Concurrent COVID-19 and leptospirosis: A case report on dual infections

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SUMMARY

Malaysia has a long history of fighting tropical diseases including leptospirosis, dengue fever, malaria, enteric fever, and Chikungunya. During the ongoing pandemic of coronavirus disease 2019 (COVID-19), it is crucial for clinicians to have high level of suspicion for detection of COVID-19 co-infection with endemic illnesses, and not to neglect the management of dual infections. We present a case of young man from the East Coast Malaysia, who presented with short history of high-grade fever, non-productive cough, shortness of breath, and haemoptysis, after recently swimming in a river at an oil palm plantation. Both COVID-19 reverse transcription polymerase chain reaction (RT-PCR) and Leptospira microscopic agglutination test (MAT) were positive. He was diagnosed with concurrent COVID-19 and leptospirosis infection. We treated the patient as per national COVID-19 protocol and antibiotic coverage for leptospirosis. Despite the development of acute respiratory distress syndrome (ARDS) with multiorgan impairment during hospitalisation, he responded well to treatment and had a favourable outcome.

INTRODUCTION

Diagnosis of co-infection of *Leptospira spirochete* and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is challenging. Both diseases have similar presentations such as fever, malaise, headache, abdominal pain, or vomiting. Due to the COVID-19 pandemic, other differentials could be neglected, and delay in diagnosis would lead to delay in initiating appropriate treatment and eventually poor clinical outcome. To our knowledge, this is the first reported case of concurrent COVID-19 and leptospirosis infection in the region of Asia.

CASE REPORT

We report a case of 16-year-old male student from Terengganu, Malaysia. He is an active smoker with one pack per day, non-alcoholic, and has no known medical illness. He presented with high grade fever, non-productive cough, and shortness of breath for two days. It was associated with large amount of haemoptysis on the day of presentation. He reported history of swimming in a river at an oil palm plantation one week prior, but denied contact with positive COVID-19 patient and denied any known dengue outbreak in his neighbourhood. On examination, he was alert but pale and tachypnoeic. His vital signs on admission were as follows: temperature, 39.8°C; heart rate, 140 beats per minute; blood pressure, 111/75mmHg; and oxygen saturation, 82% on room air. His body mass index was 23. He had otherwise no jaundice, no conjunctival suffusion, no hepatosplenomegaly, and no other bleeding tendency.

Initial resuscitation included 1-litre bolus of normal saline and two pints of pack cells. Intravenous (IV) ceftriaxone 2-gram stat was started in view of high suspicion of leptospirosis. IV tranexamic acid 1-gram stat and IV methylprednisolone 500-milligram stat were given for pulmonary haemorrhage. He was intubated for type-1 respiratory failure. Post-intubation, he developed cardiac arrest due to massive pulmonary haemorrhage. Return of spontaneous circulation occurred after two minutes of cardiopulmonary resuscitation. He was then admitted to intensive care unit (ICU) for further care. In view of ongoing COVID-19 pandemic, COVID RT-PCR sample was sent and turned out to be positive. Leptospira IgM and MAT samples were also sent and came out to be positive, with MAT titre 1:400. A full complement of laboratory studies included complete blood count, renal and liver profile, basic metabolic panel, arterial blood gas, and blood culture. The results of investigations and the trend are shown in Table I. Initial chest X-ray showed bilateral diffuse infiltrates (Figure 1), which improved subsequently (Figure 2).

After ICU admission, IV methylprednisolone another 1-gram stat was given in view of massive pulmonary haemorrhage. He developed severe ARDS and required prone ventilation for 48 hours with protective lung strategy (tidal volume of 6ml/kg and PEEP of 12). He was deeply sedated and paralysed for 48 hours during prone ventilation with continuous infusion of propofol 100mg/hour, midazolam 6mg/hour, fentanyl 100mcg/hour, and atracurium 30mg/hour. Despite all these measures, he developed left tension pneumothorax and a chest tube was inserted. His ventilation subsequently improved and extubated after seven days of intubation. He was put on IV methylprednisolone 150mg daily for four days and subsequently stepped down to IV dexamethasone 8mg OD for six days. He completed IV ceftriaxone 1-gram twice daily for two weeks. He was transferred to general ward after eight days of ICU stay with no neurological deficit and was discharged home after a total of 16 days in hospital.

