CASE IN POINT

SARS-CoV-2: A Novel Precipitant of Ischemic Priapism

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Background: Priapism is a disorder that occurs when the penis maintains a prolonged erection in the absence of appropriate stimulation. Conditions that result in hypercoagulable states and hyperviscosity are associated with ischemic priapism. COVID-19 is increasingly associated with coagulopathy. To date, there are 6 reported cases of priapism occurring in patients with COVID-19, 5 occurring in the setting of critical illness.

Case Presentation: We present a case of ischemic priapism which we suspect resulted from COVID-19–associated coagulopathy in a patient without severe COVID-19 presentation.

Conclusions: Although there have been only a handful of reported cases of COVID-19–associated coagulopathy leading to ischemic priapism, it is possible that the true incidence is much higher. While our case highlights the importance of considering COVID-19 infection in the differential diagnosis of ischemic priapism, more research is needed to understand incidence and definitively establish a causative relationship.

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Priapism is a disorder that occurs when the penis maintains a prolonged erection in the absence of appropriate stimulation. The disorder is typically divided into subgroups based on arterial flow: low flow (ischemic) and high flow (nonischemic). Ischemic priapism is the most common form and results from venous congestion due to obstructed outflow and inability of cavernous smooth muscle to contract, resulting in compartment syndrome, tissue hypoxia, hypercapnia, and acidosis.[1] Conditions that result in hypercoagulable states and hyperviscosity are associated with ischemic priapism. COVID-19 is well known to cause an acute respiratory illness and systemic inflammatory response and has been increasingly associated with coagulopathy. Studies have shown that 20% to 55% of patients admitted to the hospital for COVID-19 show objective laboratory evidence of a hypercoagulable state.[2]

To date, there are 6 reported cases of priapism occurring in the setting of COVID-19 with all cases demonstrating the ischemic subtype. The onset of priapism from the beginning of infectious symptoms ranged from 2 days to more than a month. Five of the cases occurred in patients with critical COVID-19 and 1 in the setting of mild disease.[3-8] Two critically ill patients did not receive treatment for their ischemic priapism as they were transitioned to expectant management and/or comfort measures. Most were treated with cavernosal blood aspiration and intracavernosal injections of phenylephrine or ethylephrine. Some patients were managed with prophylactic doses of anticoagulation after the identification of priapism; others were transitioned to therapeutic doses. Two patients were followed postdischarge; one patient reported normal nighttime erections with sexual desire 2 weeks postdischarge, and another patient, who underwent a bilateral T-shunt procedure after unsuccessful phenylephrine injections, reported complete erectile dysfunction at 3 months postdischarge.[4,7] There was a potentially confounding variable in 2 cases in which propofol infusions were used for sedation management in the setting of mechanical ventilation.[6,8] Propofol has been linked to priapism through its blockade of sympathetic activation resulting in persistent relaxation of cavernosal smooth muscle.[9] We present a unique case of COVID-19–associated ischemic priapism as our patient had moderate rather than critical COVID-19.

CASE PRESENTATION

A 67-year-old male patient presented to the emergency department for a painful erection of 34-hour duration. The patient had been exposed to COVID-19 roughly 2 months prior. Since the exposure, he had experienced headache, nonproductive cough, sore throat, and decreased appetite with weight loss. His medical history included hypertension, thoracic aortic aneurysm, B-cell type chronic lymphocytic leukemia (CLL), and obstructive sleep apnea. Daily outpatient medications included atenolol 100 mg, hydrochlorothiazide 25 mg, and omeprazole 20 mg. The

patient stopped tobacco use about 30 years previously. He reported no alcohol consumption or illicit drug use and had no previous episodes of prolonged erection.

The patient was afebrile, hemodynamically stable, and had an oxygen saturation of 92% on room air. Physical examination revealed clear breath sounds and an erect circumcised penis without any lesions, discoloration, or skin necrosis. Laboratory data were remarkable for the following values: 125,660 cells/µL white blood cells (WBCs), 13.82 × 10^3/ µL neutrophils, 110.58 × 10^3/ µL lymphocytes, 1.26 × 10^3/µL monocytes, no blasts, 9.4 gm/dL hemoglobin, 100.3 fl mean corpuscular volume, 417,000 cells/µL platelets, 23,671 ng/mL D-dimer, 29.6 seconds activated partial thromboplastin time (aPTT), 16.3 seconds prothrombin time, 743 mg/dL fibrinogen, 474 U/L lactate dehydrogenase, and 202.1 mg/dL haptoglobin. A nasopharyngeal reverse transcription polymerase chain reaction test resulted positive for the SARS-CoV-2 virus, and subsequent chest X-ray revealed bilateral, hazy opacities predominantly in a peripheral distribution. Computed tomography (CT) angiogram of the chest did not reveal pulmonary emboli, pneumothorax, effusions, or lobar consolidation. However, it displayed bilateral ground-glass opacities with interstitial consolidation worst in the upper lobes. Corporal aspiration and blood gas analysis revealed a pH of 7.05, P_{CO_2} of 64 mm Hg, and P_{O_2} of 33 mm Hg.

