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Life-threatening retroperitoneal bleeding in coronavirus disease 2019 patient while on full dose anticoagulation: A case report

Kirandeep Kaur, Dennis M Starr

ABSTRACT

Introduction: Thromboembolism is one of the common complications in patients presenting with coronavirus disease 2019. Studies on coronavirus disease 2019 patients recommend the use of anticoagulation to prevent thrombotic complications in these patients and have shown to decrease mortality. However, spontaneous retroperitoneal bleeding is one of the life-threatening complications of therapeutic anticoagulation.

Case Report: This case report is about an 82-year-old male who was admitted for coronavirus disease 2019 pneumonia, started on therapeutic dose anticoagulation on presentation, and developed life-threatening retroperitoneal bleeding. He was managed with conservative treatment because of the advanced age of the patient, high risk of deterioration, and guarded prognosis.

Conclusion: Although anticoagulation protects against the thrombotic complications of coronavirus-19 infection, it has life-threatening bleeding complications. The use of anticoagulation in these patients should be practiced with caution while monitoring for bleeding complications. There needs to be more clinical studies and trials to assess the risk-benefit ratio of anticoagulation in coronavirus disease 2019 patients.

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INTRODUCTION

Spontaneous retroperitoneal bleeding is described as bleeding in retroperitoneal space without any trauma or iatrogenic manipulation [1]. Various risk factors like anticoagulation therapy, antiplatelet therapy, advanced age, and hypertension are associated with spontaneous retroperitoneal bleeding [1–3]. Patients most commonly complain of acute onset abdominal pain and sometimes hip, flank, and/or back pain. Other complaints include symptoms associated with acute blood loss or hypovolemia and visible flank bruising or discoloration [1, 3, 4]. There have been reports of retroperitoneal bleeding in COVID-19 patients while on anticoagulation therapy [2, 4–6]. COVID-19 causes an increased risk of thrombosis and it has been recommended to use anticoagulation therapy to prevent these severe complications [7, 8]. But there is also an increased risk of bleeding complications with anticoagulation. This is a case report of a COVID-19 positive patient who developed retroperitoneal bleeding while he was on anticoagulation therapy in the hospital.

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CASE REPORT

An 82-year-old male with a history of essential hypertension, prostate cancer, and nephrolithiasis presented with generalized weakness, shortness of breath, and non-productive cough for 4–5 days. Nasopharyngeal swab for reverse transcriptase polymerase chain reaction was positive for COVID-19. He was started on low flow oxygen therapy, dexamethasone, and remdesivir. Computed tomography angiography (CTA) of the chest showed no evidence of pulmonary embolism. He had elevated d-dimer levels, 1.52 ug/mL FEU (Table 1), and was started on a therapeutic dose of low molecular weight heparin (1 mg/kg every 12 hours). His oxygen requirements were improving gradually during the hospital course. Then, he was found to have two minor episodes of epistaxis. Antiplatelet therapy (aspirin) was held and his therapeutic dose of low molecular weight heparin (LMWH) (1 mg/kg every 12 hours) was decreased to the prophylactic dose of LMWH for venous thromboembolism (40 mg once daily) on the 10th day of hospitalization. He also started complaining of pain in the abdomen and right hip region and had two episodes of orthostatic hypotension. His hemoglobin dropped significantly from 14.7 to 11.4 g/dL (Table 1). No obvious source of bleeding was found except for two minor episodes of epistaxis he had a few days back. Computed tomography (CT) of the abdomen and pelvis (Figure 1) was performed to look for any intra-abdominal pathology which showed prominent acute retroperitoneal bleed with involvement of right psoas muscle, extending from right posterior pararenal space to lower pelvis with some acute bleed and stranding seen along the root of mesentery artery and presacral space. Anticoagulation was held on the evidence of retroperitoneal bleeding on the 12th day of hospitalization. Interventional radiology was consulted to evaluate the patient for any therapeutic intervention. No intervention was performed due to the advanced age of the patient, high risk of deterioration, and guarded prognosis. He was managed conservatively for the retroperitoneal bleed by discontinuing anticoagulation and transfusing packed red blood cells (PRBCs) for the patient. He required 4 units of packed red blood cells during his hospital course. He also developed acute kidney injury (baseline creatinine 1.1–1.2 mg/dL) with creatinine increase from 1.1 to 2.6 mg/dL (Table 1) on the 11th day of hospitalization, reaching a maximum up to 4.2 mg/dL on the 13th day (Table 1) and then started improving after intravenous (IV) fluids and blood transfusion. Nephrology was consulted for acute kidney injury (AKI) and most likely AKI was secondary to hypovolemia (pre-renal cause). Fortunately, the patient improved gradually, and his hemoglobin was stable after discontinuing anticoagulation.

