

A Fatal Case of Chikungunya Virus Infection with Liver Involvement

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SUMMARY

Recovery from chikungunya is previously considered universal and mortality due to the virus is rare and unusual. Findings from recent chikungunya outbreaks occurred in Reunion Island and India have since challenged the conventional view on the benign nature of the illness. Malaysia has experienced at least of 4 outbreaks of chikungunya since 1998. In the present on-going large outbreak due to chikungunya virus of Central/East African genotype, a previous healthy sixty six years gentleman without co-morbidity was noted to have severe systemic infection by the virus and involvement of his liver. He subsequently passed away due to cardiovascular collapse after 5 days of illness.

KEY WORDS:

Chikungunya, Fatality, Cardiovascular Collapse, Hepatitis

INTRODUCTION

Chikungunya (CHIK) virus is a small envelope positive sense single-stranded RNA virus, belongs to the genus *Alphavirus* under the family *Togaviridae*. It was first isolated from human serum and subsequently, *Aedes aegypti* mosquitoes, during an epidemic in the Newala district of Tanzania in 1952. Since then, CHIK virus has caused occasional outbreaks and some larger epidemics throughout most of sub-Saharan Africa and tropical Asia including India and the Western Pacific Region¹. Malaysia experienced the first outbreak of CHIK in late 1998 involving a few hundred residences in Klang within the state of Selangor. Since then, a couple of outbreaks had occurred but were rapidly controlled. However, the present on-going outbreak, which started in the state of Johor in early 2008, has since then spread all over the country inclusive the state of Sarawak².

Chikungunya virus is transmitted to human beings by infective mosquitoes of the *Aedes* genus. The symptoms of CHIK virus infection are characterized by fever, headache, severe backache and joint pain, rash, and lymphadenitis. Most illnesses are self-limiting and recovery is considered universal though arthritis and arthralgia can be prolonged and excruciating for several months¹. We report a previously healthy man without co-morbidity from Sarawak who succumbed to the illness due to circulatory collapse with liver involvement following CHIK virus infection.

CASE REPORT

W.R, a sixty six years old Iban gentleman was admitted to a district hospital on the night of 15 January 2010 with the complaints of multiple joints pain, limbs swelling and fever of 2 days duration. The illness was associated with chills, rigors, myalgia, vomiting, loss of appetite, decrease urine output and loss of weight. There was no associated cough, diarrhoea, retro-orbital headache, skin rashes or bleeding tendency, loss of consciousness or seizure. He was previously well, healthy and worked as a policeman but has since retired and is currently self-employed and engaged in vegetable farming. He was non-alcoholic and non-smoker. He was admitted to hospital in 2003 with acute hepatitis which presented as acute liver failure but had recovered fully since then. There was no history of recent visit to jungle or oversea trip or any contact with dead animals. His daughter and a few of his neighbours developed similar acute febrile illness with arthralgia at around the time of onset of his present illness but recovered.

Physical examination on admission showed that he was pink with no jaundice or cyanosis but was dehydrated. There was no clinical feature of chronic liver disease or hepatosplenomegaly. There was no palpable lymphadenopathy. The lungs were clear with good air-entry. There were swelling of hands and pitting oedema on both lower limbs up to mid-shin but there was no obvious knee or elbow joints swelling. His axillary body temperature was 37.1°C and with blood pressure of 139/78 mmHg and pulse rate of 101/minute. Urine examination showed trace albumenuria. An initial clinical diagnosis of acute bacterial infection with dehydration was made and he was started intravenous (I/V) ampicillin 500 mg QID and oral erythromycin 800 mg BD. Over the night, his systolic blood pressure fluctuated between 93 to 124 mmHg with diastolic 73 to 79 mmHg overnight. On review at the following morning, he was given a bolus pint of physiological saline and put on I/V fluid of 1.5 litre/day as his blood urea was noted to be increasing. By mid-day, he developed shortness of breath and complained of severe epigastric pain. He was subsequently intubated for respiratory distress prior to being transferred to Sarawak General Hospital (SGH) for further management.

