

CASE REPORT

Leptospirosis with Pulseless Electrical Activity (PEA) Cardiac Arrest in Multiple Comorbid Patient

AMIRUDIN S, ISMAIL MS

Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia

ABSTRAK

Leptospirosis adalah salah satu penyakit yang endemik di Malaysia. Ia mempunyai pelbagai manifestasi klinikal bermula daripada yang ringan sehingga yang boleh membawa maut. Kami melaporkan sebuah kes tentang seorang lelaki berumur 56 tahun dengan pelbagai masalah kesihatan terdahulu, dengan sejarah tidak sihat kerana demam, batuk dan sakit perut selama dua hari. Pesakit datang ke Jabatan Kecemasan dalam keadaan tidak sedarkan diri dengan Pulseless Electrical Activity (PEA) cardiac arrest. Pesakit telah diresusitasi dan berjaya dipulihkan dengan mencapai peredaran darah spontan (return of spontaneous circulation) tidak berapa lama selepas itu. Keadaan pesakit dirumitkan lagi dengan keadaan Hyperosmolar Hyperglycemic State (HHS), oliguric acute kidney injury, dan non-ST elevation myocardial infarction (NSTEMI). Pesakit kemudian dimasukkan ke unit rawatan rapi dan dirawat dengan IV Ceftriaxone 2 g sekali sehari selama empat hari, dan kemudian ditukar kepada IV Cefazidime 2 g dua kali sehari untuk seminggu disebabkan ventilator acquired pneumonia (VAP). Keadaan pesakit bertambah baik dan akhirnya di benarkan pulang ke rumah pada hari yang ke 18.

Kata kunci: kematian mengejut akibat serangan jantung, leptospirosis, zooneos

ABSTRACT

Leptospirosis is one of the endemic diseases in Malaysia. It has a broad spectrum of clinical manifestation ranging from mild illness to life-threatening illness. We report a case of 56-year-old male with multiple comorbidities, who came with history of fever, cough, abdominal pain, vomiting and diarrhea for two days. He presented to the Emergency Department (ED) unresponsive with pulseless electrical activity (PEA). He was resuscitated and achieved return of spontaneous circulation (ROSC)

Address for correspondence and reprint requests: Ismail Mohd Saiboon. Department of Emergency Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia. Tel: +6019-3200297 Email: fadzmail69@yahoo.com.my/ismail@ppukm.ukm.edu.my

shortly after it. It was complicated with hyperosmolar hyperglycemic state (HHS), oliguric acute kidney injury and non-ST elevation myocardial infarction (NSTEMI). He was then admitted to intensive care unit (ICU) and treated with IV Ceftriaxone 2 g daily for 4 days then was changed to IV Ceftazidime 2 g twice per day for 1 week because of ventilator acquired pneumonia (VAP). His condition improved and was discharge home well after 18 days of admission.

Keywords: cardiac arrest, leptospirosis, zoonoses

INTRODUCTION

Leptospirosis is one of the common re-emerging zoonotic diseases caused by pathogenic spirochetes of genus *Leptospira*. The disease can be divided into two types, which are anicteric leptospirosis and icteric leptospirosis based on the clinical presentation (Lim et al. 2011). In this case, we highlight the findings in a patient with multiple comorbid features, who presented with atypical symptoms of leptospirosis. Leptospirosis can be underdiagnosed and proper management might not be delivered if the disease is not considered at the beginning.

CASE REPORT

A 56-years-old male who was brought to the Emergency Department (ED) by his friend, collapsed just before arrival. He was unwell for the past two days with complaint of generalised lethargy, fever, and chesty cough. It was associated with abdominal pain, vomiting, and diarrhoea. He had a known case of diabetes mellitus type 2 and hypertension but defaulted his treatment for almost two years. He also had a history of pulmonary

tuberculosis in 2012 and completed anti-tuberculosis treatment for 6 months. In 2014, he had lacunar infarct with left hemiparesis. The patient was single, with daily active living being independent, and he stayed alone.

Upon arrival at the ED, his Glasgow coma scale (GCS) was 3/15 and cardiac monitor showed sinus bradycardia with Pulseless Electrical Activity (PEA) (no recorded cardiac monitoring available). Cardiopulmonary resuscitation (CPR) was commenced immediately and return of spontaneous circulation (ROSC) was achieved after one minute. He was intubated and inotropes was started for haemodynamic support. Clinical examinations were unremarkable except that he was clinically dehydrated; but was not jaundiced. The examination of the cardiovascular system, respiratory system and abdomen were unremarkable.

