Peripheral Ischemia… a Sign of COVID-19?

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Background

Severe acute respiratory system coronavirus 2 (SARS-CoV-2) has been responsible for over 2.76 million deaths worldwide. It is characterized by an exaggerated inflammatory response that ranges from a mild respiratory infection to acute respiratory distress syndrome.

We are now discovering that it is associated with many other complications, including a prothrombotic state. To enter target cells, SARS-CoV-2 uses the angiotensin-2 receptor. After binding, the receptor activates the renin-angiotensin system, which results in an increase in angiotensin II. Angiotensin II is a potent vasoconstrictor and it increases hypercoagulability.

Case

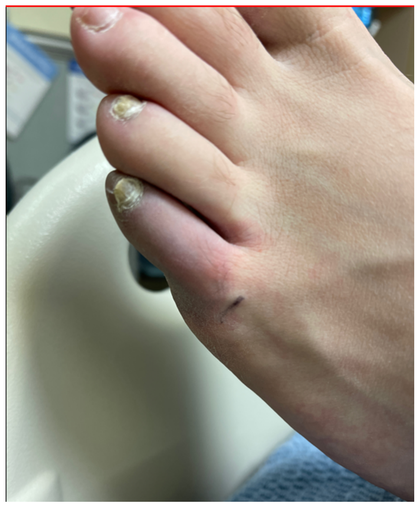
A 38-year-old male presented to the emergency department for darkening color and pain in his left fifth toe. His symptoms started two days prior and progressively worsened. On presentation to an outside hospital, an ultrasound of his left lower extremity showed no hemodynamically significant stenosis. A CTA abdominal aorta and lower extremity runoff showed a thrombus involving the left common iliac artery and extending slightly into the left external iliac artery. He was started on a heparin drip and transferred to our hospital. On arrival, he denied fever, shortness of breath, or gastrointestinal symptoms. A rapid COVID-19 swab returned positive. He was evaluated by vascular surgery and, with his COVID infection, it was determined he would be high risk for surgical intervention, and he was continued on the heparin drip. His symptoms improved and he was discharged on anticoagulation for three months.

Results

The patient's wife had tested positive for COVID-19 10 days before his presentation to the ED. He had two negative tests prior to presenting to our hospital. He had no prior history or family history of blood clots or pulmonary embolism. On presentation, his CBC showed a hemoglobin of 18.6 and a hematocrit of 58.1. His d-dimer was also elevated at 726. With the arterial thrombus seen on CTA, it is likely his left fifth toe discoloration was caused by a microvascular embolic event.

Of note, he had previously received several phlebotomy treatments, secondary to elevated hematocrit, thought to be related to testosterone use. This could have been related to his ischemic presentation. However, his hemoglobin corrected to 16.6 and his hematocrit improved to 52.3 with fluids. Given the known hypercoagulability associated with COVID-19, it is probable that his infection precipitated this event. Unfortunately, this patient was lost to follow-up.

Figure 1



The patient's fifth toe with ischemic color changes.

Discussion

Risk factors for severe symptoms of COVID-19 include advanced age, male sex, and the presence of comorbidities. Developing severe complications from COVID-19 also puts patients at a higher risk of thrombosis.

Coagulopathy has been reported in up to 50% of patients with severe COVID symptoms. SARS-CoV-2 leads to an increase in angiotensin II, which in turn increases hypercoagulability by increasing expression of tissue factor and plasminogen activator inhibitor 1. It can also cause an increase in pro-inflammatory cytokines, which are involved in abnormal clot formation and platelet hyperactivation. Pro-inflammatory cytokines also cause downregulation of important physiological anticoagulant pathways.

Low-molecular-weight heparin (LMWH) has been shown to block replication of the COVID-19 virus and have an anti-inflammatory effect. Elevated levels of D-dimer decreased significantly after treatment with LMWH. These factors have made it a cornerstone for the prevention and treatment of ischemic complications. Currently, most patients with COVID-19 receive a low prophylactic dose of LMWH. Despite prophylaxis, thrombosis can still occur, and further studies are needed to guide increased dosing to prevent clots from forming.

References

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