CASE REPORT

Triple whammy in a patient with portal vein thrombosis

Elamein Yousif[1,*], **Elamin Dahawi**[2], **Sarah Premraj**[3], **Wissem Melki**[2]

[1] Derriford Hospital, University Hospitals Plymouth NHS foundation Trust, Plymouth, UK. [2] Al-Ahli Hospital, Doha, Qatar. [3] East Suffolk and North Essex NHS Foundation Trust, Colchester, Essex, UK.

*Correspondence: Elamein Yousif, Derriford Hospital, University Hospitals Plymouth NHS foundation Trust, 11 Research Way, Plymouth PL6 8BT, UK. Email: elamein.yousif@nhs.net

How to cite this article: Yousif E, Dahawi E, Premraj S, Melki W. Triple whammy in a patient with portal vein thrombosis. Arch Clin Cases. 2024;11(1):16-18. doi: 10.22551/2024.42.1101.10280

ABSTRACT

Infection with SARS-CoV-2 has been shown to predispose to thromboembolic events. The risk of such thromboses further increases in those with underlying inherited or acquired prothrombotic states. The authors present a 30-year-old lady who developed acute abdominal pain, three days after recovery from a mild COVID-19 infection. She was also using oral contraceptive pills. Laboratory investigations revealed elevated inflammatory markers, and a contrast-enhanced abdominal CT scan demonstrated portal vein thrombosis (PVT). Due to the unusual site of thrombosis, a thrombophilia screen was performed, which detected a heterozygous Factor V Leiden mutation (FVL). Thus, her PVT was attributed three simultaneous risk factors, namely COVID-19 infection, OCP use and FVL mutation. She was initiated on anti-coagulation, with which she improved significantly. In patients presenting with thromboses at uncommon sites, investigation for evidence of recent Covid-19 infection and screening for inherited and acquired thrombophilia should be considered, while discontinuing any offending medications.

KEYWORDS: SARS-CoV-2; COVID-19; portal vein thrombosis; Factor V Leiden mutation; oral contraceptive

INTRODUCTION

The novel coronavirus SARS-CoV-2 (COVID-19) has been the focus of attention of healthcare professionals, and indeed the entire world, since late 2019. Although primarily a respiratory virus causing manifestations ranging from mild patchy pneumonia to severe respiratory failure, a plethora of extrapulmonary manifestations have been reported. Several reports of thromboembolic complications following infection with Covid-19 have been published, the commonest being pulmonary embolism. However, thrombosis in other locations is relatively uncommon.

CASE PRESENTATION

A 30-year-old lady of Mediterranean origin, presented to the Emergency Department with abdominal pain of six days duration. The pain was sudden in onset, gradually progressive, with a score of 9/10 on the VAS. It was localized to the epigastrium and right upper quadrant, with no radiation. She did not report any fever, vomiting, diarrhea, or distention. Her history was notable for a mild infection with COVID-19, ten days prior to this hospitalization, during which she experienced flu-like symptoms. She underwent self-isolation at home, with an uneventful clinical course, following which she tested negative on Day 7. She was on a Combined Oral Contraceptive Pill (COCP - *Yasmin* 0.03 mg/3 mg of ethinylestradiol/drospirenone) for polycystic ovarian syndrome (PCOS), which she been on for the past 7 years. She had no other significant past surgical or family history.

On examination, she was in pain and dehydrated, with heart rate 108/minute, respiratory rate 20 breaths/min, blood pressure 110/78 mmHg, and oxygen saturation of 98% on room air. There was no pallor, jaundice, or edema. On examination of her abdomen, there was exquisite tenderness and voluntary guarding over the epigastrium and right upper quadrant, with no hepatomegaly or evidence of ascites. Per rectal examination was normal, with no melena.

Laboratory investigations are shown in Table 1. She had a raised CRP, elevated d-dimer levels, with normal WBC counts, LFT, and U&E. She was admitted and commenced on intravenous proton pump inhibitor, fluids, and pain relief measures. However, she continued to be symptomatic and hence an abdominal CT scan was performed, which revealed a slightly hyperdense appearance of the portal vein. A subsequent Contrast enhanced CT scan (CECT) showed a mildly enlarged liver with signs of complete thrombosis of the left portal vein and its branches. The main portal vein and the right portal vein were normal with normal enhancement and no obvious filling defect. There was no evidence of cirrhosis (Figure 1). CT pulmonary angiogram showed no evidence of pulmonary embolism.