On arrival at SGH, he was noted to be restless, tachycardic with poor peripheral circulation. His blood pressure was 123/71 mmHg with a pulse rate of 106/minute. Other than a palpable liver, physical findings concurred with those in the

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Table I: Blood profile of the patient with fatal chikungunya virus infection.

Date (Time)	15/1/10 (2200)	16/1/10 (2100)	17/1/10 (0430)	17/1/10 (1500)	17/1/10 (1800)	17/1/10 (2300)	18/1/10 (0430)
Haemoglobin (g/dl)	17.6	14.4	11.7	12.8	16.2	17.8	14
Total white (10 ⁹ /L)	20.9	23.7	17.6	37.0	34.3	36.3	31.4
Platelet (10 ⁹ /L)	127	85	58	103	74	109	83
Haematocrit (%)			34.5	39.2	49.6	55.2	43.2
Prothrombin Time (sec)			29.4	30.6		27.5	34.1
aPTT (sec)			103.9	152.2		175.5	142
INR			2.7	2.8		2.5	3.2
Sodium (mmol/L)	119	126	134	137			140
Potassium (mmol/L)	5.6	5.8	lyse	lyse			lyse
Urea (mmol/L)	26	26.7	25.6	22.1			22.7
Creatinine (µmol/L)		421	378	302			358
Bilirubin (µmol/L)			2				
AST (U/L)			251				
ALT (U/L)			124				
Albumen (g/L)			3				
Alk. Phosphatase (U/L)			128				

aPTT = Activated Partial Thromboplastin Time,

INR = International Normalised Ratio

district hospital. After an initial I/V fluid resuscitation and a bolus dose of ceftriaxone 2 gm, he was immediately admitted to intensive care unit (ICU) and ventilated using bilateral mode ventilation. In ICU, he started to develop cardiac decompensation and was started triple inotropic support (dopamine/noradrenaline/dobutamine) with intermittent voluven infusion and sodium bicarbonate for severe metabolic acidosis. On 17/1/2010, he developed intravascular coagulopathy and was transfused with cryoprecipitate and fresh frozen plasma. He developed cardiac arrhythmia and was given I/V amiodarone. Despite all the intensive management, his condition continued to deteriorate and he passed away at 5.52 a.m. on 18/1/2010.

His chest X-ray taken at admission was normal with no evidence of pleural effusion. Table I shows the patient's blood profile since admission. Culture of his blood taken prior starting antibiotics had no growth of micro-organism after 5 days of incubation. Laboratory tests for hepatitis B and C were negative. Anti-dengue IgM was detected in his serum but no dengue virus specific non-structural protein (NS1) was detected by dengue NS1 antigen-capture ELISA. Molecular detection for dengue virus RNA by RT-PCR was negative and no dengue virus was isolated from his serum and post-mortem biopsy liver tissue. CHIK virus RNA was detected in his serum and liver tissue. CHIK virus of Central/East African genotype, closely related to the strain that was first introduced into Malaysia in the state of Johor in early 2008, was isolated from both his serum sample and post-mortem liver biopsy tissue.

DISCUSSION

Clinicians generally consider CHIK to be a relatively benign self-limiting illness with joint involvement as the main manifestation. Recently, numerous case-series and case reports from recent outbreaks occurred in Reunion Island and

India have since challenged the conventional view on the benign nature of the illness. Atypical presentations and complications of CHIK virus infections involving nervous system, heart, kidney, and liver leading to serious consequences and deaths have been reported. The incidence of serious disease associated with increase risk of mortality appears to be higher in patients with pre-existing comorbidity and those of aged 65 years and above.

This report records the first case of mortality due to CHIK virus infection in Malaysia. Though the patient did not have pre-existing co-morbidity, his age could have contributed to the development of serious complications. In previous reports, neurological and cardiac complications were often described as the common cause of mortality though hepatitis due to the virus had also been reported. Severe systemic infection with cardiovascular collapse was probably the terminal event for this patient though there were clinical and laboratory evidence of hepatitis. This case also demonstrates that the positive detection of anti-dengue IgM based on single serum sample should be interpreted as recent dengue and not acute dengue, especially in dengue hyperendemic countries.

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