An unusual case of fulminant leptospiral myocarditis: a case report

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Background
Fulminant myocarditis secondary to leptospirosis is rare and associated with poor outcomes.

Case summary
We describe a 60-year-old gentleman with fulminant leptospiral myocarditis and profound cardiogenic shock requiring veno-arterial extracorporeal membrane oxygenator (VA-ECMO) support. He was given high-dose pulse steroids early on post-VA-ECMO implantation and achieved full recovery. To our knowledge, this is the first reported case of leptospiral myocarditis with multiorgan dysfunction successfully managed by VA-ECMO and high-dose pulse steroids.

Discussion
This case report highlights the potential benefits of steroids in the management of leptospiral myocarditis which requires further validation. Early aggressive supportive management with ECMO should be considered in patients with fulminant leptospiral myocarditis.

Keywords
Case report • Fulminant leptospirosis • Myocarditis • Extracorporeal membrane oxygenator • Pulse steroids

Introduction
Leptospirosis is a zoonosis caused by the spirochaetes of the genus *Leptospira*. Clinical course is variable. A myriad of organ dysfunction may result. It runs a biphasic course characterized by an acute septicemic phase followed by an ‘immune’ phase. 1–3 Severe leptospirosis carries a high mortality rate. Myocarditis usually occurs beyond the first week of illness. 4 Myocardial involvement may be subclinical or may result in electrocardiogram abnormalities. 1,3,5 Severe cardiac dysfunction is rare. 6

We report a case of acute fulminant myocarditis with cardiogenic shock secondary to leptospirosis. Our patient required veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support and was treated with high-dose pulse steroids and antimicrobial therapy early on. He achieved complete myocardial recovery and was discharged well.
A 60-year-old Chinese male visiting from Australia presented to our hospital with syncope. He had been having cough, fever, myalgia, and malaise for the past 4–5 days. Past medical history included atrial fibrillation (AF) and hypertension. Drug history includes aspirin, perindopril, and atenolol. No history of illicit drug use. He reported contact with water from his outdoor inflatable pool 2 weeks ago in Australia.

Patient was hypotensive on arrival at the emergency department and required fluid resuscitation with improvement in blood pressure. He had Type 1 respiratory failure requiring non-rebreathable mask. Pulse was irregularly irregular; heart rate was 100 b.p.m. There were no audible murmurs. Coarse crepitations were heard in the left lung.

Laboratory investigations on admission were notable for elevated transaminases and elevated troponin T levels. Serum troponin T was 1041 ng/L. Serum alanine transaminase was 181 U/L while aspartate transaminase was 137 U/L. Chest radiograph showed cardiomegaly with bilateral infiltrates and a right pleural effusion. Ultrasound-guided pleural aspiration revealed haemorrhagic contents. Electrocardiogram showed AF with a right bundle branch block pattern (Figure 1A).

Transthoracic echocardiogram (TTE) on admission showed moderately depressed left ventricular ejection fraction (LVEF) of 42%.

Patient was initially treated as for respiratory tract infection and possible Type 2 myocardial infarction with intravenous (IV) ceftriaxone and doxycycline.

On Day 2 of admission, the patient’s rhythm was noted to be in alternating right and left bundle branch block (Figure 1B). He then developed a transient episode of pulseless electrical activity. There was return of spontaneous circulation within seconds after resuscitation with a bolus dose of IV adrenaline 1 mg and cardiopulmonary resuscitation. Monomorphic ventricular tachycardia (VT) followed. This was terminated within a minute with a bolus dose of IV amiodarone 150 mg. He subsequently developed recurrent runs of non-sustained VT (NSVT) and was given 100 mg of IV lignocaine.

Dual inotropes were required to maintain blood pressure. Patient was in bradycardia with ventricular escape rhythm and had recurrent runs of NSVT. Temporary pacing wire was inserted. Coronary angiogram showed minor coronary artery disease. Veno-arterial extracorporeal membrane oxygenator (VA-ECMO) inserted. Urgent endomyocardial biopsy is done.

After ECMO implantation, patient continued to have runs of monomorphic VT of varying morphologies. The recurrent runs of VT were not amenable to chemical and electrical cardioversion or overdrive pacing. Ablation was not considered in view of varying morphologies of VT and underlying aetiology was deemed secondary to myocardial inflammation.

