Case report

Case of COVID-19 infection and polycythaemia presenting with massive acute pulmonary embolism

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SUMMARY

We are reporting a middle-aged male patient with polycythaemia vera comorbidity. The patient was exhibiting symptoms including fever, cough and shortness of breath and was found to have acute pulmonary embolism. He was diagnosed with SARS-CoV-2. This case suggests that a high index of suspicion should be taken into consideration for thromboembolic events, when treating patients with COVID-19 with breathing difficulty and low oxygen saturation levels, especially in those who have underlying predisposing conditions for coagulopathy.

BACKGROUND

The outbreak of SARS-CoV-2, characterised as pandemic by the WHO on 11 March 2020, has presented novel challenges for both the healthcare and public officials to manage its fallouts. It is presenting with diverse clinical manifestations in patients with pre-existing medical conditions. Polycythaemia rubra vera is rare in young populations. Any patient who contacts COVID-19 with a pre-existing hypercoagulable condition carries an increased risk of thrombotic complications. Prompt detection of life-threatening conditions like pulmonary embolism (PE) is important in decreasing mortalities.

CASE PRESENTATION

A 46-year-old expatriate man presented to a primary healthcare facility of Dubai Health Authority with a fever, cough and shortness of breath for 3 days. On initial examination, his pulse oximeter readings were recorded low at 84% saturation of oxygen. The patient's medical history includes type 2 diabetes mellitus requiring insulin, hypertension and polycythaemia vera (PV) (which was diagnosed 3 months prior to the current admission). Based on medical assessment, he was placed on supplemental oxygen therapy and transferred to the emergency department (ER) of Dubai Hospital in an ambulance.

A physical examination in ER revealed a well-built man who was conscious, alert and oriented to person, place and time. He was afebrile but tachypnoeic, with a respiratory rate of 28 breaths/min. Oxygen saturation was 96% on pulse oximetry while on 4 L/min of supplemental oxygen via face mask. His blood pressure was 100/67 mm Hg. Lower limb examination revealed that extremities were warm, and pulses felt equally bilaterally with fair volume. Chest auscultation was clear with no audible crackles or wheezing, and the air entry was good bilaterally. Other systemic examinations were unremarkable except for a finding of mild splenomegaly.

In view of the current pandemic, a chest X-ray was performed, which showed changes in favour of a diagnosis of COVID-19 infection.

A nasal swab was taken for the novel coronavirus test. Blood diagnostics results, presented in table 1, reveal a full blood count of haemoglobin 22 g/dL, haematocrit of 70.8%, white blood cell 7.8 $10^3/\mu$L, (neutrophil absolute 7.8 $10^3/\mu$L, lymphocyte absolute 0.3 $10^3/\mu$L), platelets 247 $10^3/\mu$L, blood glucose 425 mg/dL, ketones negative, N-terminal pro B-type natriuretic peptide (NT-proBNP) 307 pg/mL, procalcitonin 1.77 ng/mL, C reactive protein 78.1 mg/L, urea 86 mg/dL and normal creatinine. Subsequently, a throat swab sample for SARS-CoV-2 by real-time reverse transcription PCR came positive.

ECG indicated non-specific changes, though not the classical pattern of PE.

As his blood pressure further dropped to 86/64 mm Hg, the patient received a bolus of intravenous normal saline. Shortly, after the fluid infusion, his breathing difficulty increased, and he desaturated despite high flow of oxygen via a non-rebreather mask (15 L/min). He was put on a non-invasive mode of ventilation (continuous positive airway pressure (CPAP)). A CT pulmonary angiogram (CTPA) was requested immediately to rule out PE.

Arterial blood gas showed severe acidosis with pH 7.191, PCO_2 49 mm Hg, PO_2 50 mm Hg and HCO_3 18.1 mmol/L. A decision was made to proceed to venesection and adjust his non-invasive parameters. An estimated 1.25 litres of blood was removed and 2.5 litres of saline was infused during the procedure.

The CTPA (figure 1) revealed filling defects in the pulmonary artery of the right lower lobe and its multiple segments representing thrombosis. Also, thrombosis was noted in pulmonary artery segments on the left side, and cardiac chambers did not show enlargement of the right ventricle (RV). However, the transverse diameter of the main pulmonary artery at its bifurcation measured 31.9 mm, more than the transverse diameter of the aorta 29.5 mm, which signified pulmonary artery hypertension (figure 2).

