Concomitant renal and splenic infarction as a complication of COVID-19: a case report and literature review

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SUMMARY

The prothrombotic state contributes to diverse and devastating prognoses of severe COVID-19. We describe a unique COVID-19 case with concomitant splenic and renal infarcts. Based on this, clinicians should have a low threshold to suspect a diagnosis of deep vein thrombosis/pulmonary embolism (DVT/PE), especially in the abdominal visceral region if a patient comes in several days after a COVID-19 diagnosis with abdominal pain. Whether or not empiric full dose anticoagulation is needed in patients without definite diagnosis of thromboembolism is still controversial. Further studies need to be done; meanwhile, we advocate the use of regular dose thromboprophylaxis in all hospitalized patients and therapeutic anticoagulation only when there is a confirmed diagnosis of thromboembolism.

Keywords: Renal thrombosis, splenic thrombosis, COVID-19, anticoagulation.

INTRODUCTION

The prothrombotic state associated with SARS-CoV-2 infection contributes to diverse and devastating prognosis of severe COVID-19 [1, 2]. Existing data do not present a clear consensus on management of thrombotic events in COVID-19 patients. Several authors recommend that high-risk COVID patients should be on empiric therapeutic anticoagulation, while others advocate the use of full-dose anticoagulation only in cases of confirmed thromboembolism [2].

Herein, we describe a COVID-19 case with concomitant splenic and renal infarcts, and perform a literature review of COVID-19 cases with a similar presentation. Furthermore, we review the recommendations for full-dose anticoagulation and prophylaxis in COVID-19 patients in the hospital and ambulatory settings.

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CASE REPORT

A 54-year-old obese man with no medical history presented in September 2020 with dry cough, shortness of breath, and subjective fever for two days. He was febrile to 39.6°C and tachycardic to 106 beats per minute (BPM) saturating 95% on room air (RA), otherwise hemodynamically stable. Laboratory data showed a D-Dimer of 0.54 mcg/mL, CRP 6.0 mg/dL, ferritin 580 ng/mL, and LDH 1639 unit/L. He tested positive for SARS-Cov-2 via RT-PCR (Xpert Xpress SARS-CoV-2, Cepheid Infinity). A chest x-ray showed bilateral heterogeneous patchy opacities. He was given 6 mg of oral (PO) dexamethasone, and discharged on albuterol as needed with dexamethasone 6 mg PO twice daily (BID) for seven days with instructions to quarantine. He was not given prophylactic anticoagulation during this visit.

Eleven days later, he developed sudden, constant, and sharp abdominal pain with nausea and vomiting for 5 hours, requiring hospitalization. A computed tomography (CT) abdomen/pelvis with contrast was done and revealed patchy

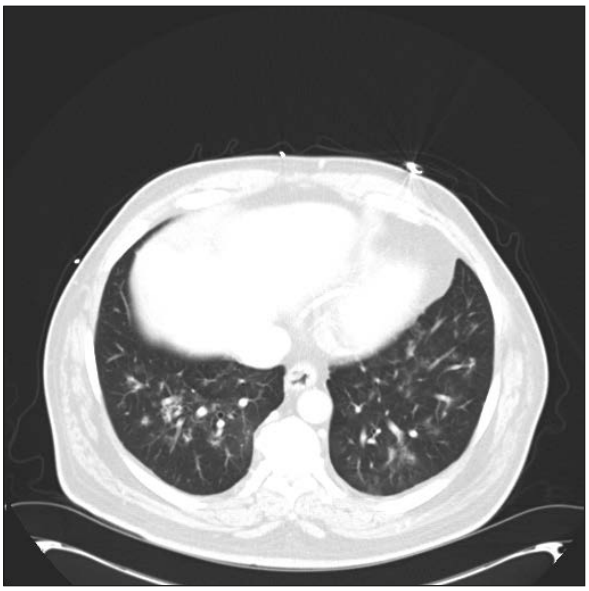

Figure 1 - CT abdomen/pelvis with intravenous (IV) contrast showing ground-glass opacities in the lungs.

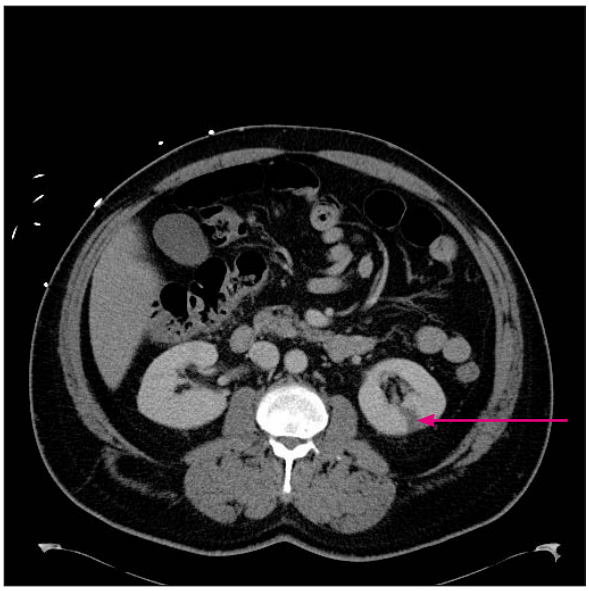

Figure 2 - CT abdomen/pelvis with IV contrast showing the renal infarcts.