DISCUSSION

Globally, we have been burdened with COVID-19 caused by SARS-CoV-2 virus since December 2019. According to data released by WHO on 28 February 2020, presentation of

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Table I: Summary of results during ICU stay

Investigation	9/11	10/11	11/11	12/11	13/11	14/11	15/11
Hb (g/L)	7.7	9.0	10.9	9.4	9.9	9.4	10.0
TWC (10^9/L)	22.4	18.6	19.8	18.4	17.3	19.9	23.2
Plt (10^9/L)	259	148	237	208	214	262	352
ALC (10^9/L)	6.37	0.96	0.74	1.31	1.55	2.11	1.57
Na (mmol/L)	139	140	141	146	146	146	141
K (mmol/L)	4.9	4.8	4.5	4.8	5.4	5.0	5.4
Urea (mmol/L)	8.7	19.7	26.1	30.7	27.5	23.9	21.0
Creat (mmol/L)	189	292	275	244	201	164	140
Ca (mmol/L)	1.71		1.95		1.93		
Mg (mmol/L)	0.98		0.84		0.84		
PO4 (mmol/L)	3.22		1.14		1.20		
TB (µmol/L)	7.5		4.1				
DB (µmol/L)	18.4		14.8				
ALT (U/L)	95		156		91		
AST (U/L)	149		118		66		
ALP (U/L)	80		61		61		
Alb (g/L)	29		29		29		
CK (U/L)		1424	3057		2021		
CRP (mg/L)	113.9	184.7	138.6	84.1	60.8	30.4	42.9
LDH (U/L)	853	1561	1025	1643	1708	1625	2118
Ferritin (µg/L)	427.2	879.2	647.8	367.0	542.8	440.5	557.9
D-dimer (ng/ml)	52583	27097	16175	14292	14163	14819	13412
INR	1.38	1.33	1.29	1.14	1.11	1.12	
PT (second)	15.6	15.1	14.6	12.9	12.5	12.7	11.8
APTT (second)	28.4	27.0	29.6	24.8	25.1	23.6	26.7

Note: Haemoglobin (Hb), total white cell count (TWC), platelet (Plt), absolute lymphocyte count (ALC), sodium (Na), potassium (K), creatinine (Creat), calcium (Ca), magnesium (Mg), phosphate (PO4), total bilirubin (TB), direct bilirubin (DB), alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), albumin (Alb), creatine kinase (CK), C-reactive protein (CRP), lactate dehydrogenase (LDH), international normalised ratio (INR), prothrombin time (PT), activated partial thromboplastin time (APTT)

