Title: Splenic Rupture in a COVID-19 Patient – Case Report

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Highlights:

- Presentation of a unique case of COVID-19 complicated by non-traumatic splenic rupture
- Diagnostic dilemma of conflicting coagulation studies in a COVID-19 patient with chronic renal failure requiring hemodialysis and valve replacement requiring warfarin therapy, leading to splenic rupture, a complication that is associated with hypocoagulable state
- Highlights possibility of fatal splenic rupture in COVID-19 patients with comorbid renal disease and complex coagulation states, reminding clinicians that rapid diagnosis and surgical correction can be life-saving

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Authors Contribution Statement:

Contributor Role	Role Definition	Authors 1	2	3	4	5	6
Conceptualization	Ideas; formulation or evolution of overarching research goals and aims.	X	X	X			
Data Curation	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse.	X					
Formal Analysis	Application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data.						
Funding Acquisition	Acquisition of the financial support for the project leading to this publication.						
Investigation	Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection.	X					
Methodology	Development or design of methodology; creation of models						
Project Administration	Management and coordination responsibility for the research activity planning and execution.	X					
Resources	Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools.						
Software	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components.						
Supervision	Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team.		X				
Validation	Verification, whether as a part of the activity or separate, of the overall replication/reproducibility of results/experiments and other research outputs.		X				
Visualization	Preparation, creation and/or presentation of the published work, specifically visualization/data presentation.	X		X			
Writing – Original Draft Preparation	Creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation).	X					
Writing – Review & Editing	Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre- or post-publication stages.		X	X			

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Discussion points:

1. A case of non-traumatic splenic rupture occurred In a COVID-19 patient with chronic renal failure and fluctuating coagulation studies while receiving therapeutic warfarin.
2. In high-risk patients with COVID-19, everyday activities which increase intra-abdominal pressure, such as sneezing, coughing, and defecation, can trigger splenic rupture, with fatal results; a high index of suspicion can be life-saving.
3. In patients with COVID-19, non-traumatic splenic rupture should be considered as one of the differential diagnosis in patients who present with abdominal pain and early recognition of the same, owing to a high index of suspicion, can be lifesaving.

ABSTRACT:

Background: It is well known that Coronavirus disease 2019 (COVID-19) causes coagulation changes, requiring frequent monitoring for potential sequelae such as myocardial infarction and stroke. Non-traumatic splenic rupture is a rare and poorly understood occurrence in the clinical setting. Possible causes of nontraumatic splenic rupture include neoplasm, infection, inflammatory disease, iatrogenic and mechanical causes. Furthermore, increased intrasplenic tension, increased abdominal pressure, and thrombotic vascular occlusion are three possible mechanisms.

The Case: We report a case of splenic rupture in a COVID-19 patient. Our patient was a 52 year old black man, presenting with diarrhea and moderate dyspnea, who was found to be COVID-19 positive. He had a past medical history significant for end-stage renal disease, chronic anemia, and aortic valve replacement. In an otherwise uneventful, 7-day hospital course, the patient's stay abruptly resulted in a nontraumatic splenic rupture and demise. In this report, we have evaluated the likelihood of COVID-19 causing splenic rupture in a patient with no prior splenic disease.

Conclusion: This case highlights the possibility of splenic rupture in otherwise normally recovering COVID-19 patients, particularly in the presence of comorbid conditions of renal failure and anticoagulation, with increased abdominal pressure during routine defecation. This information may assist in furthering the pathophysiology of COVID-19 and its life-threatening complications. In patients with COVID-19, non-traumatic splenic rupture should be considered as one of the differential diagnosis in patients who present with abdominal pain and early recognition of the same, owing to a high index of suspicion, can be lifesaving.

Key Words: case report, COVID-19, splenic rupture

INTRODUCTION.

While Coronavirus disease 2019 (COVID-19) is known to present with significant pulmonary and cardiac manifestations, other systemic complications and interactions with pre-existing pathology are being recognized.[1] As the pandemic has evolved, hypercoagulability and microvascular changes are becoming more prevalent causes of mortality.[2] Here we describe a case of nontraumatic splenic rupture in a COVID-19 patient being treated with anticoagulants and routine hemodialysis. Atraumatic splenic rupture is exceedingly rare and a potentially fatal condition. Causes of atraumatic splenic rupture include neoplasms, infection, iatrogenic, mechanical and inflammatory states.[3] This case illustrates how interactions with chronic renal disease and anticoagulation use may be important considerations in the treatment of complicated COVID-19 patients.

