Cardiac Haemorrhage: An Extreme Presentation of Leptospirosis

Razuin R[1,2], Nurquin F. S[2], Nur A. R. P.[2], Julina M. N.[3]

[1]Centre for Pathology Diagnostic & Research Laboratories, Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia, [2]Department of Forensic Medicine, Hospital Sungai Buloh, Ministry of Health Malaysia, [3]Department of Emergency Medicine, Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia

Abstract

***Introduction*:** Leptospirosis is a worldwide disease with significant morbidity and mortality. The severe form of the disease may present with cardiac and pulmonary involvements resulting in multi-organ failure. Cardiac manifestations of leptospirosis include arrhythmia, cardiomegaly, petechial haemorrhages, pericarditis and myocarditis. ***Case report*:** We report a case of a 10-year-old boy who was having shortness of breath and collapsed at home. At the emergency department, he was having refractory hypotension with electrocardiogram (ECG) showing sinus tachycardia. The liver and cardiac enzymes were markedly raised. The full blood count showed leukocytosis. It was concluded that he was in septicaemic state with acute multi-organ failure of unknown cause. He succumbed to the illness approximately 8 hours after the hospital admission. At autopsy, the lungs, liver and spleen were markedly congested. Pericardial effusion was noted. The heart showed extensive areas of petechial and confluent haemorrhages involving almost the entire epicardial surface of the right and left ventricles. Massive subendocardial haemorrhage was also observed upon sectioning of the left ventricular chamber. Histopathology examination corroborated that haemorrhages were present in the heart, lungs and the liver. Laboratory investigations revealed positive *Leptospira* IgM antibody, confirmed by positive *Leptospira* PCR. The cause of death was concluded as cardiac and pulmonary haemorrhages secondary to leptospirosis. ***Conclusion*:** Cardiovascular involvement in leptospirosis may manifest as rapidly deteriorating illness with clinical evidence demonstrable from the ECG changes and raised cardiac enzymes. Recognizing these signs early may help to improve outcomes.

Keywords: *Leptospirosis; Myocarditis; Pulmonary haemorrhage; Autopsy; Cardiac haemorrhage*

Introduction

Leptospirosis is a worldwide zoonotic disease caused by pathogenic spirochetes of the genus *Leptospira*.[1,2] Transmission primarily occurs from direct contact with infected animals, or water contaminated with urine of infected animals, commonly rodents.[3,4] The clinical manifestations include simple febrile episodes, classified as self-limiting anicteric febrile disease to complex clinical features known as Weil's disease.[2,5] A severe and fatal form of this illness may present with cardiac and pulmonary involvement, renal failure, liver failure or a combination of multi-organ involvement with haemorrhagic diathesis.[3,6]

Cardiac manifestations of leptospirosis include arrhythmia, cardiomegaly, petechial haemorrhages, pericarditis and myocarditis.[2,7,8] Studies have shown that cardiac involvement occurred in 20% to 93% of the cases.[7,9] At autopsy, petechial haemorrhages and myocarditis are the most common presentations indicating cardiovascular involvement in leptospirosis.[2,7,9]

We report a case of a 10-year-old boy who appeared to be slightly unwell, collapsed at home and passed away approximately 8 hours after the hospital admission. He was diagnosed with acute multi-organ failure and sepsis of an unknown cause. At autopsy, massive cardiac

Corresponding author:
Dr Nur Atiqah Azman Roslan Petra,
Department of Forensic Medicine, Hospital Sungai Buloh, Jalan Hospital, 47000 Sungai Buloh, Selangor, Malaysia.Tel.:+60 132331727; Fax: +60 3 61401632.
Email address: fourseven75@yahoo.com.

haemorrhages were observed. *Leptospira* IgM antibody and polymerase chain reaction (PCR) were positive. In this case report, we wish to highlight that fatal leptospirosis may have very minimum presentations, thus, high index of suspicion is needed in order to improve outcomes. We also wish to describe an extreme cardiac presentation associated with leptospirosis.

Case Report

A 10-year-old boy was brought to a hospital after he was found collapsed in a bathroom at home. According to the parents, he appeared slightly unwell and less active for two days. At the emergency department, he was unresponsive with Glasgow Coma Scale (GCS) of 3/15. His heart rate was 180/min, blood pressure of 110/40, SpO2 99%, and temperature was 38.4ºC. The electrocardiogram (ECG) showed sinus tachycardia. He also had cool peripheries. Blood investigations revealed normal haemoglobin (15.5 g/dL), high total white cell count (38 x 10^9/ L) and mild thrombocytopenia (149 x 10^9/ L). Cardiac enzymes such as troponin I, creatine kinase (CK), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) were all raised, at 15439 ng/ml, >42670 mml/L, 995 U/L and 2904 U/L respectively. The creatinine level was 309.7 mg/dl, indicating acute renal failure. The liver function test showed increased alanine aminotransferase (232 U/L). Computed tomography for the brain was performed, showing no evidence of intracranial bleed or space occupying lesion. The working diagnoses at this point were severe sepsis with acute multi-organ failure. He was promptly intubated and resuscitated. Shortly after the admission, his blood pressure began to show a downward trend. Systolic pressured ranging from 50-60 mmHg and diastolic pressure 30-40 mmHg. His blood pressure remained low despite maximum inotropic supports and multiple fluid boluses given. Eventually, he succumbed to the illness approximately 8 hours after the admission. A medico-legal autopsy was performed to ascertain the cause of death.