The initial laboratory work-up showed evidence of hyperosmolar hyperglycaemic state (HHS) with blood gas showing severe metabolic acidosis, serum glucose of 26 mmol/L, serum ketone of 0.6 mg/dL, and serum osmolarity of 333.3 Osm/kg. Full blood count (FBC) was normal

Table 1: Blood investigation trends of the patient.

Test	Day 1	Day 2	Day 3	Day 4	Day 5	Day 7	Day 12	Reference range	Unit
Hb	15.3	13.7	11.5	11.0	9.9	8.6	8.3	13.5-17.4	g/dL
WCC	11.3	8.5	5.7	5.5	7.4	8.3	12.2	4.1-11.4	$\times 10^3 \mu\text{L}$
Plt	256	215	154	143	143	235	238	142-350	$\times 10^3 \mu\text{L}$
Alb	34	25	18	15	15	16	16	35-50	g/L
ALP	91	60	62	-	63	70	91	40-150	U/L
ALT	58	92	241	-	183	119	72	0-55	U/L
TB	18.9	12.0	39.3	-	16	10.7	7.5	3.4-20.5	mg/dL
Urea	29.3	32.3	37.5	24.7	39.0	36.2	18.8	3.2-7.4	mmol/L
Cr	382.6	454.4	701.8	598.4	775.6	709.7	360.5	63.6-110.5	mg/dL
K	4.1	4.8	4.4	4.1	4.4	4.6	3.6	3.5-5.1	mmol/L
Na	131	133	138	138	139	140	140	136-145	mmol/L
CK	1506	19652	40292	21227	9734	2038	468	30-200	U/L

Hb = Hemoglobin; WCC = White cell count; Plt = Platelet; Alb = Albumin; ALP = Alkaline Phosphatase; ALT = Alanine Transaminase; TB = Total bilirubin; Cr = Creatinine; Na = Sodium; CK = Creatinine Kinase

with white cell count $11.3 \times 10^3 \mu\text{L}$, haemoglobin 15.3 g/dL, and platelet $256 \times 10^3 \mu\text{L}$. Renal function showed acute kidney injury (AKI) with urea and creatinine being 29.3 mg/dL and 362.8 mg/dL, respectively. Liver function test (LFT) results were slightly deranged with alanine transaminase (ALT) 58 U/L; alkaline phosphatase (ALP) 91 U/L, and bilirubin 18.9 mg/dL (Table 1). Cardiac enzymes post-CPR were elevated with creatinine kinase (CK) 1066 U/L and Troponin I was 1166 ng/L with electrocardiogram (ECG) showed ST depression at lead II,III, aVF, V3-V6 (Figure 1). Chest X-ray was unremarkable. Computed tomography brain showed old right lentiform nucleus and right thalamic lacunar infarction with underlying small vessel disease. He was given 4L of IV crystalloid and was started on IV insulin infusion. Then, he was transferred to the intensive care unit

(ICU).

Serum ELISA for leptospirosis showed IgM positive and IgG negative, which was confirmed with microscopic agglutination test (MAT) done at Institute for Medical Research (IMR) Malaysia. He was treated as leptospirosis infection. He was given IV Ceftriaxone 2 g daily for 4 days and then was changed to IV Ceftazidime 2 g

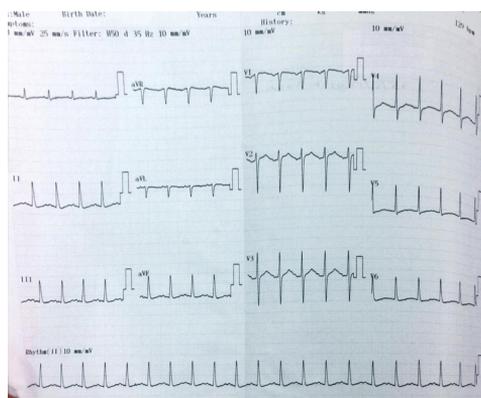


Figure 1: Patient ECG 1 hour after ROSC



Figure 2: Left: Patient's CXR post intubation on day 1; Right: Patient's CXR day 4 post-intubation, noted that there was new changes on the left side of the lungs.

twice daily for 1 week as it complicated with ventilator associated pneumonia (VAP) (Figure 2). Blood cultures taken had no growth but the tracheal aspiration secretion culture growth *Burkholderia Cepacia sp.* which was sensitive to Ceftriaxone. Subcutaneous enoxaparin sodium 1 mg/kg was given for five days for the Non-ST elevation myocardial infarction and Sustained Low-Efficiency Dialysis (SLED) was done as patient went to oliguric state after day-4 of illness. Patient condition continued to improve and responded to treatment. He was finally extubated and sent to the ward for recovery. Patient was discharged home after 18 days of admission.