THE CASE.

History of Present Illness: A 52-year-old black male presented to the Emergency Department with a chief complaint of diarrhea for 1 day followed by moderate dyspnea. At the time of admission, the BUN/Cr ratio was 44/11.3, and on admission, the SARS-CoV-2 Antigen by IFA (in-house, Sofia) was positive. The patient was afebrile (36.9 °C), and the oxygen saturation was 100% on room air.

Past Medical History: He had a past medical history of hypertension, hepatitis B (2006), end-stage renal disease (2005), hyperlipidemia, severe anemia (2008), and aortic valve replacement (2019). Current medications included warfarin (10mg daily, in addition to supplemental 5mg on M/W/F) due to past mechanical aortic valve replacement. The patient's goal INR was 2.5-3.5. The patient has a history of hemodialysis noncompliance and often did not attend the recommended treatments. From laboratory data in 2019, the patient's average BUN/Cr was 34.2/6.5, respectively. Patient denied any recent travel. He did not have any personal or family history of leukemia, lymphoma, coagulopathies, DVT/PE, auto-immune pathology, or other neoplasms.

Investigations: Laboratory results on admission were significant for pancytopenia, elevated inflammatory markers, and elevated coagulation studies. From laboratory data in 2019, the patient had a history of leukopenia, anemia, platelet count of 160.7 ($10^3/\mu L$), and an average Hgb/Hct of 8.2/25.6 (g/dL/%), repectively. Physical exam revealed normal lung sounds, no hepatosplenomegaly, or lymphadenopathy. Prior to this current admission, the patient was evaluated for further renal disease progression in December 2018. There was no evidence of splenic injury or splenomegaly on the 2018 abdominal CT. The patient's pancytopenia was evaluated during his stay at the hospital; both nutritional and viral etiologies, as well as bone marrow failure, were ruled out with appropriate investigations, as shown in Table 1. Peripheral smear was unremarkable.

Hospital Course: On the second day of admission the patient received dialysis, and over the next six days underwent a total of three hemodialysis treatments coupled with three separate packed RBC transfusions because of his severe anemia. His chest radiograph remained clear and diarrhea subsided by Day 2. Due to the belief that the patient's symptoms were due to COVID-19 initially, no abdominal imaging was performed on admission. On Day 5 the INR increased to 5.13 and remained above therapeutic range (2.5-3.5) for the remainder of his hospital course. After the patient's increase in coagulation studies, his regular warfarin treatment regimen (10mg daily, in addition to supplemental 5mg on M/W/F) was discontinued on day 6.

On the eighth inpatient day, when attempting defecation, the patient felt a "pop" and developed tearing and burning LLQ flank pain at 8:00. This bowel movement was blood-tinged and loose. His abdominal

pain progressed throughout the day, and at 16:00, the internist's physical examination revealed a firm abdomen with no rebound tenderness. CT scan of the abdomen was compatible with acute splenic hemorrhage. Before emergency splenectomy could be performed, the patient became hypotensive, developed cardiac arrest at 18:55, and expired at 19:12.

The abdominal CT detected a large amount of heterogenous material surrounding the spleen with small to moderate amount of free fluid around the spleen, compatible with acute splenic hemorrhage as shown in Figure 1. Due to abrupt onset of acute intra-abdominal hemorrhage, the patient died prior to splenectomy or other life-saving interventions. No autopsy was performed.

Throughout the patient's stay, he received the standard in-house COVID-19 treatment including five days of Ascorbic acid (50 mL 2000mg/4 mL IV), Thiamine HCl (2mL 200 mg/2 mL IV), and Zinc Sulfate (20 mg oral QD), along with his continued warfarin anticoagulation as previously prescribed until its discontinuation on day 6.

DISCUSSION.

We believe this case of non-traumatic splenic rupture in a COVID-19 patient was caused by interactions from COVID-19-related coagulation changes. Based on recent data, COVID-19 has been shown to cause both hypercoagulable and hyperfibrinolyic states in patients.[2] Because our patient was on chronic warfarin therapy and reached supratherapeutic levels during hospital days 5-8, we believe the effects of COVID-19 affected our patient's coagulability and possibly led to his hemorrhagic state and splenic rupture.