Autopsy examination showed an obese and appropriately built male child measuring 146 cm in length and 85 kg in weight. The lungs, liver and spleen were markedly congested. Detailed gross examination of the cardiovascular system showed pericardial effusion amounting to 55 ml. The heart showed extensive areas of petechial and confluent haemorrhages involving almost the entire epicardial surface of the right and left ventricles. Massive subendocardial haemorrhage was also noted upon sectioning of the left ventricular chamber (Fig. 1). The serial cut sections showed softening of the cardiac parenchyma associated with transmural petechial haemorrhages, mostly prominent at the antero-septal region of the left ventricle. 'Shock' kidneys appearance was observed, exhibiting pale cortex with dark medulla. The spleen was also congested, soft and friable.

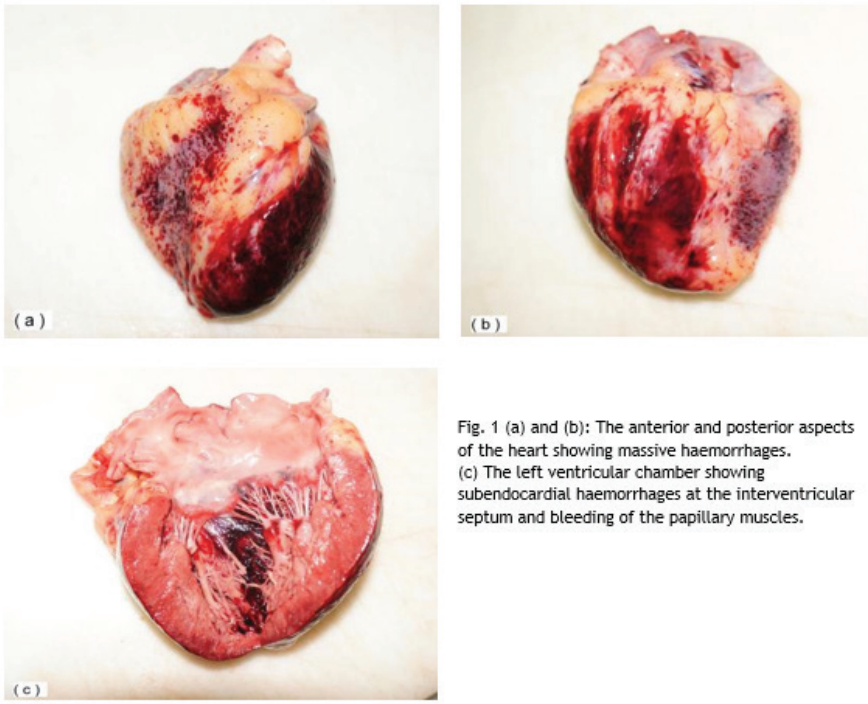

Fig. 1 (a) and (b): The anterior and posterior aspects of the heart showing massive haemorrhages. (c) The left ventricular chamber showing subendocardial haemorrhages at the interventricular septum and bleeding of the papillary muscles.

Representative tissue samples from the heart, lungs, liver, spleen and kidneys were obtained for microscopy examination. On histology, the heart shows extensive transmural haemorrhages involving both the right and left ventricles. Occasional acute inflammatory cells are present and contraction band necrosis is also observed, in keeping with ischaemic changes (Fig. 2 a&b). Haemorrhages are also present on the liver and lungs sections. The spleen shows massive neutrophilic infiltration and central necrosis of the white pulps. These features are in keeping with septicaemia. The kidneys show features of acute tubular necrosis, corroborating the high creatinine level from the blood investigation. Myoglobin globules are observed in the kidneys, which, in combination with the markedly raised creatine kinase, confirming presence of rhabdomyolysis in this case (Fig. 2d). The lungs show oedema, congestion and massive intra-alveolar haemorrhages (Fig. 2c). An area showing pulmonary infarction is also observed. In summary, the histology examination confirmed that the deceased was having an acute multiple organ failure, cardiac and pulmonary haemorrhages, as well as severe rhabdomyolysis.