ground-glass-opacities throughout his lungs and multiple wedge-shaped hypodensities, likely infarction, in both kidneys (Figure 1 and 2). There were also large areas of hypoattenuation in the splenic parenchyma consistent with infarcts (Figure 3). On laboratory studies, he had INR 1.0, PT 13.4, PTT 31, D-dimer 1.55 mcg/mL, CRP 5.7 mg/dL, ferritin 1633 ng/mL, LDH 2136 unit/L, ESR 23 mm/hr, WBC of 14.4 x 10^3/mcL with lymphopenia of 0.9, AST 118 unit/L, ALT 183 unit/L, alkaline phosphatase 128 unit/L, and lactic acid 2.9 mmol/L. Creatinine was 0.6 mg/dL. Hepatitis panel was negative. He was not considered a candidate for Remdesivir, as he was saturating 98% on RA. He was started on therapeutic heparin drip at 18 units/kg/hr. Ultrasounds of upper and lower extremities were negative for thrombosis. The patient was discharged, 4 days later with improving laboratory studies, on Apixaban 10mg PO BID for seven days, followed by 5mg PO daily for thirty days with an anticipated duration of 3 months.

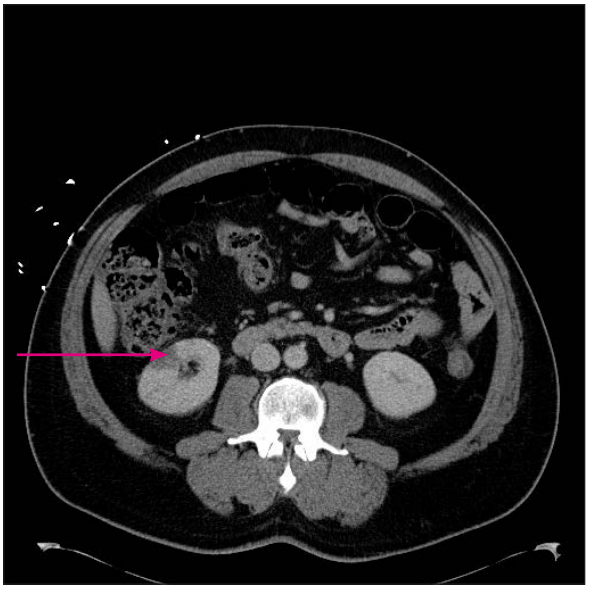

Figure 3 - CT Abdomen/Pelvis with IV contrast with splenic infarcts.

DISCUSSION

There has been an increased frequency of thrombosis in COVID-19. Klok et al. showed that in 184 ICU COVID-19 patients in three hospitals, the cumulative incidence of thrombosis was 31% [5]. PE was most commonly seen. However, there have been recent reports of abdominal visceral infarctions [4, 5].

Renal infarctions are rare, with an incidence of 0.1-1.4%. COVID-19 is thought to affect the kid-

Table 1 - Literature review of cases of COVID-19 with splenic and renal infarcts.

Article	*Age (years)*	*Gender*	*Past medical history*	*Days after COVID diagnosis to infarct presentation (days)*	*Area of infarct*	*Treatment*	*Outcome*
1 (1)	71	Male	None	9	Renal and Ascending Aortic Infarct	IV heparin; discharged on Apixaban 5 mg PO BID x 3 months	Recovered
2 (11)	46	Male	Kidney - pancreas transplant	8	Renal allograft infarct	Enoxaparin 80 mg every 12 hours; no anticoagulation at discharge	Recovered
3 (12)	62	Male	Hypertension, Henoch-Schonlein purpura, kidney trasplant	9	Multiple wedge shaped infarcts in the renal allograft	Dalteparin, 15,000 units then acenocoumarol	Recovered
	58	Male	Obstructive sleep apnea	10	Multiple wedge shaped infarcts in the renal allograft	Nadroparin	Discharged to rehabilitation center
4 (13)	56	Male	None	9	Renal artery thrombosis and infarct	0.5 mL/kg/h Enoxaparin	Recovered
5 (4)	60s *	Male	None	7	Acute splenic thrombosis and infarct	Heparin drip for 24 hrs; then to enoxaparin 1 mg/kg bid. Discharge on Rivaroxaban	Recovered
6 (14)	35	Male	None	6	Spontaneous Hemoperitoneum with splenic infarct	3 units PRBC	Recovered
7 (15)	64	Male	Gastric and duodenal ulcer	15	Multiple Cerebral Infarcts, Bilateral Renal Infarcts, Splenic Infarction	Favipiravir, Ciclesonide, Lovenox	Died on day 26 of hospitalization
8 (6)	67	Male	Hypertension	Same day	Pulmonary thromboembolism and Splenic infarct	No information	Recovered
	53	Female	Rheumatoid arthritis	Same day	Splenic infarct	No information	Recovered
9 (16)	54	Male	Ulcerative colitis, asthma, former smoker	6	Right kidney arterial infarct	LMWH (6,000 UI 2×/d)	Recovered
	53	Male	Hypertension and MVR	6	Spleen and the left kidney	LMWH (6,000 UI 2×/d)	Recovered
	72	Male	Stage 3 kidney failure, hypertension, myocardial infarction, and type 2 diabetes,	2	Spleen infarct	Heparin in continuous infusion	Recovered
10 Present case	54	Male	None	11	Bilateral renal and splenic infarcts	3 months of Apixaban	Recovered

