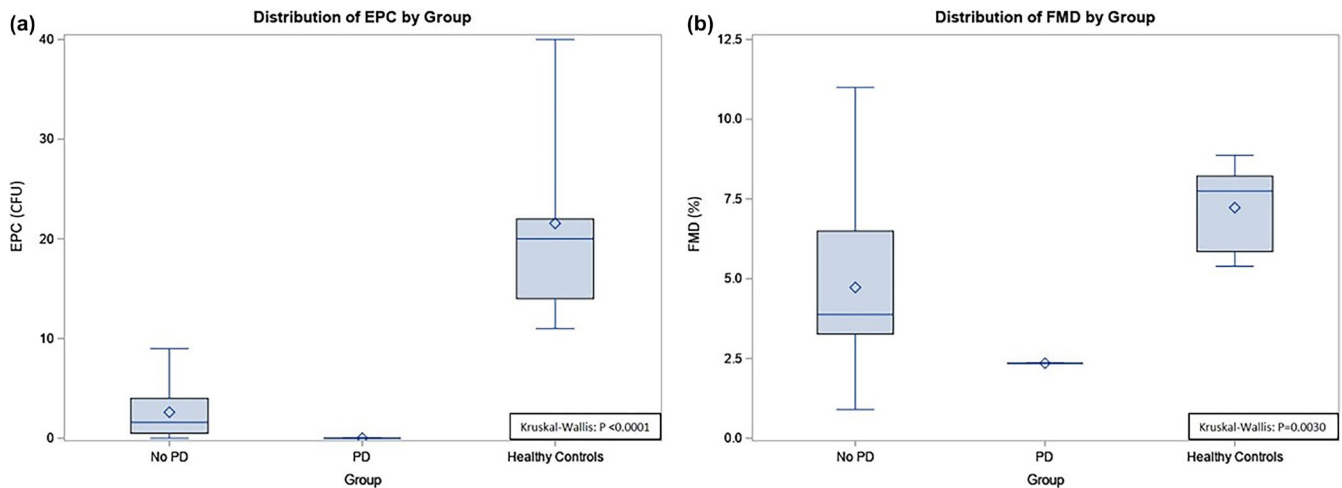
FIGURE 2 (A) Endothelial function in each patient group. Patient with Peyronie's Disease (PD, *n* = 1) and negative controls ('No PD', *n* = 27) have impaired endothelial progenitor cell-colony forming units (EPC-CFUs) compared to healthy controls (*n* = 9, *p* < .0001). (B) Patient with PD (*n* = 1) and negative controls ('No PD', *n* = 27) have reduced brachial artery flow-mediated vasodilation (FMD%) compared to healthy controls (*n* = 9, *p* = .003)

protein priming (Hoffmann et al., 2020). Endothelial cells possess both receptors, and endothelial damage is evident in one-third to three-quarters of patients with COVID-19, regardless of symptom severity (Guney & Akar, 2021; Umbrajkar et al., 2021). Although the pathophysiology of Peyronie's disease is still uncertain, it appears to involve endothelial or epithelial damage, inflammation, and poor wound healing (Campbell & Alzubaidi, 2017). Therefore, it is possible that widespread endothelial damage seen in COVID-19 infections may lead to Peyronie's disease and/or erectile dysfunction in susceptible individuals.

The possibility of sexual dysfunction as a result of COVID-19 has been studied since the start of the COVID-19 pandemic. In a study by Achua et al. (2021), SARS-CoV-2 was found within in the testicles on autopsy in one of four men who had died of COVID-19 related pneumonia and one live biopsy patient, suggesting that SARS-CoV-2 can cross the blood-testis barrier. COVID-19 infection in men can acutely decrease total sperm number (TSN) in ejaculate, one study found that there was a median of 12.5 million TSN in COVID-19 patients (*n* = 30) versus 59.2 million TSN in a COVID-19 negative control group (*n* = 30) (Best et al., 2021). A systematic review by Gonzalez et al. examined the current literature studying the possible presence of SARS-CoV-2 in the semen of men with a history of COVID-19 (Gonzalez et al., 2020). Of the eight studies found, one demonstrated the presence of SARS-CoV-2; six of the 160 compiled semen samples were found to have the presence of viral RNA. The possibility of sexual transmission is still a matter of debate.

There is evidence of affiliated androgen deficiency in the context of COVID-19. A prospective cohort study consisting of 262 men examined three different groups: 89 hospitalised men with COVID-19 (group 1), 30 hospitalised men with non-COVID-19 respiratory tract infection (group 2), and 143 age-matched controls admitted to urology outpatient clinic for reproductive function

evaluation (group 3) (Kadihasanoglu et al., 2021). This study found a median testosterone level of 185.52 ng/dl in group 1, which was significantly less than group 2 (288.67 ng/dl) and group 3 (332 ng/dl). The prevalence of testosterone deficiency in group 1 was 74.3%, which was significantly greater than group 2 at 53.3% and group 3 at 37.8%. Furthermore, median serum luteinizing hormone (LH) and prolactin (PRL) levels were significantly higher in group 1 and 2 (group 1: LH = 5.67 U/L, PRL = 9.6 µg/L, group 2: LH = 5.39 U/L, PRL = 9.61 µg/L) when compared to group 3 (LH = 4.1 U/L, PRL = 7.5 µg/L), but there was no significant difference between group 1 and 2. The increase in LH is an expected outcome of compensated hypogonadism and elevated LH is triggered by increased interleukin (specifically 1, 2, and 6) levels.

In addition to testicular inflammation and hypogonadism, it has been proposed that COVID-19 may cause erectile dysfunction due to the endothelial invasion demonstrated by SARS-CoV-2 (Sansone, Mollaioli, Ciocca, Colonnello, et al., 2021). A survey conducted in Italy, completed by 100 subjects (25 COVID-19 positive and 75 COVID-19 negative controls), found that the prevalence of erectile dysfunction, according to SHIM scores, was significantly higher in the COVID-19 positive group, 28% versus 9.33% (Sansone, Mollaioli, Ciocca, Limoncin, et al., 2021). Interestingly, subjects with erectile dysfunction, often an indication of poor vascular health, were predisposed to have a COVID-19 infection with an odds ratio of 5.27. Furthermore, extracellular COVID-19 viral particles have been identified on transmission electron microscopy of penile tissue from patients undergoing penile prosthesis for treatment of erectile dysfunction onset after COVID-19 infection (Kresch et al., 2021). Taken together, these studies indicate that COVID-19 likely affects the reproductive system of many patients and further studies should evaluate the long- and short-term effects of COVID-19 infection on sexual function and fertility.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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