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Case Report

Leptospirosis complicated by fatal myocarditis and cardiogenic shock requiring multiple ionotropic support; a tale of a double-edged sword: a case report

Charles JC[1], KGKU Kiriwandeniya[2], KV Liyanapathirana[2], RDS Gunarathna[2], S Mendis[2], GG Liyanarachchi[2]

[1]Postgraduate Institute of Medicine, University of Colombo, [2]National Hospital of Sri Lanka

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Corresponding Author: Charles JC, E-mail:< chrishtheboss@gmail.com >

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Introduction

Leptospirosis is a zoonotic illness caused by *Leptospira* spp which has more than 200 serovars [1]. The majority of patients are asymptomatic. Symptomatic patients go through two phases of the disease, which are septicaemic and immune phases [2]. Cardiac involvement in leptospirosis is uncommon and usually occurs in the immune phase of the illness [3]. Cardiac involvement can range from non-specific ECG abnormalities to fatal myocarditis and arrhythmias [3]. Sri Lanka is hyperendemic for leptospirosis, with a morbidity of 300.6 and a mortality of 17.98 per 100,000 population, annually [4]. Myocarditis in leptospirosis is well known and can cause fatality. It is usually associated with other organ involvement, which makes management more difficult [3]. Myocarditis with cardiogenic shock is generally managed with supportive care with inotropes.

There is neither a definitive treatment for myocarditis nor evidence-based mortality benefit management [5]. Ascertaining definitive myocarditis is also tricky, given the procedural difficulties in endomyocardial biopsy (EMB) in an unstable patient [6]. A possible diagnosis can be made with history, examination, ECG abnormalities and positive and serial troponins with echocardiography evidence [7]. When septic shock is combined with cardiogenic shock, the need for multiple ionotropic arises. There is an imbalance when using multiple inotropes to maintain optimal blood pressure. Vital organs are perfused at the expense of under-perfused peripheries, which causes ischaemic skin necrosis and myocyte ischaemia. Veno arterial ECMO is one modality of

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treatment that resulted in a successful recovery, as reported in a few case reports [8]. Other modalities are steroid pulse therapy and plasmapheresis [8].

Case report

A 44-year-old, previously healthy, South Asian male was transferred from a local hospital (LH). He presented to the LH with fever, arthralgia myalgia and reduced urine output for one-week. On admission, he was ill-looking, icteric and was in shock. There was no neck stiffness or focal neurological signs, and his GCS was 15/15. His pulse rate was 110/min and his SpO2 was 97% on room air. He had bilateral basal crepitations on the respiratory examination and an increased respiratory rate with increased work of breathing. He had severe right hypochondrial tenderness on abdominal examination. The rest of the examination was normal. Initial resuscitation was done with intravenous fluid (IV) boluses and noradrenaline was started and escalated. He was haemodynamically stable after initial resuscitation. His urine output was nil since admission and initial serum creatinine was 10.2 mg/dl. An urgent dialysis was arranged for him.

Table 1: Summary of the events

Summary of events	
Day 01	Diagnosis of leptospirosis with multiorgan involvement with shock, presumptive diagnosis of myocarditis made
Day 02	Four inotropes to maintain a minimum MAP of 65mmHg; patient transferred to ICU, evidence of pulmonary haemorrhage.
Day 03	Atrial tachycardia, one episode of cardiac arrest
Day 05	Five inotropes to maintain a minimum MAP of 65mmHg, one episode of ventricular fibrillation
Day 07	Purpura fulminans
Day 08	The patient succumbed to illness and expired.

A presumptive diagnosis of leptospirosis with multiorgan involvement was made. He was started on IV ceftriaxone 2g daily. Despite initial resuscitation, his BP began to drop with the first inotrope. Then, the second inotrope dobutamine was started at five micrograms/kg/min and escalated. His initial ECG revealed widespread T inversion sinus tachycardia. A bedside two-dimensional echo revealed global hypokinesia and a dilated heart with an ejection fraction (EF) of 30%. The presentation evolved as a refractory shock with desaturation which warranted ICU care with invasive ventilation. He was transferred to the ICU immediately for further management on the same day. The persistent pulse rate of 180/min in the absence of fever was an ominous sign and warranted a rate controller medication, and the patient was started on ivabradine on day 01 of ICU admission. He was electively intubated. Plasmapheresis was commenced and he had five cycles of plasmapheresis during the ICU stay. He was given three cycles of slow, low-efficiency dialysis (SLED). His leptospiral MAT was significantly positive with titres of more than 1600. MAP remained suboptimal despite combined management with plasmapheresis, SLED, multiple inotropes and IV antibiotics. He was started on adrenaline as a third inotrope.

