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COVID-19-Associated Thromboembolic Events Causing Acute Mesenteric Ischaemia

From:
Bingwen Eugene Fan

From the Department of Haematology, Tan Tock Seng Hospital, Singapore, Singapore (B.E.F.); Department of Laboratory Medicine, Khoo Teck Puat Hospital, Singapore, Singapore (B.E.F.); Lee Kong Chian School of Medicine, Singapore, Singapore (B.E.F.); Yong Loo Lin School of Medicine, Singapore, Singapore (B.E.F.).

I read with great interest "Acute Mesenteric Ischaemia in Severe Coronavirus-19 (COVID-19): Possible Mechanisms and Diagnostic Pathway" by Parry et al (1). Acute mesenteric ischaemia (AMI) in COVID-19 is rare but carries a high morbidity. Four common causes for AMI include acute mesenteric artery thrombosis, acute mesenteric artery embolism, acute mesenteric vein thrombosis and non-occlusive mesenteric ischaemia. Thrombogenesis in COVID-19 can be attributed to the direct and indirect cytotoxic effects of the SARS-CoV-2 virus on vascular endothelium, due to the coronavirus' affinity to the ACE-2 receptor on endothelial surfaces. This results in direct viral toxicity, endothelial dysfunction with thromboinflammation; and dysregulation of the renin-angiotensin-aldosterone system (2). The combination of endothelial injury, a hypercoagulable state and stasis of blood due to immobility contribute to the classic Virchow's triad of thrombosis.

Radiologists and clinicians should be aware that AMI in COVID-19 can manifest acutely or sub-acutely without classic cardiovascular risk factors or a significant history of arteriosclerotic disease. Parry et al (1) recognized COVID-19-associated coagulopathy as one of the key drivers of mesenteric vascular thrombosis; however, they mentioned there was lack of both radiologic and histologic evidence then, for large arterial and venous mesenteric vessel thrombosis. Recent case reports have now emerged of COVID-19 cases confirmed on SARS-CoV-2 polymerase chain reaction (PCR) having acute mesenteric vein or artery thrombosis, with Fan et al (3) describing a 30-year-old male with both radiologic and histologic features of superior mesenteric vein thrombosis and Cheung et al (4) reporting a 55-year-old male with "absence of major predisposing factors for thromboembolic formation" developing superior mesenteric artery thrombosis. Both cases were complicated by AMI, necessitating surgical resection of necrotic small bowel and anticoagulation.

Embolism from aortic thrombi superior to the mesenteric vessels is another notable cause of COVID-19-associated AMI, where a free-floating thrombus of the aortic arch was associated with an occlusion of the superior mesenteric artery (5). Norsa et al (6) described a 62-year-old male with cardiovascular risk factors who was SARS-CoV-2 PCR negative on nasopharyngeal and bronchoalveolar lavage, who had thromboembolism found in the inferior vena cava and superior mesenteric vein, resulting in mesenteric ischaemia requiring small intestine resection. Histologic examination showed severe endothelitiis with RNA in situ-hybridisation assay confirming SARS-CoV-2 presence in the intestinal mucosa, suggestive that superior mesenteric venous thrombosis with AMI can also present in the subacute phase of COVID-19 illness.

While no cases of AMI have yet been described in the convalescent phase of COVID-19, radiologists and clinicians should be mindful of the potential development of AMI even in the post-recovery population of COVID-19 patients. Cases with thromboembolism presenting during the convalescent phase of COVID-19 infection have been described, with patients having negative nasopharyngeal swabs for SARS-CoV-2 PCR but testing positive for SARS-CoV-2 IgG assay. Péré et al (7) discussed a 68-year-old male who was seropositive for SARS-CoV-2 IgG, with no significant co-morbidities and without evidence of arteriosclerosis, who had acute limb ischaemia secondary to an embolism from an infrarenal thrombus that caused a complete occlusion of the left popliteal artery. Goh et al (8) described a 35-year-old male who initially presented with right foot drop for 3 weeks with negative nasopharyngeal PCR swabs but a strongly positive serology for SARS-CoV-2 IgG. He had presented with an eccentric infrarenal abdominal aorta thrombus with embolization causing occlusion to the right external iliac artery. The diagnosis of an acute thrombosis of unusual site in patients with COVID-19 without obvious risk factors will also require exclusion of other known thrombophilic aetiologies, particularly the antiphospholipid syndrome, paroxysmal nocturnal haemoglobinuria, myeloproliferative neoplasms, protein C, S, and anti-thrombin III deficiencies, Factor V Leiden mutation and G20210A mutation in the prothrombin gene.

Patients with COVID-19 may present with a raised D-dimer, where higher levels prognosticate for a higher inpatient mortality rate and a poorer clinical course. While a raised D-dimer is non-specific and can be elevated in liver disease, disseminated intravascular coagulopathy, malignancy, trauma, and pregnancy; the presence of an *unexplained* elevated D-dimer together with raised serum lactate and acute abdominal symptoms should raise a high index of suspicion for AMI. Close clinical monitoring, together with CT imaging of the abdomen should be performed when clinically warranted. COVID-19-associated thromboembolic events continue to cause significant mortality and morbidity, hence pharmacologic thromboprophylaxis should be strongly considered for all hospitalized COVID-19 patients.

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