DISCUSSION

Leptospirosis is a bacterial infection cause by a species of pathogenic *Leptospira* genus called Spirochetes which are known as *Leptospira interrogans*. It occurs in both temperate and tropical regions with the incidence in the tropics being approximately 10

times higher than temperate regions (Lim et al. 2011). Leptospirosis was considered as differential diagnosis for this case in the beginning because of its endemicity in Malaysia. The study done provides documented evidence that leptospirosis is an emerging public health concern in Malaysia with an incidence rate of 1.15/100,000 population and rising to 15.87/100,000 in 2013 (Tan et al. 2016).

Leptospirosis is spread by *Leptospira* which are pathogenic or saprophytic. Pathogenic leptospirosis is normally found in the renal tubules of host animals while saprophytic leptospirosis is commonly isolated from wet or humid environments. Wild and domestic animals, including rats, mice, sheep, cattle, pigs, dogs, racoons, and goats are the reservoir of leptospirosis. Infected animals excrete *Leptospira* in the urine, and can persist for several months in the environment with appropriate temperature (28° to 32°C) with moisture. Direct contact with the urine of infected animals or exposure to the soil, water, or other

matter contaminated with *Leptospira* can infect human. Thus, risk factors for the infection include occupational factors such as outdoor activities, presence of cut or wound at body parts during work and environmental factors such as contact with rodents through using the food materials ate by infected rat and contact with contaminated soil or water with rat urine (Kamath et al. 2014). In our case, background social history was very limited as the patient lived alone and he was unconscious on arrival at the ED. The initial signs and symptoms were not typical of leptospirosis. However, due to the epidemiologic data and abnormal LFT, we decided to send serum ELISA for leptospirosis.

Leptospiral infection symptoms in human can range from no symptom at all to the severe spectrum of the disease which are Weil's disease, and death. It also can present as ocular symptom only, which is known as ocular leptospirosis (Shao Yin et al. 2018). Ninety percent of cases are anicteric leptospirosis, which means that jaundice does not occur in the patient. Anicteric leptospirosis patient will undergo phase 1 and phase 2 of the illness. In phase 1 (acute or septic phase), patients have flu-like symptoms such as severe headache, sudden high-grade fever of 39°C or more, eyes inflammation, muscle ache, diarrhoea, fatigue, nausea and vomiting, chills, rigors and maculopapular rashes. Phase 1 usually lasts around 3-5 days. In phase 2 (the immune phase), anti-spiral antibodies start to multiply and infected patients will fall sick again lasting for up to 30 days or more.

However, some patients do not go into phase 2 of the illness. Another 10% of cases fall into icteric leptospirosis which is also known as Weil's diseases. Weil's disease is a more severe form than anicteric leptospirosis where it can develop into a more fatal condition (Sharma & Yadav 2008). Organ damage including liver, kidneys, brain, heart and central nervous system are affected within 10 days of infection. This fatal infection tends to prolong the period of severe fever, jaundice, azotaemia, hypotension as well as haemorrhagic vasculitis (Lim et al. 2011). In our patient, there was history of generalised lethargy, fever, chesty cough, abdominal pain, vomiting, and diarrhoea as revealed by his friend who saw him just before he collapsed. Compared to the other cases described in the literature, severe form of leptospirosis is usually icteric leptospirosis where patient will have frank jaundice with and other organ damage (Lim et al. 2011). However, our patient did not have jaundice at the first place. Our patient falls into the category of Weil's diseases because of its abrupt and severe presentation despite no jaundice.

Non-survivors were usually older, and had higher frequency of oliguria, cardiac arrhythmia, dyspnoea and pulmonary rales (Daher et al. 1999) and had higher frequency of oliguria, cardiac arrhythmia, dyspnea, and pulmonary rales. Logistic regression showed that the only independent factor associated with death was oliguria (odds ratio [OR] 8.98). The mortality rate also increase if there is co-existing infection such as dengue

fever (Zyneelia & Hashim 2017). Other common symptoms were fever (38-40°C), rigors, headache, conjunctival suffusion, dry cough, nausea and vomiting, diarrhoea and muscle pain. In Weil's disease, the clinical manifestation will be more severe and this includes frank jaundice, renal failure with oliguria, haemorrhagic features and systemic inflammatory syndrome or shock (Sandra et al. 2018). Our patient at the age of 56, with multiple comorbid and presented with PEA, HHS, oliguric AKI, non-ST elevation myocardial infarction (NSTEMI), and subsequent lungs infection was a rare case of survivors. His kidneys involvement manifested by elevated serum blood urea nitrogen and creatinine levels. Unfortunately we did not do any urinalysis to detect pyuria, haematuria or urine protein which was also reported to be the findings of AKI secondary to Leptospirosis (Katz et al. 2001) a zoonosis with global distribution, commonly occurs in tropical and subtropical regions; most reported cases in the United States occur in Hawaii. All laboratory-confirmed leptospirosis cases in the State of Hawaii from 1974 through 1998 (n=353).

