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A rare but potentially lethal complication of dengue

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ABSTRACT

Severe rhabdomyolysis is an uncommon but potentially fatal complication of dengue fever that is not well characterised and may be underreported. With the resurgence and continued rise of dengue cases worldwide, physicians must be aware of the less common but serious complications of dengue. Here, we report a patient who presented with severe rhabdomyolysis secondary to dengue fever with a serum creatine kinase of 742 900 U/L.

1. Introduction

Severe rhabdomyolysis is an uncommon but potentially fatal complication of dengue fever that is not well characterised and may be underreported. Dengue fever, a mosquito-borne flavivirus endemic in Southeast Asia and Western Pacific regions, has been increasingly reported worldwide[1]. With the resurgence and continued rise of dengue cases in endemic regions, physicians must maintain not only a high index of suspicion for the diagnosis but also an awareness of the less common but serious complications of dengue. Here, we would like to report a patient who presented with severe rhabdomyolysis secondary to dengue fever with a serum creatine kinase (CK) of 742 900 U/L on admission.

2. Case report

An active 50 year old Chinese male with a medical history of hypertension and hyperlipidemia on daily long term amlodipine 5 mg and simvastatin 10 mg, presented with fever of 5 d duration associated with myalgia. In the initial 2 d of illness, his symptoms were mild and he proceeded

with a mountain hike in Malaysia. He reached the summit of 2 000 feet above sea level with little difficulty. Upon return, his symptoms worsened and he developed abdominal pain and vomiting 2 d prior to admission. No medications were recently initiated and the patient denied illicit drug use. There was no history of fall or injury. There was also no family history of muscle diseases.

On admission, the patient was alert and ambulant. He was noted to be tachypnoeic with a respiratory rate of 35 breaths/min, a blood pressure of 174/85 mmHg and a pulse rate of 85 beats/min. His laboratory tests are as follow: serum CK: 742 900 U/L, creatinine: 1 036 mmol, arterial bicarbonat: 7.4 mmol/L. The diagnosis of dengue fever was confirmed with both a positive dengue IgM and a positive dengue virus PCR. His blood and urine cultures demonstrated no growth of organisms and the leptospiral and rickettsia serologies were negative. His platelet count on admission was $33 \times 10^3 / \mu\text{L}$. Soon after admission, he was transferred to the intensive care unit (ICU) for continuous renal replacement therapy.

However, within 24 h, his condition deteriorated in the ICU. He required both inotropic and ventilatory support. His stay was complicated by the development of acute compartment syndrome of bilateral lower extremities from severe rhabdomyolysis and likely intramuscular bleed, acute liver failure and disseminated intravascular coagulation. He also had seizures from generalised cerebral edema and gastrointestinal bleeding requiring massive blood transfusions. On day 19 of his illness, he suffered a cardiorespiratory collapse and eventually demised.

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3. Discussion

Severe rhabdomyolysis is an uncommon complication of dengue[2–5]. Its pathogenesis has remained elusive although the release of cytokines, particularly tumour necrosis factor, has been implicated[6–9]. The causal relationship between dengue and rhabdomyolysis is often confounded by the presence of established shock and multiorgan complications of the critically ill patient. However, in our patient, it was clear that the rhabdomyolysis occurred before the development of shock, suggesting that this may be a true complication of dengue.

It is also interesting to note that in our patient, there was a history of significant physical activity early in his illness. Acharya *et al*[2] reported a patient with rhabdomyolysis from dengue who was involved in labour work during the period of illness while Lim *et al*[3] reported a case of readmission for myalgia with rhabdomyolysis following resumption of exercise 2 d after a prior hospital discharge for dengue fever. It seems plausible that strenuous physical activity may be a potential risk factor for severe rhabdomyolysis peri-illness. Hence, it may be prudent to advise dengue patients to avoid aggressive physical activity during the period of acute illness or convalescent phase. This is especially so for those who are engaged in laboriously demanding occupations or patients who enjoy strenuous recreational activities.

We concede that our patient was on long term low dose statin medication. However, fatal rhabdomyolysis associated with statins is rare[10] and appears to be dose dependent[11,12]. Studies have also attempted to look at exertion-induced muscle injury in patients on statins. In a study by Thompson *et al*, CK levels were 62% to 77% higher after treadmill exercise in patients on lovastatin versus placebo[13]. Nevertheless, exertion-triggered rhabdomyolysis in patients on statin therapy resulting in acute renal failure requiring dialysis is extremely rare and the levels of CK reported were generally far below that of our patient[14]. Exercise and rhabdomyolysis has also been well described. However, exercise -induced rhabdomyolysis leading to dialysis-requiring acute renal failure is rare too. In a series by Sinert *et al*, none of the 35 patients with pure exercise-induced rhabdomyolysis developed acute renal failure in the absence of nephrotoxic cofactors[15]. In addition, other reports of severe exercise-induced rhabdomyolysis have implicated predisposing factors such as the concomitant use of performance enhancing compounds[16], sickle cell trait[17] and genetic factors[18].

Hence, given the clinical picture, simvastatin or exercise alone was unlikely to have accounted for our patient's extreme level of CK. To our knowledge, it is the highest level of CK reported in a dengue patient with rhabdomyolysis. On the other hand, it is possible that the unfortunate combination of all 3 factors – dengue virus infection, coupled with statin use and exercise led to his fatal rhabdomyolysis.

In conclusion, severe rhabdomyolysis is a rare but potentially lethal complication of dengue. The mechanism as well as risk factors for this complication including exercise peri-illness or concomitant statin use, remains to be determined. In Southeast Asia, dengue is endemic, statin use is common, and there is an increasing number of people engaging in endurance sports, with many more involved in physically demanding occupations. Thus, physicians must

be aware of this complication, and possibly the 'high-risk' patient profile as described in our report. We hope that future studies may continue to further our understanding of this enigmatic disease, thereby leading to improvements in patient care and clinical outcomes.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

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