While the exact etiology of nontraumatic splenic rupture is not fully understood, three possible mechanisms could explain this patient's unfortunate clinical course: increased intrasplenic tension, increased abdominal pressure, and altered coagulation.[4] We believe the supratheraputic warfarin levels and hyperfibrinolytic state caused by COVID-19 led to our patient's altered coagulation studies. The process of defecation is a known inciting event for splenic rupture due to the rising intrabdominal pressure and stretching of the splenocolic ligament causing rupture of pre-existing subcapsular hematoma. While the patient had no evidence of pre-existing splenic hematoma or splenomegaly, we believe this was the chief inciting event leading to splenic rupture.[5]

It is relevant to eliminate the other causes of nontraumatic splenic rupture. Because our patient did not receive an autopsy following his death, we cannot be certain that our patient didn't have an underlying primary splenic neoplasm (i.e. splenic marginal zone lymphoma) or primary myelofibrosis. However, these etiologies are extraordinarily rare.[6] Our patient did not present with any clinical or laboratory findings suggestive of an underlying hematological malignancy, and there was no hepatosplenomegaly, enlarged lymph nodes, or systemic B symptoms. Mature B or T cell leukemias are unlikely because the patient's lymphocyte count is within normal range. Hairy cell leukemia can be ruled out because peripheral blood smear typically reveals a pancytopenia with monocytopenia. Primary myelofibrosis typically presents with an enlargared spleen and liver with tear drop cells on blood smear, which was not detected in our patient. Epstein Barr Virus and Cytomegalovirus are not suspected due to absence of atypical lymphocytes and leukocytosis.

Even though microvascular changes, coagulation changes, and defecation can be regarded as the principal causes of splenic rupture in this case, the consequences of repetitive hemodialysis from CRD cannot be overlooked. This is a rare reported complication of hemodialysis, and its exact incidence is not known. However, in a previous study of nontraumatic splenic rupture in a hemodialyzed patient, important risk factors included use of anticoagulants during hemodialysis, uremic coagulopathy, susceptibility to infections, and impaired immune function. These risk factors can occur as long-term complications of hemodialysis, but they are also complications of severe coronavirus infection, which paradoxically is

associated with coagulation changes.[7] The exact etiology and pathogenesis cannot be confirmed due to lack of autopsy, but because of the extremely low incidence of splenic rupture due to hemodialysis, and the absence of known risk factors in our patient (e.g., infectious mononucleosis, hematologic disease, splenomegaly, neoplasm), we believe COVID-19 infection is a contributing cause of splenic rupture in our patient.

There have been other recently reported cases of nontraumatic splenic rupture in the setting of COVID-19. Research demonstrates COVID-19 has a direct effect on the body's secondary lymph tissue. Following these studies, there is further reason to suspect the virus has the potential to have a direct effect on the spleen by causing "lymphoid follicle attrition and nodular atrophy in addition to microvascular thrombosis and necrosis," as stated in a case report by Shaukat, I. and the British Infection Association.[8]

In monitoring COVID-19 progression, clinicians monitor inflammatory markers, such as C-reactive Protein (CRP), Lactate dehydrogenase (LDH), ferritin, lymphocytes, etc. As shown in Table 1, several other laboratory values are now closely monitored to evaluate the coagulation changes related to the COVID-19 pathogenesis including d-dimer, fibrinogen, prothrombin time, partial thromboplastin time, platelet count, and other specific quantifications such as calcium.[9] Although the mechanism is still unknown, elevated coagulation markers support studies documenting many critically ill COVID-19 patients who suffer from a thrombotic microvascular event.[10] Studies have suggested that in the setting of COVID-19, symptoms such as abdominal pain may be an indication for abdominal CT scan on admission and frequent monitoring throughout the patient's disease progression. In a case of splenic rupture in Poursina Hospital in Rasht, Iran, a COVID-19 patient had vague abdominal symptoms and subsequent signs of decompensation. Urgent laparotomy was performed, revealed atraumatic splenic rupture, and splenectomy was performed. Fortunately, the acuity of these physicians' actions were able to save their patient's life.[11]

Due to the multisystem involvement of COVID-19, coagulation studies are becoming increasingly relevant in that the virus can cause both hypercoagulable and hemorrhagic changes. We are assuming that our patient's hyperfibrinolytic state led to his splenic hemorrhage. While coronavirus remains a heavily studied topic both microbiologically and clinically, it is pertinent that clinicians grow more cognizant of emerging complications related to COVID-19. This case highlights the importance of monitoring coagulation studies while maintaining a high index of suspicion for rare but life-threatening intra-abdominal complications. In patients with COVID-19, non-traumatic splenic rupture should be considered as one of the differential diagnosis in patients who present with abdominal pain and early recognition of the same, owing to a high index of suspicion, can be lifesaving.

