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Editorial

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PULMONARY EMBOLISM IN ESKD AND COVID-19 – A KNOWN COMMON PROBLEM YET TOO MUCH UNKNOWN

Go Zher Lin[1], Irene Wong[1], Khairul Anuar Abd Manaf[1], Norleen Zulkarnain Sim[1], Shahnaz Shah Firdaus Khan[1]
[1]Department of Nephrology, Hospital Tengku Ampuan Rahimah Klang

ABSTRACT

Venous thromboembolism (VTE) is common in COVID-19 infection, particularly in those with severe disease. Here we report a case of pulmonary embolism (PE) in an end stage kidney disease (ESKD) patient on maintenance haemodialysis with COVID-19 infection. The clinical manifestations of PE in this case were non-specific, and were masked by the other concurrent illnesses. Patient was persistently hypoxic despite optimal management of the other concurrent illnesses, and PE was eventually diagnosed based on CT pulmonary angiogram. This case highlights a few important issues that, VTE incidence is unacceptably high despite pharmacological prophylaxis, and clinical manifestations of PE in CKD patients with COVID-19 are non-specific and are frequently thought to be due to other concurrent illnesses. Optimal treatment of PE in COVID-19 is unknown, and data is even more scarce in CKD population. Current treatment recommendations are largely extrapolated from data of non-COVID-19 population, though large prospective trials are underway.

Keywords: *Pulmonary Embolism, COVID-19, Chronic Kidney Disease, End Stage Kidney Disease*

INTRODUCTION

At the time of writing up this case report, the COVID-19 pandemic has already been around for more than a year. As we have seen more cases of COVID-19, and more data on this novel disease has been published to date, we slowly understand this disease better, though there are still lots of unknown.

Venous thromboembolism (VTE) is extremely common in COVID-19 infections, particularly those with severe disease, with incidence up to 46%, even with pharmacological prophylaxis (1). On the other hand, VTE is also very common in CKD populations, with an estimated two to three times higher incidence in those with CKD stage 3-4 compared to those with normal kidney function, and carries higher mortality (2). Pulmonary embolism (PE) is the commonest VTE in COVID-19 infection, and is associated with more severe disease and poorer mortality outcome (3). Although scientific data on covid-19 has been explosive in the last one year, data on incidence of PE in CKD population with COVID-19 is scarce. Much is also unknown on the optimal diagnostic, prophylactic and therapeutic approach of this condition in COVID-19 patients, and current guidelines are largely extrapolated from data of general population. Here we reported a case of PE in an end stage kidney disease (ESKD) patient receiving maintenance haemodialysis with COVID-19 infection. It is not an uncommon scenario in our present routine practice but it highlighted a few learning points, revealing there are in facts lots of unknown.

CASE REPORT

Our patient was a forty-four-year-old gentleman with ESKD on maintenance haemodialysis for 4 years. He presented to us with sudden onset of shortness of breath after the end-of-week gap of dialysis. He gave a history of dry cough for three days but denied fever. He was tachypneic on arrival, blood pressure was 210/123 mmHg, and his arterial blood gas showed marked hypoxemia requiring non-invasive ventilation. He was clinically overloaded, with bilateral crepitations on auscultation of the lungs and pedal oedema up to mid shin.

**Correspondence:* Go Zher Lin
Hospital Tengku Ampuan Rahimah Klang,
Jalan Langat, 41200 Klang, Selangor.
Tel: +603-33757000
Email: zher_lin@hotmail.com

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Blood investigations noted leucocytosis with total white cell count of 17.5 x109/L and raised C-reactive protein (CRP) at 134 mg/dL. Plain chest radiograph was done showing bilateral heterogenous patchy opacities (figure 1).

He was treated as acute pulmonary oedema and community acquired pneumonia. He was started on intravenous ceftriaxone and urgent haemodialysis was commenced with an ultrafiltration volume of 3 litre. Nevertheless, his tachypnoea and hypoxia did not improve much after haemodialysis. His nasal and oropharyngeal COVID-19 PCR were positive. He was immediately