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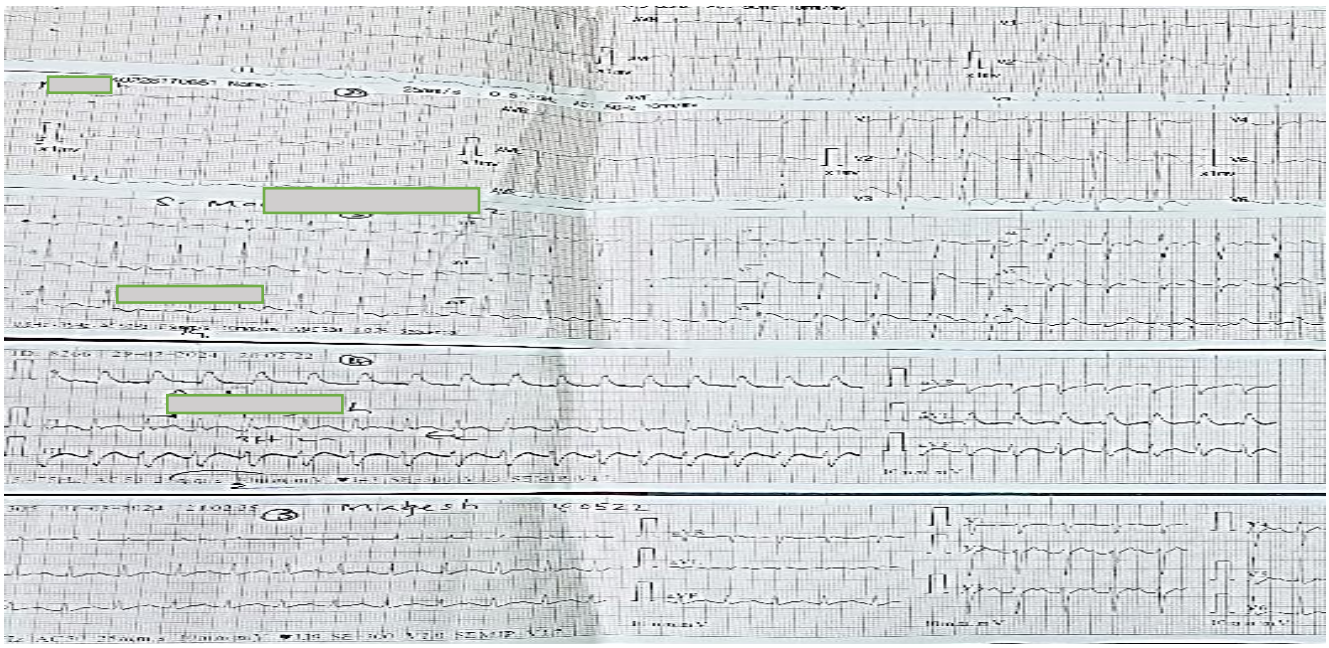

Figure 1: Serial ECGs of the patient showing sinus tachycardia and widespread T inversions, coveted ST elevation in v2

His BP was 60/40 at the time and he was kept on three inotropes with maximum doses. He was started on a fourth inotrope milrinone to maintain a minimum MAP of 65mmHg. The summary of use of inotrope is mentioned in Table 2. Persistent disproportionate tachycardia, cardiogenic shock, ECG changes, elevated troponin, and global reduction in cardiac contractility in two-dimensional echocardiography collectively favored the diagnosis of leptospirosis-associated myocarditis.

Table 2: Summary of use of multiple inotropes

Inotrope	Dose of ionotropic support							
	D1	D2	D3	D4	**D5**	D6	D7	D8
Norepinephrine(microgram/kg/min)	0.4	2	1.5	0.8	**0.2**	0.7	0.8	0.8
Dobutamine (microgram/kg/min)	15				**10**	20	10	10
Adrenaline (microgram/kg/min)		1	0.8	1	**0.5**	0.1	0.5	0.35
Vasopressin (unit/min)		4	4	4	**2**	2	2	2
Milrinone (microgram/kg/min)		0.5	0.5	0.5	**0.4**			

ECMO was not available in our hospital; it is only available at Galle Hospital, Sri Lanka. The patient was unstable to mobilize for ECMO modality in another centre. The maximum pressure achieved was 90/50 mmHg with four inotropes. His biochemical parameters started to normalize with the treatment, but he began to deteriorate clinically. He had overt peripheral cyanosis up to elbow and knee level bilaterally. He had ecchymotic patches in the limbs and developed purpura fulminans. This turn of events clearly revealed his poor outcome. A summary of the events since admission is mentioned in Table 1. Eventually, he had two cardiac arrests and ventricular fibrillation. He was resuscitated with defibrillation and amiodarone was commenced as a low-dose infusion. He succumbed to illness on the seventh day of his ICU stay due to multiorgan failure, cardiac arrest, and coagulopathy.