Both lungs fields showed extensive patchy areas of ground-glass infiltrates consistent with known acute lung injury due to COVID-19 infection[1] (figure 3).

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Table 1 Biochemistry Tests

Blood test	Reference range	Date: 25 May 2020	Date: 28 May 2020	Date: 2 June 2020
WBC Count	3.6–11 10^3/µL	7.8	12.4	10.7
Neutrophil absolute	2–7 10^3/µL	7.8	11.4	9.8
Lymphocytes absolute	1.0–3.0 10^3/µL	0.3	0.5	0.5
Haemoglobin	13–17 g/dL	22	17.2	14.2
Haematocrit	40%–50%	70.8	54.5	45
RBC count	4.5–5.5 10^3/µL	9.76	7.65	6.19
Platelets	150–410 10^3/µL	247	246	295
CPK (Creatine Phosphokinase)	0–190 U/L	45	20	19
CK-MB (Creatine Kinase Myocardial Band)	0–24 U/L	18	14	17
Troponin	<14 ng/L	9		
Urea	12–40 mg/dL	86	47	20
NT-proBNP	<125 pg/mL	5307	4903	3589
K	3.3–4.8 mmol/L	5.5	3.8	3.5
Na	136–145 mmol/L	130	137	136
Cl	98–108 mmol/L	94	110	103
Bicarbonate (HCO_3)	20–28 mmol/L	21.1	18.9	24.8
Creatinine	0.7–1.2 mg/dL	1.1	0.3	0.2
Procalcitonin	<0.05 ng/mL	1.77	5	0.45
C reactive protein	<5.0 mg/L	78.1	18.2	30.1
Dimer	<0.05 µg/mL FEU	6.81	10.44	2.31
Fibrinogen	200–400 mg/dL	318.26	356.85	
Ferritin	30–400 ng/mL	366.8	238.9	244.9
Prothrombin time	9.7–11.4 s	29.3	16.3	27.6
INR*(International Normalized Ratio)	0.8–1.1	2.91	1.6	2.73
APTT (Activated Partial Thromboplastin Time)	27–40 s	67.1	44.9	60.2

*Creatine Kinase Myocardial Band
APTT, Activated Partial Thromboplastin Time; CK-MB, Creatine Kinase Myocardial Band; CPK, Creatine phosphokinase; INR, International Normalized Ratio; NT-proBNP, N-terminal pro B-type natriuretic peptide; RBC, red blood cell; WBC, white blood cell.

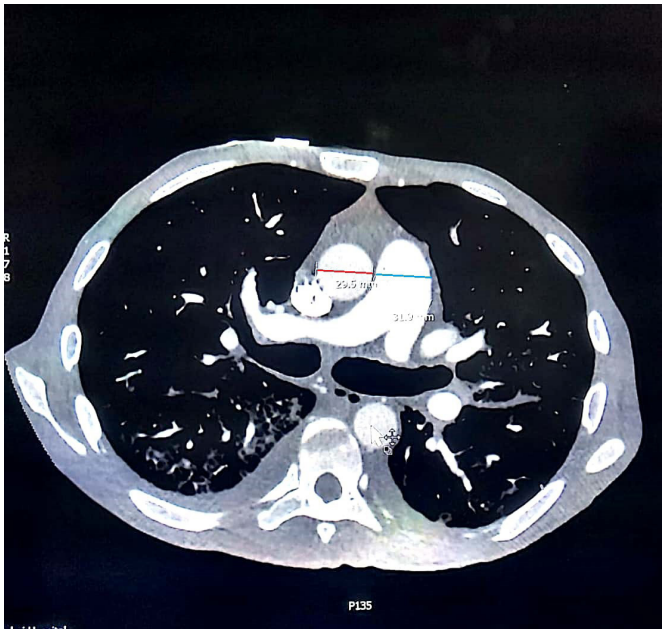

Figure 2 CT pulmonary angiogram showing the transverse diameter of the main pulmonary artery at its bifurcation measures 31.9 mm (blue line) and the ascending aorta measures 29.5 mm (red line).