Differential Diagnosis

The first consideration in the differential diagnosis of priapism is to differentiate between ischemic and nonischemic. Based on the abnormal blood gas results above, this case clearly falls within the ischemic spectrum. Ischemic priapism secondary to CLL-induced hyperleukocytosis was considered. It has been noted that up to 20% of priapism cases in adults are related to hematologic disorders.[10] While it is not uncommon to see hyperleukocytosis (total WBC count > 100 × 10^9/L) in CLL, leukostasis is rare with most reports demonstrating WBC counts > 1000 × 10^9/L.[11] Hematology, vascular surgery, and urology services were consulted and agreed that ischemic priapism was due to microthrombi or pelvic vein thrombosis secondary to COVID-19–associated coagulopathy (CAC) was the most likely etiology.

Treatment

After corporal aspiration, intracorporal phenylephrine was administered. Diluted phenylephrine (100 ug/mL) was injected every 5 to 10 minutes while intermittently aspirating and irrigating multiple sites along the lateral length of the penile shaft. This initial procedure reduced the erection from 100% to 30% rigidity, with repeat blood gas analysis revealing minimal improvement. CT of the abdomen and pelvis with IV contrast revealed no evidence of pelvic thrombi. A second round of phenylephrine injections were administered, resulting in detumescence. The patient was treated with 2 to 3 L/min of oxygen supplementation via nasal cannula, a 5-day course of remdesivir and low-intensity heparin drip. Following the initial low-intensity heparin drip, the patient transitioned to therapeutic enoxaparin and subsequently was discharged on apixaban for a 3-month course. Since discharge, the patient followed up with hematology. He tolerated and completed the anticoagulation regimen without any recurrences of priapism or residual deficits.

DISCUSSION

Recent studies have overwhelmingly analyzed the incidence and presentation of thrombotic complications in critically ill patients with COVID-19. CAC has been postulated to result from endotheliopathy along with immune cell activation and propagation of coagulation. While COVID-19 has been noted to create lung injury through binding angiotensin-converting enzyme 2 receptors expressed on alveolar pneumocytes, it increasingly has been found to affect endothelial cells throughout the body. Recent postmortem analyses have demonstrated direct viral infection of endothelial cells with consequent diffuse endothelial inflammation, as evidenced by viral inclusions, sequestered immune cells, and endothelial apoptosis.[12,13] Manifestations of this endotheliopathy have been delineated through various studies.

An early retrospective study in Wuhan, China, illustrated that 36% of the first 99 patients hospitalized with COVID-19

demonstrated an elevated D-dimer, 6% an elevated aPTT, and 5% an elevated prothrombin time.[14] Another retrospective study conducted in Wuhan found a 25% incidence of venous thromboembolic complications in critically ill patients with severe COVID-19.[15] In the Netherlands, a study reported the incidence of arterial and venous thrombotic complications to be 31% in 184 critically ill patients with COVID-19, with 81% of these cases involving pulmonary emboli.[16]

To our knowledge, our patient is the seventh reported case of ischemic priapism occurring in the setting of a COVID-19 infection, and the first to have occurred in its moderate form. Ischemic priapism is often a consequence of penile venous outflow obstruction and resultant stasis of hypoxic blood.[7] The prothrombotic state induced by CAC has been proposed to cause the obstruction of small emissary veins in the subtunical space and in turn lead to venous stasis, which propagates the formation of ischemic priapism.[8] Furthermore, 4 of the previously reported cases shared laboratory data on their patients, and all demonstrated elevated D-dimer and fibrinogen levels, which strengthens this hypothesis.[3,5,7,8] CLL presents a potential confounding variable in this case; however, as we have reviewed earlier, the risk of leukostasis at WBC counts < 1000×10^9/L is very low.[11] It is also probable that the patient had some level of immune dysregulation secondary to CLL, leading to his prolonged course and slow clearance of the virus.

CONCLUSIONS

Although only a handful of CAC cases leading to ischemic priapism have been reported, the true incidence may be much higher. While our case highlights the importance of considering COVID-19 infection in the differential diagnosis of ischemic priapism, more research is needed to understand incidence and definitively establish a causative relationship.

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Ethics and consent

Informed consent was obtained from the patient reported in this case report.

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