She was started on Enoxaparin, 60 mg, subcutaneously, twice daily, and hydration was continued. The COCP was

Received: February 2024; **Accepted after review:** March 2024; **Published:** March 2024.

Table 1. Laboratory investigations.

Lab investigation	Result		Reference range
	At admission	After 3 weeks	
White blood cell count (103/uL)	4.12	5.31	4.00-11.00
Hemoglobin (g/dL)	15.5	15.0	12.00-14.50
Platelet count (10e3/uL)	266	284	150-450
C-Reactive Protein (mg/L)	35	<3	0-10
Creatinine (umol/L)	56	-	53-115
Sodium (mmol/L)	135	-	136-145
Potassium (mmol/L)	4.2	-	3.6-5.1
Bicarbonate (mmol/L)	25	-	22-32
ALT (SGPT) (IU/L)	23	26	12-78
AST (SGOT) (IU/L)	19	20	15-37
Alkaline phosphatase (IU/L)	62	81	45-117
Lipase (U/L)	245	-	73-393
Amylase (U/L)	102	-	25-115
Prothrombin Time (seconds)	10.3	10.8	8.41-12.00
INR	0.96	0.96	
Partial Thromboplastin Time (seconds)	28.2	27.6	24.50-32.80
d-dimer (mg/L)	2.14	0.29	0.00-0.53
Factor V Gene Mutation (Leiden Mutation)	Heterozygous (Mutation detectable on one allele)	-	
Lupus Anticoagulant (LAC)	Negative	-	Negative
Factor II Gene Mutation (Prothrombin gene mutation)	Wild type (no mutation present)	-	
Protein C	0.33	0.81	0.69-1.56
Protein S	39%	62%	60-114
Anti-nuclear antibody screen	1.4	-	<20 CU
Anti-Cardiolipin antibodies (IgM & IgG)	Negative	-	

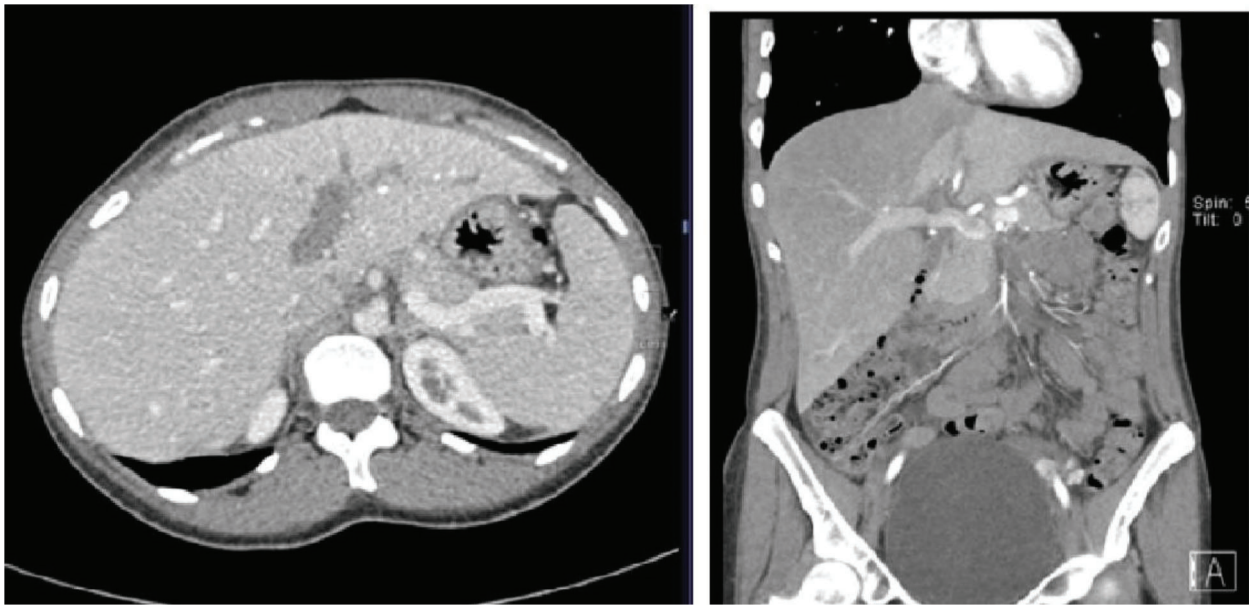

Fig. 1. Contrast enhanced CT scan of the abdomen demonstrating Left Portal Vein Thrombus.