The bedside echocardiogram revealed a dilated RV with global hypokinesis, which in context of high B-type natriuretic peptide and hypotension, signified RV stress.[2] The patient was given thrombolysis with alteplase 100 mg over 2 hours, followed by heparin infusion.[3] He received inotropic support as well in addition to routine intensive care support.

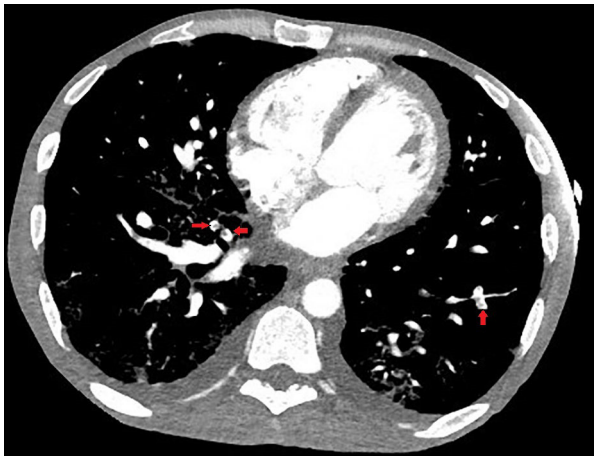

Figure 1 CT pulmonary angiogram showing multiple filling defects in right anterior descending and left posterior descending branches of pulmonary arteries.

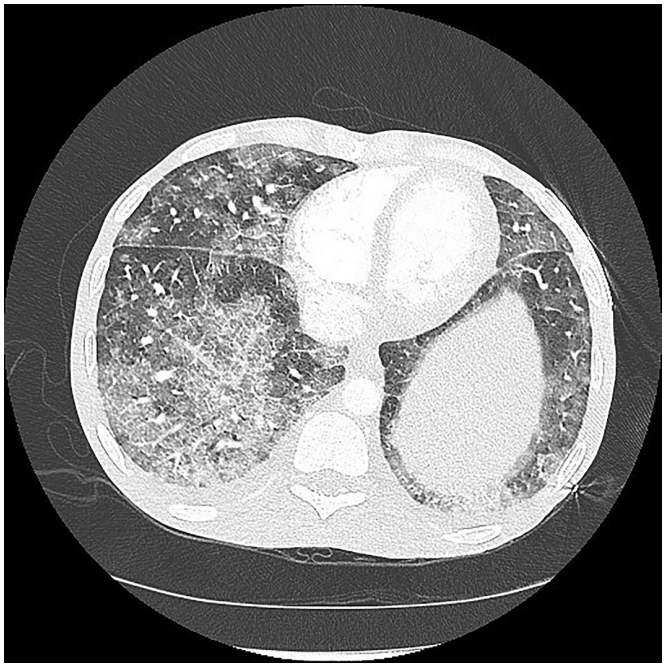

Figure 3 CT scan of lungs, bilateral peripheral and central patchy areas of ground-glass infiltrates consistent with known acute lung injury due to COVID-19 pneumonia.

OUTCOME AND FOLLOW-UP

The general condition of the patient improved gradually. He was weaned off from CPAP and supplemental oxygen. Similarly, his inotrope was tapered off as his blood pressure stabilised, recorded at 100/69 mm Hg. The patient was discharge from the hospital with advice of self-monitoring of capillary blood sugar at home and a follow-up visit to the haematology, cardiology and anticoagulation clinics for monitoring of INR. He was placed on medications, which include warfarin 5 mg once a day, hydroxyurea 1 g two times a day[4] and allopurinol 300 mg, along with subcutaneous insulin.