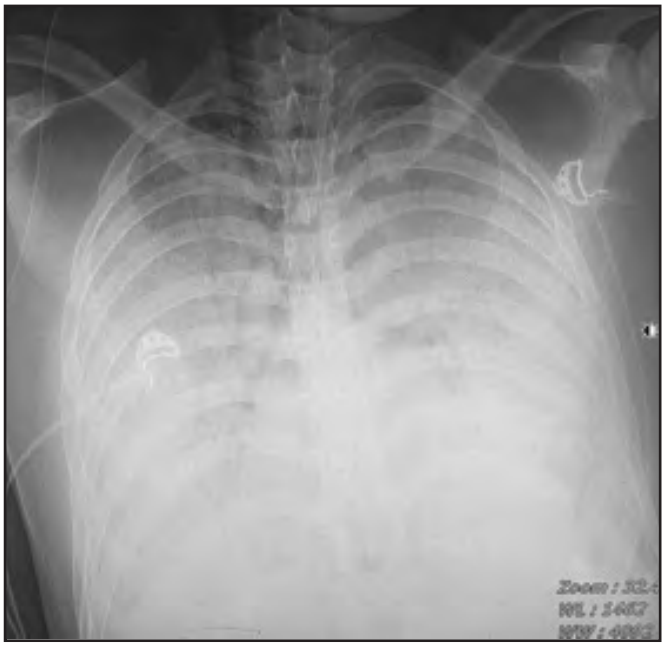

Fig. 1: Chest X-ray with bilateral diffuse infiltrates

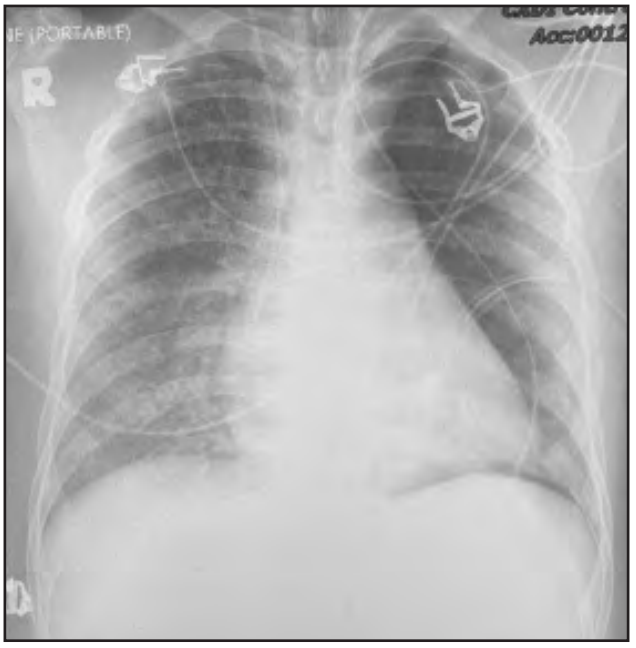

Fig. 2: Chest X-ray on day 7 of ICU admission

COVID-19 includes fever (87.9%), dry cough (67.7%), fatigue (38.1%), and less commonly haemoptysis (0.9%). These presentations of COVID-19 are common to most of the acute febrile illness (AFI), which is an umbrella term used for infectious febrile illness of short duration (<14 days) in tropical and sub-tropical countries.[1] The common causes of AFI include leptospirosis, dengue, malaria, enteric fever, and chikungunya. Leptospirosis is a zoonosis caused by gram-negative spirochetes genus *Leptospira*. Infected reservoir animals, typically rats, will carry the pathogen in their renal tubules and shed the bacteria into their urine.

Leptospirosis is not uncommon in Malaysia. Concurrent COVID-19 and leptospirosis have made the diagnosis of dual infections challenging. Delay in such diagnosis might lead to delay in antibiotic and hence poor outcome.[2] Majority cases of leptospirosis are asymptomatic with only 10% developing severe illness, which is characterised by increased leptospiraemia, multiorgan failure, and increased mortality rate.[3] It is difficult to distinguish between COVID-19 and leptospirosis based on clinical grounds alone, as leptospirosis could also present with fever, dry cough, and fatigue. Conjunctival suffusion, one of the most important signs suggestive of leptospirosis, is not present in this case. In this case, leptospirosis was suspected due to massive pulmonary haemorrhage with a history of swimming in a river at an oil palm plantation. This is supported by the finding of Ludwig et al.,[4] who suggested leptospirosis should be considered in case of rapid multiorgan failure presenting with pulmonary haemorrhage.

Other than similar clinical presentation, laboratory tests of severe leptospirosis and severe COVID-19 share similarity. Presence of acute kidney injury and liver enzyme derangement could be present in both severe leptospirosis and COVID-19. The elevated inflammatory marker levels, such as LDH, ferritin, and D-dimer, could be present due to the cytokine storm from COVID-19 and severe leptospirosis. The higher level of white blood cells, C-reactive protein, and creatine kinase had raised the suspicion of leptospirosis in our patient, as suggested by a study of Li et al.[5] However, elevated level of creatine kinase was also shown to be associated with increased mortality and severity in patients with COVID-19.[6] Hence, the use of rapid diagnostic tests is helpful in early diagnosis and initiation of treatment. In this case, we had sent the samples for both the rapid and diagnostic COVID-19 and leptospirosis testing at presentation, which had aided us in rapid diagnosis and timely antibiotic initiation.

Cytokine storm is an umbrella term encompassing several disorders of immune dysregulation characterised by constitutional symptoms, systemic inflammation, and multiorgan dysfunction, which can lead to multiorgan failure if inadequately treated.[7] Both COVID-19 and increased leptospiraemia will trigger a cytokine storm, which may lead to ARDS and death.[8] High-dose steroids have been used to mitigate the effects of cytokine storm in leptospirosis and COVID-19 with observed benefit in survival. The RECOVERY trial supports the use of steroid in ARDS due to COVID-19.[9] However, there is no well-designed randomised clinical trial to support the effectiveness of high-dose steroid in severe leptospirosis.[10] In our case, we treated cytokine storm with intravenous methylprednisolone and then stepped down to intravenous dexamethasone, which is in accordance with our COVID-19 management guidelines in Malaysia 2020. Additionally, ceftriaxone was started from the beginning, which could lead to the good outcome. A prophylactic anticoagulant, subcutaneous heparin, was only started on day-11 of illness due to persistent haemoptysis.

CONCLUSION

Concurrent infection of leptospirosis and COVID-19 are becoming increasingly common in the background of pandemic COVID-19. Hence, a high index of suspicion should be maintained especially when dealing with acute febrile illness presented with pulmonary haemorrhage and rapid development of multiorgan failure. The suspicion should be further heightened if the patient has epidemiological exposure including water activity. Diagnostic test should be considered early along with other routine laboratory and imaging tests. Early diagnosis and treatment are pivotal as the outcome can be rewarding.

CONFLICT OF INTEREST

None

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