In view of the physical examination, laboratory investigations results and autopsy findings, a diagnosis of leptospirosis was suspected. Several post mortem blood samples were obtained for infectious disease screening. Serological analysis revealed a positive *Leptospira* IgM antibody. A subsequent confirmatory test by PCR was performed, the result was positive. Therefore, the cause of death was concluded as cardiac and pulmonary haemorrhages secondary to leptospirosis. The mechanism of death was septicaemia in combination with multiple organ failure.

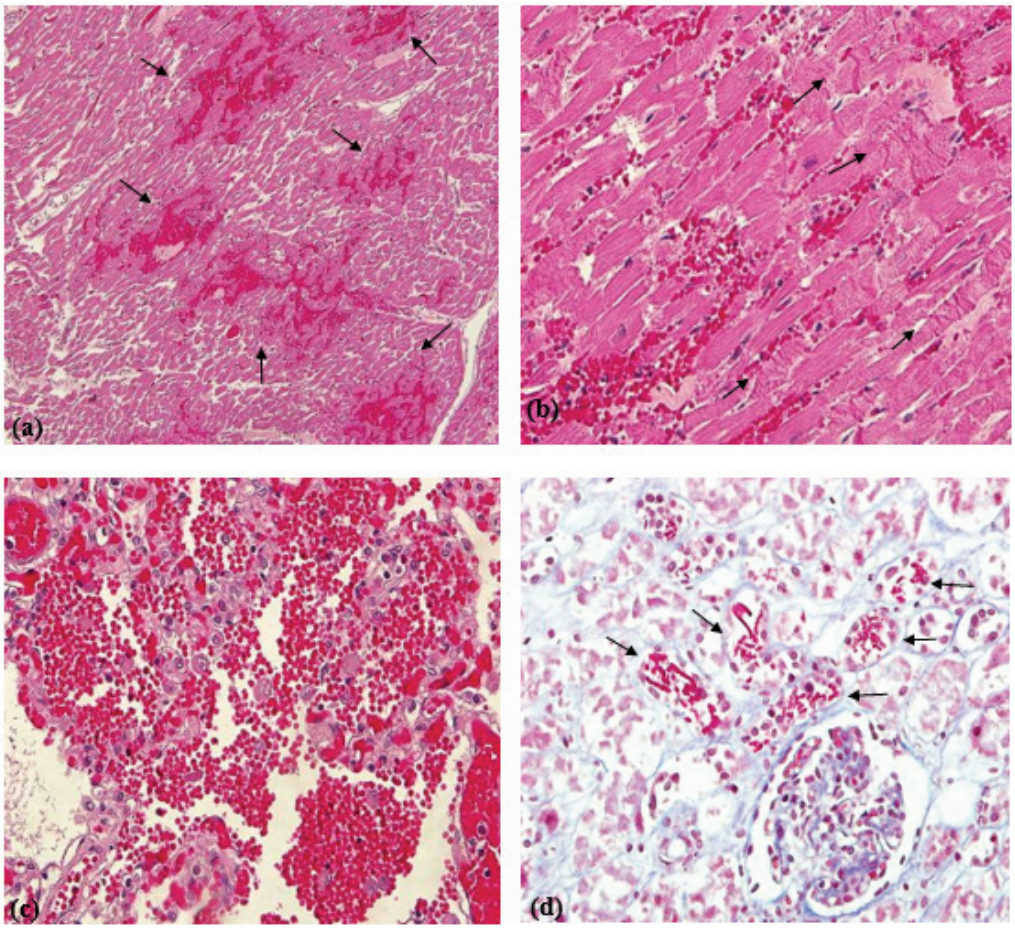

Fig. 2 (a) The myocardium showing multiple foci of haemorrhages (arrows). (b) Scattered intraparenchymal haemorrhages and contraction band necrosis of the myocardium (arrows). There is no inflammatory cell infiltrate observed. (c) The lung section shows thickened alveolar walls with red blood cells in the alveoli sacs. (d) Masson's trichrome stain of the kidney, showing myoglobin globules in the distal convoluted tubules (arrows).

Discussion

Cardiovascular involvement in leptospirosis has variable degrees and potentially life threatening. Presentations such as arrhythmia, pericarditis, myocarditis, congestive heart failure and cardiogenic shock are well documented in studies before.[2,6,7,9] Clinical evidence is frequently demonstrable from cardiac enzymes assays, ECG and echocardiography (ECHO). Manifestations such as refractory hypotension, AV conduction block and sinus tachycardia are the most common ECG findings in leptospirosis.[2,7] Raised cardiac enzymes may be an indication of myocarditis and an important prognostic marker. [2] In our case, the child presented with refractory hypotension and sinus tachycardia on ECG. All the cardiac enzymes were markedly raised. We hypothesized that the child was having cardiogenic shock when he was admitted to the hospital.