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Discussion

The pathogenesis of leptospiral myocarditis is complex. It occurs in the immune phase of illness with vasculitic phenomena and interstitial inflammation, as evidenced by previous autopsy studies of fatal myocarditis (3). Cardiac involvement in leptospirosis is uncommon and ranges from asymptomatic nonspecific ECG abnormalities, atrial fibrillation, conduction block, ventricular arrhythmias, cardiac tamponade to fulminant myocarditis (3). A possible diagnosis of myocarditis was made in our patient with ECG abnormalities with a serial rise in the highly sensitive troponins titres from 0.3 to 32 with echocardiographic evidence of global hypokinesia with an ejection fraction of 30%. We could not clinch the definitive diagnosis because of the instability of the patient and the unavailability of cardiac MRI in our hospital. Endomyocardial biopsy also could not be done due to procedural complications and difficulties.

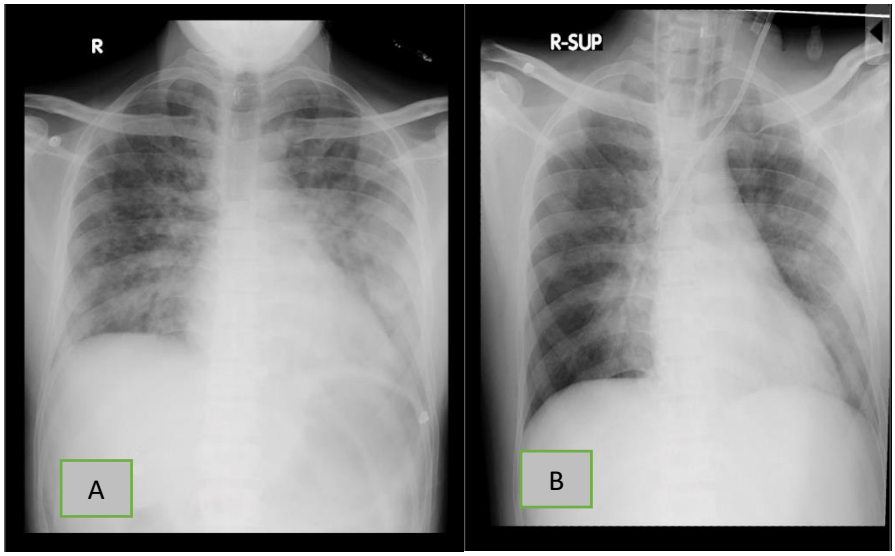

Figure 2: A- First X-ray showing evidence of pulmonary haemorrhage, B- serial x-ray showing resolution of pulmonary haemorrhage

In Sri Lanka, leptospirosis contributes to significant mortality through SPHS and myocarditis, in seasonal epidemics especially in urban areas [4]. SPHS can be managed with plasmapheresis and steroid pulses with a certain level of success, although the evidence is insufficient [9]. Myocarditis cannot be managed in the same arm as SPHS. Our patient had both SPHS and myocarditis. VA- ECMO is identified as a successful therapeutic modality, as evidenced in a few case reports [10,11,12]. The availability of VA-ECMO for seriously ill patients in Sri Lanka remains a difficult dream to achieve even in the near future, given the financial constraints. Plasmapheresis can be given for leptospiral myocarditis, but there is no clear evidence-based benefit (9). There are no professional guidelines to address leptospiral myocarditis, as yet, in spite of the global burden of leptospirosis with significant mortality annually [3].

Initially, our patient received one inotrope at low doses and then each inotrope was added up to maintain optimal blood pressure. Higher doses of inotropes are cardiotoxic

and increase the risk of fatal arrhythmias and peripheral ischaemic necrosis [13]. Careful use of inotropes can maintain optimal vital perfusion. Still, distal limb ischaemia is inevitable, with a small ecchymotic patch that can become fertile soil for infection, especially in the ICU setup with multidrug-resistant colonizers [13]. Sepsis also contributed to the refractory shock in our patient, but the absence of fever, serial blood culture negativity, serial drop in lactate, and CRP are against septic shock. Despite the aforementioned biochemical parameters, the serial rise in highly sensitive troponins suggested that an injured cardiac reserve was the predominant cause of shock rather than sepsis.

Conclusion

Leptospirosis with fulminant myocarditis is a difficult entity to clinch a diagnosis and even more challenging to treat. It contributes to significant mortality. Multiple inotropes are required to maintain optimal perfusion at the cost of distal limb ischaemia. Further studies are needed to explore the definitive management of leptospiral myocarditis, as no regional or international guidelines exist on this topic. The availability of ECMO for these critically ill patients could be a solution in Sri Lanka to prevent mortality in seasonal epidemics.

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