**Timeline**

| Events                                                                 | Events                                                                                   |
|------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Contact with outdoor inflatable pool, likely the index exposure to Leptospira. | Transthoracic echocardiogram (TTE) showed normal LV cavity size and LVEF 65%. Renal function normalized. Patient was discharged well after a period of rehabilitation. |
| Fever, myalgia, and cough. Flew to Singapore from Australia. Syncope on day of admission | After 3 weeks of admission showed normal LV cavity size and LVEF 65%. Renal function normalized. Patient was discharged well after a period of rehabilitation. |
| Hypotensive on arrival which was fluid responsive. Had Type 1 respiratory failure requiring non-rebreathable mask. Treated as respiratory tract infection with antibiotics. | Days 5-11 Gradual return of cardiac rhythm and improvement in blood pressure. LVEF improved on serial TTE. Inotropes weaned off. Extracorporeal membrane oxygenation explanted on D11 of admission. |
| Developed alternating bundle branch block and transient pulseless electrical activity. | After 3 weeks Transthoracic echocardiogram showed normal LV cavity size and LVEF 65%. Renal function normalized. Patient was discharged well after a period of rehabilitation. |
| Coronary angiogram showed minor coronary artery disease. Rapidly developed refractory cardiogenic shock. Veno-arterial extracorporeal membrane oxygenator (VA-ECMO) inserted. Urgent endomyocardial biopsy is done. | Days 5-11 Gradual return of cardiac rhythm and improvement in blood pressure. LVEF improved on serial TTE. Inotropes weaned off. Extracorporeal membrane oxygenation explanted on D11 of admission. |
| Days 2–3 of admission                                                  | Days 2 weeks prior to admission                                                          |
| Days 2–3 of admission                                                  | 4–5 days prior to admission                                                              |
| Day of admission                                                       | Day 2–3 of admission                                                                     |
| Day 4                                                                  | Day 4                                                                                    |
| No pulse pressure or cardiac rhythm while on VA-ECMO support. Bedside TTE showed severely depressed LVEF of <10%. Continuous renal replacement therapy initiated in view of acute kidney injury. Given pulse intravenous (IV) methylprednisolone. A total of 2 g of IV methylprednisolone was given over the first 3 days followed by tapering doses of prednisolone in the following 7 days. | Transthoracic echocardiogram (TTE) at admission showed left ventricular ejection fraction (LVEF) of 42%. |

**Case presentation**

A 60-year-old Chinese male visiting from Australia presented to our hospital with syncope. He had been having cough, fever, myalgia, and malaise for the past 4–5 days. Past medical history included atrial fibrillation (AF) and hypertension. Drug history includes aspirin, perindopril, and atenolol. No history of illicit drug use. He reported contact with water from his outdoor inflatable pool 2 weeks ago in Australia.

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After ECMO implantation, patient continued to have runs of monomorphic VT of varying morphologies. The recurrent runs of VT were not amenable to chemical and electrical cardioversion or overdrive pacing. Ablation was not considered in view of varying morphologies of VT and underlying aetiology was deemed secondary to myocardial inflammation.
Repeat TTE showed severely depressed LVEF of <10%. There was subsequently no pulse pressure or cardiac rhythm while patient was on VA-ECMO support. Continuous renal replacement therapy was commenced for acute kidney injury. Decision was made to empirically pulse high-dose IV methylprednisolone as endomyocardial histology confirmed acute myocarditis without obvious pathogens or viral cytopathic features present. One gram of IV methylprednisolone was given, then 500 mg per day over the next 2 days, followed by tapering doses of prednisolone, 30 mg b.i.d. for 2 days, 25 mg b.i.d. for 2 days, 20 mg b.i.d. for 2 days, and then 15 mg b.i.d. for 2 days. Haemodynamic status improved over the following week. Inotropes were weaned off by Day 6 of admission. Veno-arterial extracorporeal membrane oxygenator was successfully explanted after ten days of support. A total of 14 days of IV ceftriaxone and oral doxycycline was given.

He was extensively evaluated for an underlying infective aetiology. Multiple blood cultures were negative. Respiratory virus polymerase chain reaction test was negative. A search for evidence of parvovirus, Epstein–Barr virus, cytomegalovirus, herpes simplex virus, dengue virus, Zika virus, chikungunya virus, human immunodeficiency virus, hepatitis B/C virus, toxoplasma, rickettsia from blood, serum, and urine did not yield any

Figure 1 Electrocardiogram of patient. (A) On presentation, showing atrial fibrillation with right bundle branch block pattern. (B) Electrocardiogram when patient went into alternating right bundle branch block and left bundle branch block.
positive results except for a paired convalescent leptospira enzyme-linked immunosorbent assay (ELISA). The initial leptospira IgM at admission was negative, but a convalescent repeat 2 weeks later returned positive, supporting the diagnosis of acute leptospirosis.