At autopsy, cardiac manifestations in leptospirosis include cardiomegaly, petechial haemorrhages, inflammation of the cardiac muscles and complications such as congestive cardiac failure.[2,7,9] Microscopically, interstitial myocarditis with predominant lymphocytes and macrophages infiltrations with some degree of myocardial injuries such as degeneration or necrosis are commonly observed.[7,9] In our case, massive haemorrhages were observed affecting almost the entire epicardial surface and all layers of the heart. On microscopy, the cardiac parenchyma generally showed evidence of haemorrhages with minimum inflammation. Therefore, our case illustrates an extreme and unusual form of cardiac presentation where the heart was essentially having severe bleeding, instead of inflammation as commonly observed in leptospirosis.

Another highlight of the case is rapid deterioration of a patient with cardiovascular involvement. Retrospectively, the parents only noticed his reduced activity for two days, as he was lying down and taking nap a little longer than usual. Still, he did not complain of feeling ill or appear very sick. However, the fact that paracetamol and salicylate were present in the blood suggested that the child did have fever and myalgia. According to the parents, the boy was quite independent and most probably had taken the medications by himself. As he came in with acute multi-organ failure with sepsis, the rapid worsening of his conditions baffled the attending clinicians. Unfortunately, leptospirosis was not suspected to be the cause.

Contact tracing revealed that he was most probably infected during a recreational activity at a waterfall. Two weeks prior to his death, the family went to a waterfall for picnic and swimming. A week later, he probably began to have fever as further checks showed that he bought some fever medications at a convenient store near his home. However, all this while, he appeared well and was able to carry out his daily activities including going to school and playing football in the afternoon. A day prior to his demise, he appeared slightly unwell, as he spent longer nap in the afternoon and did not go out to play football. His final symptom was difficulty in breathing amid the high fever. Observing the sequence of events, we hypothesized that after a week of contracting the disease, he began to have fever as a manifestation of the first phase of leptospirosis. The first phase is usually associated with high fever, headache, myalgia, abdominal pain, nausea and vomiting.[3] Subsequently, the child went into the second phase which is characterized by jaundice, renal and liver failures and pulmonary haemorrhages.[3] When he was brought to the hospital, two weeks after contracting leptospirosis, he was having cardiogenic shock, multiple organ failure and septicaemia.

Conclusion

Cardiovascular involvement in leptospirosis may manifest as rapidly deteriorating illness with clinical evidence demonstrable from the ECG changes and raised cardiac enzymes. Despite a vague medical history, leptospirosis should always be kept in mind as early identification and appropriate treatments may help to improve outcomes.

Conflict of Interest: None.

Funding: None.

Ethical Clearance: None.

Acknowledgement: The authors would like to thank the Director General, Ministry of Health Malaysia for the permission to publish this paper.

References

1. Lim T.S.C., Jun T.Y., Fah T.R. Pulmonary Hemorrhage Associated With Severe Leptospirosis–The Role Of Low Dose Intravenous Methylprednisolone. Mal J Med Health Sci 2018; 14(1): 69-72.
2. Pushpakumara J., Prasath T., Samarajiwa G., Priyadarshani S., Perera N., Indrakumar J.

Myocarditis causing severe heart failure-an unusual early manifestation of leptospirosis: a case report. BMC research notes 2015; 8.1:80.

3. Razuin R., Omar E., Tuan Soh T.S., Mohd Nawi S.F.A., Md Noor S. Leptospirosis in pregnancy: A lesson in subtlety. Malays J Pathol 2018; 40(2): 169-173.

4. Ludwig B., Zotzmann V., Bode C., Staudacher D.L., Zschiedrich S. Lethal pulmonary hemorrhage syndrome due to Leptospira infection transmitted by pet rat. ID Cases 2017; 8: 84-86.

5. Daher E.D.F., Abreu K.L.S.D., Silva Junior G.B.D. Leptospirosis-associated acute kidney injury. Jornal Brasileiro de Nefrologia 2010; 32.4: 408-415.

6. Turhan V., Atasoyu E.M., Kucukardali,Y., Polat E., Cesur T., Cavuslu S. Leptospirosis presenting as severe rhabdomyolysis and pulmonary haemorrhage. Journal of Infection 2006; 52.1:e1-e2.

7. Chand P.T., Garg V.R., Wadia, M.Z., 2016. A Study on Cardiovascular Manifestation in Leptospirosis Cases in a Tertiary Care Hospital of Surat City. National Journal of Medical Research; 60(40): p.240.

8. Forbat E., Rouhani M.J., Pavitt C., Patel S., Handslip R., Ledot S. Leptospirosis presenting as severe cardiogenic shock: A case report. Journal of the Intensive Care Society 2018; p.1751143718754993.

9. Chakurkar G., Vaideeswar P., Pandit S.P., Divate S.A. Cardiovascular lesions in leptospirosis: an autopsy study. Journal of Infection 2008; 56.3: 197-203.