Myocarditis in three patients with dengue virus type DEN 3 infection

Dengue fever is caused by four dengue virus serotypes, DEN 1, 2, 3, and 4 which are antigenically related, closely [1]. Myocarditis and cardiac dysfunction are recognised complications of dengue fever, but very few studies have identified the causative dengue virus (DEN) type [2]. We report three cases of DEN 3 who had significant cardiac dysfunction suggestive of myocarditis in an outbreak of dengue fever in Kandy, Sri Lanka in April 2005.

Blood samples were obtained within four days of the onset of fever and subjected to RT-PCR-AGE (Agarose gel electrophoresis) assay and Semi-nested—PCR-AGE assay [3]. Acute sera were tested for IgM antibodies using MAC-ELISA and rapid strip test to detect high titres of both IgM and IgG.

Case 1

A 37-year old male medical doctor was admitted with high fever, headache, myalgia and nausea for 3 days. Pulse rate was 74/min, regular, low volume and blood pressure was 100/70 mmHg. He had no clinical evidence of bleeding. He felt tiredness and intermittent chest discomfort. Investigations are shown in Tables 1 and 2. On the 4th day of fever he collapsed while straining at micturition with bradycardia of 38 beats per min and blood pressure 80/50 mmHg. He was resuscitated and the ECG showed ST segment changes which reverted in five hours. The fever lasted for 5 days and ECG changes reverted to normal on the 10th day of illness. Repeated 2-dimensional echocardiograms were normal.

Case 2

A 32-year old woman was admitted with fever, headache, myalgia and nausea of one day's duration. Pulse rate was 126/min and blood pressure dropped to 84/56 mmHg on the second day of fever. There was no evidence bleeding or effusions. The ECG showed sinus tachycardia with an abnormal ST segment (Table 1). She became stable on the 4th day and the ECG reverted to normal on the 6th day of illness.

Table 1. **ECG, echocardiography, serology and dengue virus type in the patients**

Case	*1st ECG*	*2nd ECG*	*Lowest Ef* (%)*	*ELISA test*	*RT-PCR***
1	3rd day. T inversion L1, V1–V6; Flat T 11, 111, avF, avL	4th day. ST elevation L1, avL, V2–V5; ST depression 11, 111, avF	53	IgM	DEN 3
2	2nd day. ST depression V4–V6; T inversion 11, 111, avF	Same as first ECG	56	IgM	DEN 3
3	2nd day. T inversion 111, avF, V1	3rd day. T inversion V2–V5, Flat T 11, V6	59	IgG	DEN 3

*Ef = ejection fraction measured using echocardiography

**RT-PCR = Reverse transcriptase

Table 2. **Haematological and biochemical investigations of the patients**

Case	*Troponin T*	*AST (Units/l)*	*ALT (Units/l)*	*Lowest WBC ($\times 10^9$/l)*	*Lowest platelet count ($\times 10^9$/l)*	*PCV (%)*
1	+	88	Normal	1.9	100	34–45
2	–	Normal	Normal	1.8	96	35–39
3	+	342	302	2.2	94	36–39

AST = aspartate transaminase, ALT = alanine transaminase (normal <40 U/l), PCV = packed cell volume

Case 3

A 31-year old woman nursing officer was admitted with fever, headache, myalgia, nausea and vomiting for 2 days. Pulse rate was 68/min and the blood pressure was 140/80 mmHg. Her ECG was abnormal on admission (Table 1) and reverted to normal on the 8th day.

Discussion

We describe 3 cases of myocarditis caused by DEN 3 virus. The importance of this study is in the identification of the causative virus type as DEN 3 for the first time in the literature. However, we observed 5 cases of myocarditis in a series of 404 dengue cases at Peradeniya, but the causative dengue serotype was not identified [4]. DEN 2 has been identified to a cause myocardial dysfunction of children who had DHF/DSS in a series of 17 patients in India [2]. Their finding had a major impact on the elucidation of the mechanism of shock in fluid resistant DSS. Over the past two decades, DEN 3 had been identified as the cause of epidemics of dengue fever in Sri Lanka, but myocarditis has not been reported [5].

In the cases presented, cardiac involvement was detected in the early phase of the infection. T wave inversion was the commonest ECG change and relative bradycardia was the problem in 2 cases. Tachycardia was observed in one case. Serology of cases indicates presence of both primary and secondary dengue infection. This unprecedented outbreak of DEN 3 with more cardiac complications could either be due to genetic susceptibility of the host or alteration of the virulence of the viral strain or both. Further virological studies are needed to unravel these problems. For the management of myocarditis we adopted a policy of strict bed rest, oxygenation, and monitoring.

Acknowledgements

We thank Prof. SN Arsecularatne for the valuable comments.

References

1. World Health Organisation. *Dengue Haemorrhagic Fever: Diagnosis, Treatment, Prevention and Control* 1998, Geneva: WHO, Prentice-Hall of India Private Ltd: 1–47.
2. Wali JP, Biswas A, Chandra S, *et al.* Cardiac involvement in dengue haemorrhagic fever. *International Journal of Cardiology* 1998; **64**: 31–6.
3. Seah CLK, Chow VTK, Tan HC, Chan YC. Rapid, single step RT-PCR typing of dengue viruses using five NS3 gene primers. *Journal of Virology Methods* 1995; **51**: 193–200.
4. Kularatne SAM, Gawarammana IB, Kumarasiri PRV. Epidemiology, clinical features, laboratory investigations and early diagnosis of dengue fever in adults: a descriptive study in Sri Lanka. *Southeast Asian Journal of Tropical Medicine and Public Health* 2005; **36**: 282–8.
5. Messer WB, Gubler DJ, Harris E, Sivananthan K, De Siva AM. Emergence and global spread of a dengue serotype 3, subtype III virus. *Emerging Infectious Diseases* 2003; **9**: 800–9.

SAM Kularatne, *Senior Lecturer in Medicine, Department of Medicine, Faculty of Medicine, University of Peradeniya,* **Manoji MK Pathirage**, *Medical Officer, General Hospital, Peradeniya, and* **UAB Medagama**, *Senior Registrar in Medicine, General Hospital, Peradeniya, Sri Lanka, and* **Sunethra Gunasena**, *Medical Virologist, Medical Research Institute, Colombo 8, and* **Maya B Gunasekara**, *Head, Genetech Research Institute, Colombo 8.*
Correspondence: SAMK, *e-mail: <samkul@sltnet.lk>* *(Competing interests: none declared). Received 21 October 2005 and revised version accepted 20 January 2006.*