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FIGURES AND TABLES.

Figure 1. Abdominal CT confirming splenic rupture

Impression Per Radiology:

1. Large amount fo heterogenous material surrounding the spleen with small to moderate amount of free fluid in the abdomen compatible with acute splenic hemorrhage.
2. Renal findings compatible with autosomal dominant polycystic kidney disease.
3. Small bilateral pleural effusions, greater on the left.
4. Atherosclerosis.

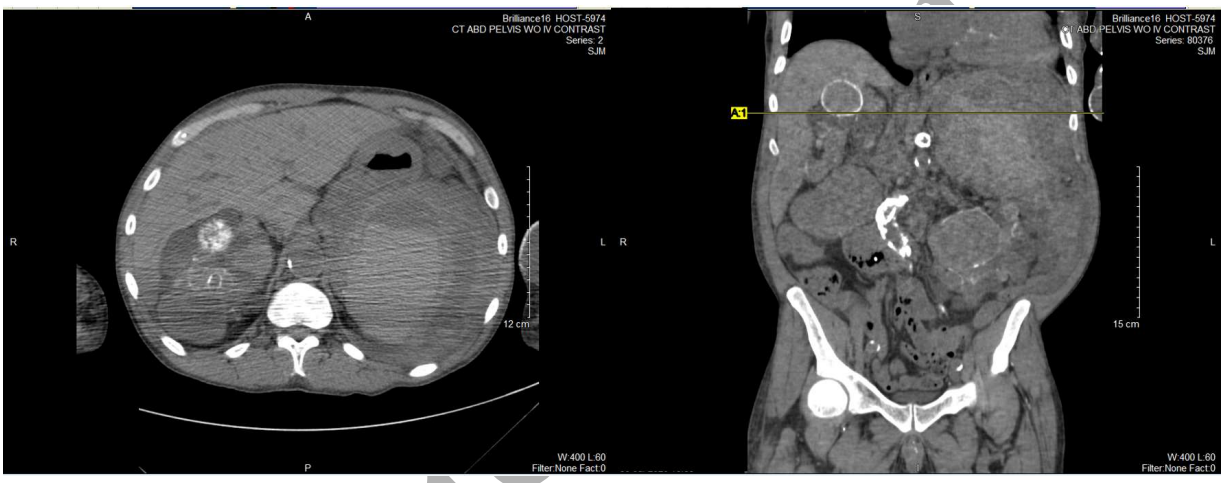

Table 1. Inpatient laboratory values

	Ref. Range	Day 0	D1	D2	D3	D4	D5	D6	D7
WBC ($10^3/\mu L$)	4.5-10.4	1.5	1.6	1.7	1.8	2.8	3.5	5.2	5.4
RBC ($10^6/\mu L$)	3.7-5.3	2.41	2.37	2.11	2.29	2.10	1.64	2.04	1.91
Hgb (g/dL)/HCT (%)	11.0-16.0/35.0-47.0	7.8/23.5	7.4/22.9	6.6/20.8	6.9/22.2	6.5/20.4	5.2/16.5	6.5/19.9	6.0/18.2
Platelet ($10^3/\mu L$)	140-440	54	62	60	59	76	68	72	69
INR		2.93	--	2.24	2.22	2.84	5.13	4.65	4.73
PT (s)	9.8-11.6	29.8	--	23.1	22.9	28.9	50.8	46.2	47
aPTT (s)	23.1-31.6	56.6	--						
AST (unit/L)	2-33	24							
ALT (unit/L)	13-61	12							
Albumin (gm/dL)	3.4-5	2.7							
Ferritin (ng/mL)	8.0-252.0	2184.6	--						
CRP (mg/L)	0.0-3.0	24.5	--						
Procalcitonin (ng/mL)	<0.10	0.52	--						
Sed Rate (mm/h)	0-30	53	--						
D-dimer	0.19-0.5	2.92	--						
LDH (unit/L)	87-241	360	--						
BUN/Cr	7-18/0.6-1.3	44/11.3	--						
Lymphocyte (%)		25.5	43.0	36.5	32.6	27.3	25.1	22.9	16.5
Monocyte (%)		9.4	13.3	17.1	11.4	9.1	13.6	12.9	11.9