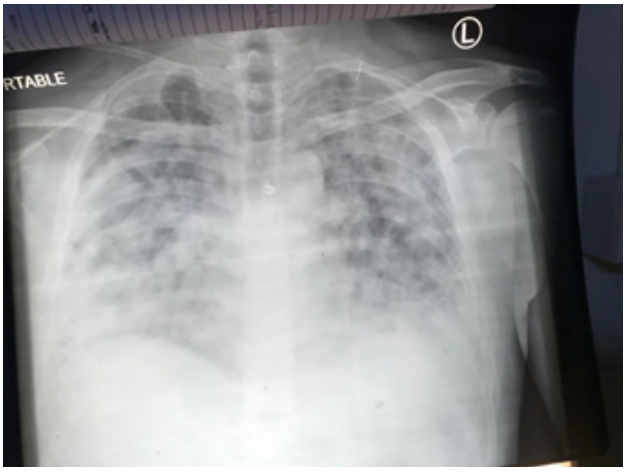

Figure 1: Plain chest radiograph showing bilateral heterogenous patchy opacities

started on intravenous dexamethasone, prophylactic doses of subcutaneous enoxaparin, and was transferred to the regional infectious disease centre for further management. After the transfer, favipiravir and intravenous methylprednisolone were started for his COVID-19 pneumonia. His low molecular weight heparin (LMWH) was continued for VTE prophylaxis. He had persistent fever and raised CRP levels and the antibiotic was escalated to intravenous piperacillin-tazobactem. Unfortunately, he suffered from non-ST elevation myocardial infarction (NSTEMI) as well, for which he was given double antiplatelets and statin. With regards to his acute pulmonary oedema and fluid retention, he was regularly dialysed every 48 hours with target ultrafiltration volume of 2.5-3.0 litre.

After one week of hospitalization, his fluid retention was much improved. Plain chest radiograph was repeated, showing improvement of pulmonary oedema, but presence of bilateral ground glass opacities likely attributable to COVID-19 pneumonia (figure 2). He became afebrile with his total white cell count and CRP levels reducing in trend. Blood culture did not show any growth. He also completed five days of therapeutic anticoagulant for his NSTEMI. Despite the above, he still remained hypoxic requiring face mask oxygen support. At this point of time, D-dimer was taken which was significantly raised at >3000 mcg/ml.

An urgent computed tomography pulmonary angiogram (CTPA) was performed, showing filling defects involving bilateral segmental branches of pulmonary arteries (figure

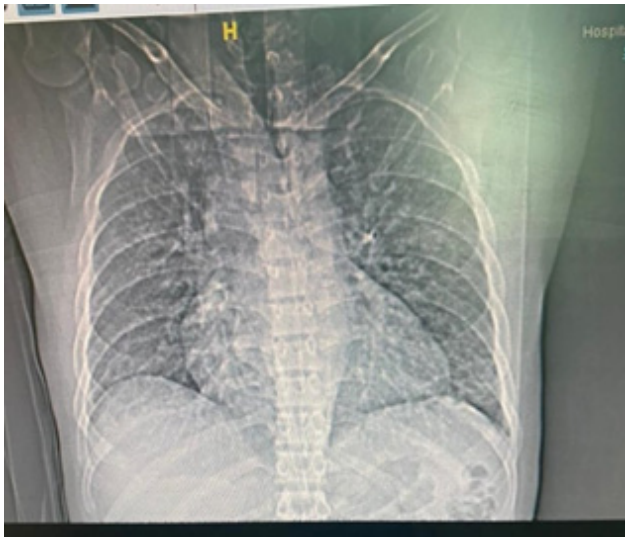

Figure 2: Repeated plain chest radiograph after one week of hospitalization showing improvement of pulmonary oedema, with presence of bilateral ground glass opacities likely attributable to COVID-19 pneumonia.

3). Bilateral pulmonary embolism was diagnosed and he was started on therapeutic anticoagulant, subcutaneous enoxaparin. After few days of therapeutic anticoagulation, his oxygen requirement was able to tapered down, and eventually, off from oxygen support. His general condition improved and he was discharged after twenty days of hospitalization. He was planned for therapeutic anticoagulation with low molecular weight heparin (LWMH) for three months.