discontinued. After consultation with the hematology team, it was decided to perform a screen for thrombophilia, since the site of thrombosis was unusual. This revealed a Heterozygous Factor V Leiden mutation, while being negative for Anti-cardiolipin antibodies, Lupus Anti-coagulant, and Anti-Beta-2 Glycoprotein antibodies. Protein-C and Protein-S were also low initially, however they normalized when repeated at follow-up, possibly after discontinuation of the OCP. Methyl-enetetrahydrofolate reductase (MTHFR) gene mutation was not investigated. Enoxaparin was continued for 5 days, after which she was initiated on Oral Rivaroxaban 15 mg, twice daily. She improved symptomatically and was discharged in a stable condition. At 3-weeks follow-up, she was completely asymptomatic, and was continued on Rivaroxaban 20 mg OD. She was educated regarding COCP being an important risk factor for the development of thromboses, especially given her underlying inherited thrombophilia. She was referred to the Gynecologist for further non-hormonal management of her PCOS, and for investigation of any underlying gynecologic malignancy that might have triggered her VTE.

She is under regular follow-up and is doing well on oral anti-coagulation, which she will continue for 6 months. Further duration of anti-coagulation will be determined after discussion in the MDT meeting (Gastroenterology/Hematology).

DISCUSSION

Thrombotic complications have been well established in SARS-CoV-2 infections, the commonest being acute pulmonary embolism (PE) and deep venous thrombosis (DVT). The coagulopathy associated with COVID-19 infection (CAC) has been attributed to several factors such as endothelial dysfunction, direct cytotoxicity of the virus and activation of pro-inflammatory cytokines [1]. Most cases of thrombosis occur in hospitalized patients with severe infections. Although the exact incidence of venous thromboembolism (VTE) following asymptomatic or mild infection is not known, there have been case reports of DVT, cerebral venous thrombosis and PE in such patients [2]. A cohort study from the UK established that a substantial risk of PE persisted until about 8 weeks after COVID-19 infection [3].

Portal vein thrombosis (PVT) is a rare cause of acute abdominal pain, and can be precipitated by various causes such as malignancies, auto-immune diseases, pancreatitis, and hypercoagulable states. There have been published reports of PVT occurring in hospitalized patients with COVID-19 [4-6]. Appenzellar et al reported a young male with extensive thromboembolism following asymptomatic COVID-19 infection, who was later found to have Factor V Leiden (FVL) mutation [7]. A cohort study by Stefely et al, concluded that there was a marked increase of Factor V activity in severe COVID-19 infection, especially in those who developed VTE [8]. Therefore, it is likely that those with a FVL mutation would be more predisposed to thrombotic events associated with COVID-19, than the general population [9].

Our patient was a young female, on the OCP, who recovered uneventfully from a mild COVID-19 infection. She presented 10 days later with acute portal vein thrombosis and her thrombophilia screen detected a heterozygous FVL mutation. The authors recognize OCP use as an important risk factor for thrombosis. However, portal vein thrombosis related solely to the use of oral contraceptives is rare. Denninger et al, based on their study of 36 patients with PVT, found that this condition was associated with one or more thrombophilic states in 26 out of 36 patients. They recommended screening for prothrombotic states in all cases of PVT, irrespective of other local predisposing factors or OCP use [10]. Hence, the multidisciplinary team concluded that this patient warranted a full thrombophilia study. According to the recommendations of the British society of Hematology: MPN panel should be performed in patients with full blood count abnormalities suggestive of a myeloproliferative neoplasm, genetic testing with JAK2 mutation in patients with splanchnic vein thrombosis is suggested in the absence of clear provoking factors and a normal FBC, and PNH testing may be considered in patients with thrombosis at unusual sites and abnormal hematological parameters [11]. Since our patients did not fit the above criteria, these investigations were not carried out.

CONCLUSION

The present case emphasizes the need to explore prior mild or asymptomatic COVID-19 as the etiology in those presenting with venous thromboembolism at any site. A thrombophilia screen should be considered in those with unusual sites of thrombosis, such as portal vein thrombosis, as this will be essential to guide the type and duration of anticoagulation. In all patients, a thorough medication history should be obtained, and offending drugs should be discontinued promptly.

Conflict of Interest statement

The authors do not have any conflict of interest.

Funding

None.

Consent

Written informed consent was obtained from the patient, and there are no patient identifiers in the submission.

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