Meanwhile, cardiac involvement can present as (ECG) abnormalities, echocardiographic evidence of myocardial dysfunction, cardiac biomarkers evidence of myocardial damage, and endocarditis. ECG changes vary which include sinus tachycardia or bradycardia, atrial fibrillation (AF), 1st or 3rd-degree heart block, ventricular and supraventricular extra-systole, bundle branch block,

low voltage QRS, changes in P-QRS-T complex and ST-T wave disturbance (Navinan & Rajapakse 2012). However, we could not find any similar case report of Leptospirosis presented with PEA which responded quickly to active resuscitation such as the present case.

The standard first-line treatment for severe leptospirosis is intravenous penicillin (Sandra et al. 2018). However, in the case of severe leptospirosis with other concurrence infection like our patient, intravenous ceftriaxone is the better choice as it has broader spectrum of antimicrobial activity. Furthermore, it is cost-effective and easier for health care personnel to administer as it is once per day dose in compared to penicillin which is 6-hourly dose (Panaphut et al. 2003) open-label, randomised trial at Khon Kaen Hospital (Thailand). It had also been updated in the latest Malaysian National Antimicrobial Guideline 2019 that suggested intravenous Ceftriaxone 2 g once per day for seven days as the first-line treatment the patient with severe leptospirosis (National Antimicrobial Guideline 2019).

CONCLUSION

Leptospirosis can present with unusual symptom and life-threatening event especially in patient with multiple comorbidity. Thus, the diagnosis should be considered especially in endemic area. Early awareness of the distinct presentations of leptospirosis and prompt antibiotic therapy can dramatically save the patients.

REFERENCES

- Daher, E., Zanetta, D.M., Cavalcante, M.B., Abdulkader, R.C. 1999. Risk factors for death and changing pattern in leptospirosis acute renal failure. *Am J Trop Med Hyg* **61**(4): 630-4.
- Kamath, R., Swain, S., Pattanshetty, S., Nair, N.S. 2014. Studying risk factors associated with human leptospirosis. *J Glob Infect Dis* **6**(1): 3-9.
- Katz, A.R., Ansdell, V.E., Effler, P.V., Middleton, C.R., Sasaki, D.M. 2001. Assessment of the clinical presentation and treatment of 353 cases of laboratory-confirmed leptospirosis in Hawaii, 1974-1998. *Clin Infect Dis* **33**(11): 1834-41.
- Lim, J.K., Murugaiyah, V.A., Ramli, A., Abdul Rahman, H., Mohamed, N., Shamsudin, N., Tan, J.C. 2011. A case study: leptospirosis In Malaysia. *Webmed Central Infectious Diseases* **2**(12): WMC002764
- National Antimicrobial Guideline (NAG) 2019, 3rd Edition. 2019. Ministry of Health Malaysia.
- Navinan, M.R., Rajapakse, S. 2012. Cardiac involvement in leptospirosis. *Trans R Soc Trop Med Hyg* **106**(9): 515-20.
- Panaphut, T., Domrongkitchaiporn, S., Vibhagool, A., Thinkamrop, B., Susaengrat, W. 2003. Ceftriaxone compared with sodium penicillin g for treatment of severe leptospirosis. *Clin Infect Dis* **36**(12): 1507-13
- Sandra, G.G., Ana, P.V., Judith, G.-M. 2018. Leptospirosis: practice essentials, background, pathophysiology [MEDSCAPE Web site]. <https://emedicine.medscape.com/article/220563-overview> [27 January 2020].
- Shao Yin, Y., Faj, N., Nro, R., Jwak, A. 2018. Case report: conjunctiva granuloma, a rare presentation of ocular leptospirosis presenting as conjunctiva granuloma: case series. *Med & Health* **13**(1): 272-8.
- Sharma, M., Yadav, A. 2008. Leptospirosis: epidemiology, diagnosis, and control. *J Infect Dis Antimicrob Agents* **25**(2): 93-103.
- Tan, W.L., Soelar, S.A., Mohd Suan, M.A., Hussin, N., Cheah, W.K., Verasahib, K., Goh, P.P. 2016. Leptospirosis incidence and mortality In Malaysia. *Southeast Asian J Trop Med Public Health* **47**(3): 434-40.
- Zyneelia, H., Hashim, E. 2017. Case report: fatal pulmonary haemorrhage in co-infection with dengue and Leptospirosis. *Med & Health* **12**(1): 131-7.

Received: 22 Jul 2019

Accepted: 19 Apr 2020