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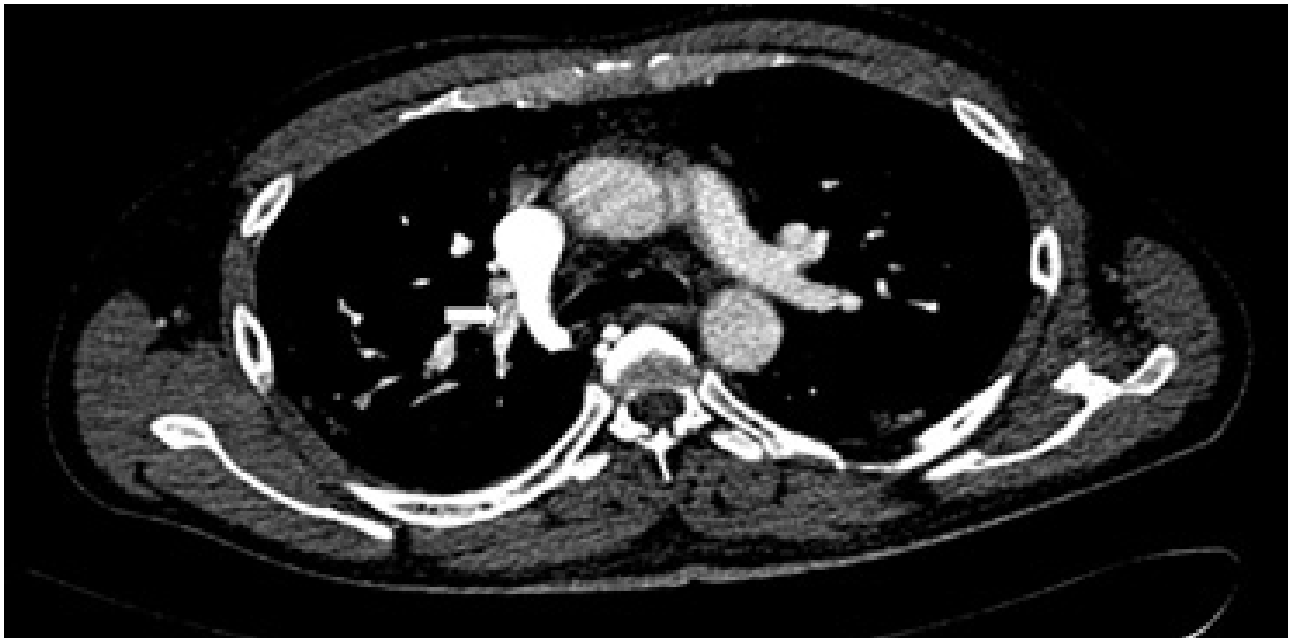

Figure 3: CTPA image showing filling defect in segmental branch of right ascending pulmonary artery (white arrow).

DISCUSSION

As mentioned in the introduction, VTE is common in CKD population while VTE is also very common in COVID-19 infection. Our patient has both the conditions predisposing him to pulmonary embolism. His initial presentations were very commonly seen in our daily nephrology practice and were typical of acute pulmonary oedema and pneumonia. The alarming sign here was that his hypoxemia did not improve despite optimal management of his concurrent illnesses, namely, acute pulmonary oedema, COVID-19 pneumonia, and acute coronary syndrome. D-dimer test was done at this juncture followed by CTPA and finally the diagnosis of PE.

This case illustrated the non-specific manifestations of PE which can be confused and easily attributed to other concurrent illnesses. Given the fact the VTE is extremely common in COVID-19 infection and also CKD populations (1-2), clinicians must have high level of suspicion and low threshold for diagnostic imaging when encountering patients with COVID 19 and CKD. Clinical scoring systems such as Wells has been widely utilized but were unreliable in inpatient settings and even less so among critically ill patients. D-dimer is widely utilized as well and has been validated in CKD population showing excellent negative predictable value yet poor positive predictive value. However, D-dimer has additional value in terms of prognosis in COVID-19 infection. It was found that higher D-dimer values are associated with higher in-hospital mortality and more severe disease among COVID-19 patients (4). Therefore, the value of D-dimer in COVID-19 is two-fold - to exclude VTE when clinical suspicion is not high, to prognosticate and risk stratify. When clinical suspicion of PE is high, diagnostic imaging is warranted without delay, regardless of clinical scoring and D-dimer value.

This case also highlighted the fact that PE can still happen in ill COVID-19 patients despite receiving prophylactic anticoagulant. There has been data showing current pharmacological prophylactic strategies are inadequate to prevent VTE in severe COVID-19 cases (5). With regards to treatment of PE in COVID-19, current guideline recommendations from societies such as ACCP (American College of Chest Physicians) and ISTH (International Society of Thrombosis and Haemostasis) are largely extrapolated from data of non-COVID-19 population. Such data is even more scarce in CKD populations, and the above mentioned guidelines did not make any specific recommendations or suggestions pertaining to CKD patients. While large RCTs (ClinicalTrials.gov Identifier: NCT04372589, NCT04505774) are underway examining the optimal prophylactic and treatment strategies for VTE in COVID-19, we look forward to data on CKD populations as this group of patients are vulnerable when facing COVID-19 with higher mortality rate, their data are desperately needed.

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CONCLUSION

Pulmonary embolism is common in COVID-19, the risk may even be higher in CKD population due to their pro-thrombotic risk, though data is lacking. Making clinical diagnosis of PE in COVID-19 is challenging as clinical manifestations are very non-specific, and scoring systems are unreliable, thus clinical suspicion must be high. D-dimers has two-fold values in COVID-19 - good negative predictive value, and prognostication. Diagnostic imaging should be pursued when suspecting PE, regardless of clinical scoring and D-dimer.

Optimal strategies of VTE prophylaxis and treatment in COVID-19 are still unknown, these data are even more scarce in CKD population. Data on optimal strategy of VTE prophylaxis and management in COVID-19 are desperately needed, while large RCTs are underway. We look forward to these new data, particularly in CKD population.

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