After recovery of haemodynamics, patient was started on heart failure treatment, including bisoprolol and hydralazine, isosorbide dinitrate combination. Angiotensin-converting enzyme inhibitors were not started, while renal function was recovering.

There were no further episodes of malignant arrhythmia. Transthoracic echocardiogram done before discharge showed normal LV cavity size and LVEF of 65%. He was discharged stable 3 weeks after admission.

Discussion

Fulminant leptospiral myocarditis is associated with a high mortality rate. Timely recognition and management including appropriate antimicrobial and supportive therapy are pivotal. Our patient had a clinical presentation and exposure history compatible with that of severe leptospirosis. Presence of bilateral pulmonary infiltrates and haemorrhagic pleural effusion with respiratory failure raise suspicion of pulmonary haemorrhage syndrome related to leptospirosis. Capillary damage in the lungs and pleurae caused by direct toxic effect of the organism have been thought to result in petechiae and ecchymoses accounting for the respiratory manifestations. This diagnosis is supported by exclusion of major causative pathogens and a supporting positive convalescent leptospira ELISA, which is highly specific at 93.4%. The gold standard for diagnosis includes the microscopic agglutination test and culture, both of which have their limitations in early diagnosis, and are not widely available. Over the years, molecular tests, including polymerase chain reaction and isothermal amplification techniques have emerged as reliable diagnostic modalities in the early diagnosis of leptospirosis, when tested on blood or urine specimens. Such rapid tests, however, are limited by their lack of availability in many laboratories.

Benefit of steroids remains unestablished although there have been case reports and small series demonstrating the efficacy of steroids in severe leptospirosis, especially the pulmonary complications. A descriptive study of the efficacy of bolus methylprednisolone in severe leptospirosis in Sri Lanka showed that steroids may improve survival outcomes in severe leptospirosis, specifically those with pulmonary complications. However, the benefit did not extend to those with established multiorgan dysfunction and comorbidities at the time of initiation of steroids in their study. All the study patients had received standard treatment with IV benzylpenicillin, with addition of IV ceftriaxone in patients who had severe leptospirosis.

Myocarditis usually occurs during the 5–7th day of leptospiral infection. This coincides with the ‘immunogenic’ phase of the disease. Anti-inflammatory properties of steroids have been postulated to reduce myocardial injury and oedema, thus improving chances of recovery. Conversely, worsening of bacterial infection can occur if steroids were administered during the initial ‘infective phase’ of the disease.

In our patient, main complication was that of acute fulminant myocarditis with cardiogenic shock requiring VA-ECMO support. Rapid deterioration occurred after at least 4–5 days of initial infective symptoms. At time of initiation of pulse steroids, he had multi-organ dysfunction involving the hepatic, pulmonary, renal, and cardiac systems. He made significant improvements in his haemodynamic status with eventual complete recovery of myocardial function. We postulate that he was in the ‘immunogenic’ phase of the disease, accounting for his good response to steroids.

Management of haemodynamic instability associated with leptospiral myocarditis is primarily supportive. In our case, VA-ECMO therapy was used as a bridge to recovery. A similar reported case of a patient with fulminant leptospiral myocarditis complicated by cardiogenic shock and VT in Sri Lanka demised despite antimicrobials, pulse steroids, and inotropic support.

Conclusion

Leptospirosis resulting in acute fulminant myocarditis should be considered in patients with risk factors such as occupational exposure, and those who stay in endemic areas. Although yet unvalidated, there may be potential benefits in the use of high-dose pulse steroids in the treatment of fulminant myocarditis caused by leptospirosis. More studies would be required to confirm the efficacy of pulsed steroids in this group of patients. Early initiation of appropriate antimicrobials and early supportive treatment such as VA-ECMO support, including consideration of high-dose pulse steroids where appropriate, can improve survival.

Lead author biography

Chun Yuan Khoo is currently an Associate Consultant in Cardiology practising in National Heart Centre Singapore. She is pursuing a fellowship in Heart Failure and has a special interest in echocardiography.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.
Conflict of interest: none declared.

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