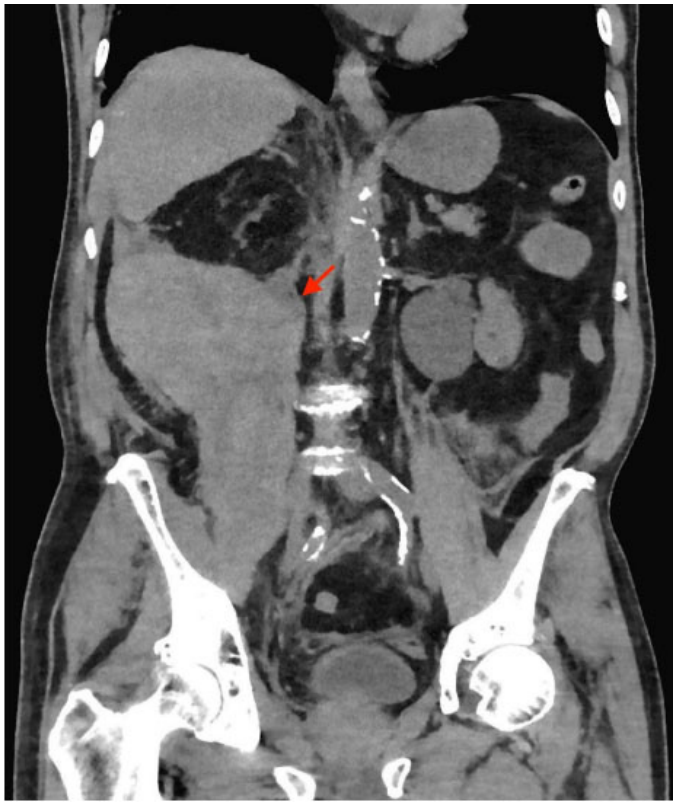

Figure 1: CT abdomen coronal view showing large right retroperitoneal bleeding (red arrow) with involvement of right psoas muscle.

DISCUSSION

Retroperitoneal bleeding can be caused by various causes including traumatic, iatrogenic, and spontaneous causes [1, 2]. Spontaneous retroperitoneal bleeding is comparatively less common and usually reported in elderly patients. Vessels usually implicated in retroperitoneal bleeding include lumbar arteries, renal artery, and superior gluteal artery [1]. Anticoagulation therapy is one of the risk factors for spontaneous retroperitoneal bleeding [1–3].

COVID-19 infection involves an increase in inflammatory markers and an increased risk for various thrombotic complications [8]. Increased d-dimer level has also been associated with an increased incidence of thrombotic events. It is recommended to use therapeutic dose anticoagulation (LMWH or Unfractionated Heparin) in noncritically ill hospitalized COVID-19 patients with d-dimer levels above the upper limit of normal and who require low flow oxygen [7]. Studies on COVID-19 patients have shown decreased mortality in these patients when they were treated with a therapeutic dose of anticoagulation to prevent thrombotic complications [8]. In contrast, there are several studies that demonstrated increased bleeding complications in COVID-19 patients when they are treated with anticoagulation to prevent thrombotic complications. Retrospective analysis of 355 COVID-19 patients by Musoke et al. [9] showed an increased risk of major bleeding with therapeutic anticoagulation in COVID-19 patients. A previous case report by Patel et al. [4] described a COVID-19 patient

who developed life-threatening psoas hematoma after he was started on therapeutic anticoagulation in hospital. Mahboubi-Fooladi et al. [6] described five COVID-19 patients who received anticoagulation therapy and developed retroperitoneal bleeding during 7–11 days after admission.

This patient on presentation to the hospital was diagnosed with COVID-19 infection. Computed tomography angiography (CTA) of the chest showed no evidence of pulmonary embolism but he had an elevated level of d-dimer (Table 1) and was requiring low flow oxygen therapy. As per National Institutes of Health (NIH) COVID-19 treatment guidelines, he was started on a therapeutic dose of anticoagulation [7]. Retroperitoneal bleeding was suspected when he started having abdominal and hip pain with symptoms of hypovolemia and a drop in hemoglobin. Computed tomography scan (CT scan) of the abdomen (Figure 1) showed evidence of acute retroperitoneal bleed with involvement of the right psoas muscle.

In regard to the management of retroperitoneal bleeding, discontinuation of anticoagulation and antiplatelet therapy, blood transfusion, volume resuscitation, and supportive measures are the initial steps [4, 10]. Surgical intervention for retroperitoneal bleeding management is a risky procedure as it can lead to further unstoppable bleeding. Arterial embolization is selectively used in some cases [10]. However, this patient was managed conservatively without any intervention as he was deemed to be at risk of further deterioration. The patient was monitored over the next few days and fortunately, he improved with conservative management.

On presentation to the hospital, our patient was considered at low risk of bleeding as he had no history of renal disease or coagulopathy. Disseminated intravascular coagulation (DIC) is considered to be another differential diagnosis as an underlying cause of bleeding in COVID-19 patients [11]. This patient had a decreasing trend of C-reactive protein (Table 1) and stable platelet count during 1–11 days (Table 1) after admission and he was found to have retroperitoneal bleeding on day 12. As he had decreasing level of inflammatory marker and normal platelet count, DIC seems to be an unlikely cause of bleeding in this patient. Heparin-induced thrombocytopenia (HIT) cannot be considered as the underlying cause of bleeding in this patient as he had normal platelet count on day 11 (Table 1).