DISCUSSION

Our knowledge of SARS-CoV-2 (also known as COVID-19) is still limited and has been continuously evolving.[5] In the majority of patients, the disease has mild symptoms or no symptom at all.[6] However, in a minority of patients, the disease may progress very rapidly and takes an aggressive course. Its complications range from minor skin manifestations to pneumonia, acute respiratory distress syndrome, thromboembolic phenomena, such as acute myocardial infarction, stroke, PE, sepsis with multiorgan failure and even death in severe cases.[7 8]

COVID-19 is a highly infectious disease, and it is obvious from our current knowledge that it is a prothrombotic RNA virus infection of the corona family.[9] The thrombotic nature of the infection is evident by serial rising levels of d-dimer,[10] fibrinogen and prothrombin time, which signify prognosis of the disease as well. Hence, anticoagulation is recommended for severe COVID-19 infection.[11]

Inherently, PV is a hypercoagulable condition due to hyperviscosity of the blood, along with a quantitative and qualitative disorders of leucocytes and platelets.[12] Therefore, the propensity of arterial and venous thrombosis increases multifold when both conditions appear simultaneously.[13]

Acute PE is a serious, and may be immediate, life-threatening condition. Clinical signs and symptoms of PE are non-specific[14]; therefore, the diagnosis is frequently missed on clinical examination and routine chest X-ray. Acute PE is suspected when biochemistry shows high levels of d-dimer, cardiac NT-proBNP and troponin with echocardiographic finding of right ventricular dilation.[15] In modern medicine, CTPA is the investigation of choice for detection of PE confidently, as it visualises pulmonary vasculature adequately up to the subsegmental level.[16]

For an appropriate therapeutic approach, risk stratification of patients presenting with acute PE is important. It can be done based on clinical criteria, laboratory biomarkers, radiological findings and integration of comorbid conditions. In this regard, the Pulmonary Embolism Severity Index (PESI) and its modified version, the simplified PESI[17] are widely used. In our case, calculated PESI score is 110, which put this patient in a class IV category, meaning high risk of in-hospital mortality at 30 days (4.0%–11.4%)[18] and need for reperfusion therapy.

The general principles of acute PE management in PV are not different from acute PE in other conditions. Treatment strategy depends on assessment of the risk of death in the patients. In this case, the levels of d-dimer and cardiac pBNP[15] were high, along with echocardiographic finding of right ventricular strain.[19] Furthermore, the patient was haemodynamically unstable as his systolic blood pressure (BP) was <90 mm Hg and he required vasopressor support for maintenance of BP. This single factor put him at high risk of mortality and qualified him for urgent reperfusion therapy[20] (class I recommendation for reperfusion therapy).

Besides the thrombosis, tendency for haemorrhage also increases in PV.[21] Therefore, extreme caution should be exercised when introducing thrombolysis and anticoagulation.

Therapeutic venesection is the single best short-term and long-term modes of decreasing haematocrit in PV. Maintenance of haematocrit below 45% is a grade 1A recommendation.[22] If venesection is intolerable, pharmacological cytoreductive agents such as hydroxyurea, busulfan and interferon alpha are alternatives.

It is prudent to decrease red cell mass by venesection while instituting reperfusion therapy in massive acute PE in patients with a background of PV presenting with high haematocrit, which was done in our case.

Alteplase and tenecteplase recombinant tissue plasminogen activator (rtPA) are preferable pharmacological agents to first-generation streptokinase and urokinase, as they are easy to institute and have less side effects. After thrombolysis, anticoagulation with unfractionated heparin or low-molecular-weight heparin should be continued followed by oral vitamin K antagonists (VKAs) or novel oral anticoagulants[23] for an extended period, as duration of treatment is defined according to patient's future risk of thrombosis.

The clinical data are lacking to determine the actual incidence of thrombosis in patients with PV contacted with COVID-19. Therefore, more studies are required to determine the actual incidence of PE in patients with myeloproliferative disorders infected with coronavirus.

Learning points

- The COVID-19 pandemic is caused by a novel coronavirus and its presentation is varied. Pulmonary embolism (PE) is a well-recognised complication in patients with COVID-19, which can easily be treated as discussed previously.
- This diagnosis should be considered in all seriously ill patients with COVID-19 who have low levels of oxygen saturation with respiratory symptoms and a pre-existing inherited or acquired hypercoagulable states, such as antithrombin III, protein C, protein S deficiencies, factor V Leiden mutation, antiphospholipid syndrome and myeloproliferative disorders (primary myelofibrosis, essential thrombocythaemia and, in particular, polycythaemia vera).
- When a patient present with multiple complex acute medical conditions, treatment provided is individualised and tailored based on international guidelines.
- Early diagnosis of PE in patients with COVID-19 may save many valuable lives.

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