*Actual age not written.

neys through systemic illness, renal hypoperfusion, cytokine storm, and direct invasion of the nephron. Splenic thrombosis is also infrequent and should be suspected in patients with left-sided abdominal pain [4, 6].

To evaluate the frequency of renal and splenic thromboses in COVID-19, we did a literature search via Pubmed for the relevant Medical Subject Headings terms, which included "COVID and renal infarcts", "COVID and splenic infarcts" and "COVID and renal and splenic infarcts". Ultimately, nine case reports of 13 patients were identified (Table 1). Overall, 92% were male and 8% were female. The mean age was 62 (46-72) years. They presented 17 days on average after COVID-19 was diagnosed. One patient died. Four patients had no past medical history, like our patient. The most common pre-existing medical condition was hypertension. There were 6 patients with renal infarcts, 5 patients with splenic infarcts and 2 patients with concomitant renal and splenic infarcts. In terms of treatment, most of the patients were treated with low molecular weight heparin (LMWH) for an average of 3 weeks. In one case, the patient was switched over to Apixaban, similar to our patient. One patient was treated with 3 months of therapy, like our patient.

The treatment and prevention of thrombotic events in COVID- 19 is controversial. The current standard of care is thromboprophylaxis for each hospitalized patient with regular heparin or LMWH doses. The controversy arises whether hospitalized patients without a definitive diagnosis of thromboembolism should empirically receive therapeutic anticoagulation. In this regard, the International Society of Thrombosis and Hemostasis (ISTH) proposed a scoring system named "sepsis-induced coagulopathy" (SIC) to evaluate the need of empiric anticoagulation [7]. Tang et. al used this system to assess 449 patients with severe COVID-19 [7]. Of them, 99 patients received therapeutic heparin or LMWH for 7 days or more [7]. The 28-day mortality between heparinized (hep+) and non-heparinized (hep-) patients was compared in different risk populations with no difference seen. However, the mortality of hep+ patients was lower than hep- patients with SIC score ≥4 or D-dimer >6-fold of upper limit of normal [7]. Despite these findings, there is no consensus for all hospitalized patients with COVID-19 to receive therapeutic anticoagulation [8]. Therapeutic anticoagulation is only recommended in patients with a diagnosis of thromboembolism or when there is a high clinical suspicion in the absence of diagnostic imaging, currently [8]. Our patient received therapeutic anticoagulation only after a CT scan confirmed renal and splenic infarcts.

In non-ICU hospitalized patients, using an intermediate-dose of LWMH for prophylaxis appeared to be feasible and safe in COVID-19 patients [9]. Paolisso et. al assessed 450 patients with severe COVID-19 retrospectively, 361 received standard DVT prophylaxis enoxaparin treatment (40-60 mg daily) and 89 patients received intermediate enoxaparin (40–60 mg BID) for 7 days. The intermediate-LMWH administration was associated with lower in-hospital all-cause mortality compared to the "standard" prophylactic LMWH dosage (18.8% vs 5.8%, p=0.02) (9). Several trials are underway to confirm the efficacy of this approach [10].

In patients who are discharged from the hospital, the NIH does not recommend universal thromboprophylaxis as an outpatient [8]. Following these recommendations, our patient was discharged after his first hospitalization without thromboprophylaxis. It is uncertain if the kidney and splenic thrombosis could have been prevented with prophylaxis.

In conclusion, clinicians should have a low threshold to suspect a diagnosis of DVT/PE of the abdominal visceral region if a patient comes in several days after a COVID diagnosis with abdominal pain. The need of empiric anticoagulation or intermediate-dose thromboprophylaxis in COVID patients without a definite diagnosis of thrombosis is still controversial. While we await further data from current clinical trials, a reasonable approach is to continue with regular dose thromboprophylaxis in all hospitalized patients and to provide therapeutic anticoagulation only in patients with confirmed thrombotic events.

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