It is debatable to say that anticoagulation therapy was the sole reason for spontaneous retroperitoneal bleeding in this patient as he had other risk factors like antiplatelet therapy, advanced age, and hypertension which might have played a role in increasing propensity for retroperitoneal bleeding and the anti-factor Xa activity testing was not done in this patient. Also, Erdinc et al. [12] reported a COVID-19 patient who was not on anticoagulation therapy and developed spontaneous retroperitoneal bleeding.

Table 1: Laboratory results

Day of hospitalization →	On admission	On 7th day	On 9th day	On 11th day	On 12th day	On 13th day	On 15th day	On 17th day	On 19th day
Hemoglobin (g/dL) reference value: 13.6–17.3	13.6	14.2	14.7	11.4	9.0	11.2	9.2	8.3	8.9
Platelets (1000/uL) reference value: 166–383	324	469	369	349	300	184	150	131	148
Creatinine (mg/dL) reference value: 0.7–1.3	1.4	1.1	1.1	2.6	3.1	4.2	2.9	1.6	1.6
D-Dimer assays (ug/mL FEU) reference value: 0.06–0.48	1.52	–	–	–	–	–	–	–	–
International normalized ratio reference value: 0.82–1.19	–	–	–	–	–	–	–	–	–
Prothrombin time (seconds) reference value: 12–15	–	–	–	–	15.2	–	–	–	–
C-reactive protein (mg/L) reference value: 0–5	17.3	8.7	–	–	–	–	–	–	–
Ferritin (ng/mL) reference value: 21.8–274.7	595.8	–	–	–	–	–	–	–	–

CONCLUSION

In conclusion, we have limited data on the use of anticoagulation therapy in COVID-19 patients. There needs to be more clinical studies and trials to assess the risk-benefit ratio of anticoagulation in COVID-19 patients. Although anticoagulation therapy is helpful to prevent and treat the thrombotic complications of COVID-19, patients should be closely monitored for any symptoms of retroperitoneal bleeding.

Disclaimer: The contents do not represent the views of VA or the United States Government.

The work has been approved by the appropriate VA IRB committee related to James H. Quillen Veterans Affairs Medical Center.

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Author Contributions

Kirandeep Kaur – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Dennis M Starr – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

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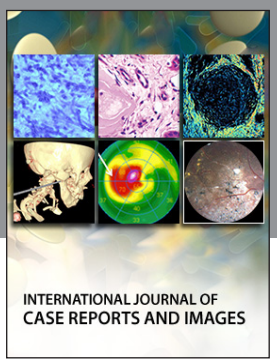
Written informed consent was obtained from the patient for publication of this article.

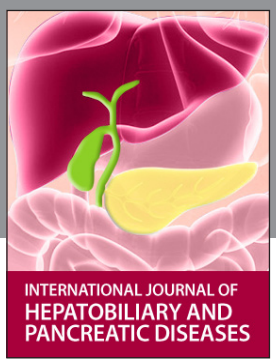
Conflict of Interest

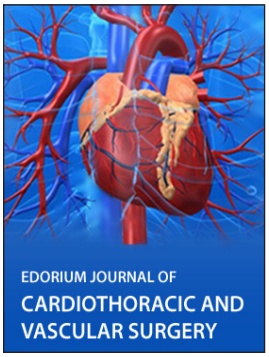
Authors declare no conflict of interest.

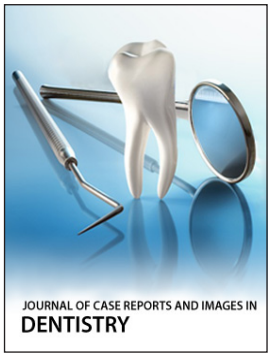
Data Availability

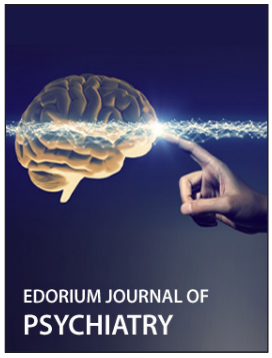
All relevant data are within the paper and its Supporting Information files.

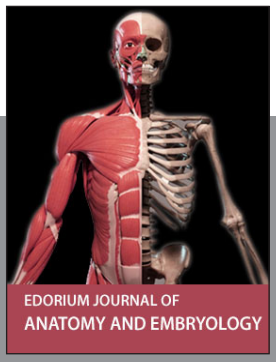


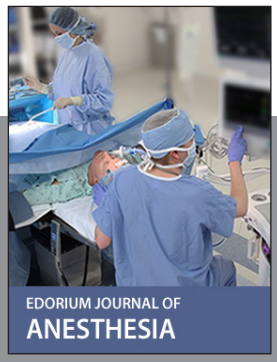












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