OUTBREAK OF DENGUE IN 2009: HISTOPATHOLOGICAL CONFIRMATION OF MYOCARDITIS BY AUTOPSY STUDIES

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Introduction

Dengue fever is caused by one of dengue viral serotypes DEN 1 – 4. Dengue viral infection has been recognized since the early 1980s in Sri Lanka. Dengue Haemorrhagic fever had been increasingly observed since 1989. The worst recorded outbreak of dengue in the island occurred in 2009 with 245 deaths and 24629 cases. During this epidemic, General Hospital, Peradeniya received a substantial number of dengue cases. Of them, a proportion of patients died despite meticulous management in the Intensive Care Unit (ICU). What exactly caused these deaths during their acute illness remains unclear. Therefore, we performed limited number of autopsies and the tissue materials were subjected to histopathological examination. Aims of this study are to describe the outbreak of dengue at General Hospital, Peradeniya in 2009, to identify the pattern of complications and to identify the cause of death based on histopathological evidence.

Methodology

Data were collected prospectively from all clinically diagnosed patients with dengue infection admitted to the Professorial Medical Unit, General Hospital, Peradeniya from May to August 2009. Patients were managed according to the routine protocols of the hospital. Data collection was done by medical personnel, using a structured data sheet. Confirmation of the diagnosis was done at Medical Research Institute, Colombo using serological tests. Dengue specific IgM and IgG ELISA, HIA and RT-PCR technique were used. Blood samples were collected during routine collection. Further, the routine investigations such as Full blood count, Liver biochemical tests, Ultra Sound Scan of the abdomen, ECG, and 2D Echo Cardiogram were used to identify the complications. Autopsy findings and histopathological results were considered in identifying causes of death in deceased. Histopathological examination was done at Department of Forensic Medicine.

Table 1. Histopathological results with clinical details

Age/ Gender	Clinical data	Histology	Diagnosis
16/ Female	Pleural effusion Hypotension Tachycardia	Heart - interstitial oedema, inflammatory cells, necrosis of myocardial fibers Lung – diffuse alveolar damage	Myocarditis
28/Male	Pleural effusion Hypotension Tachycardia, Bleeding	Heart - interstitial oedema, inflammatory cells, necrosis of myocardial fibers, Pericarditis	Myocarditis
28/Male	Pleural effusion Hypotension Tachycardia	Heart - interstitial oedema, inflammatory cells, necrosis of myocardial fibers Lung - septal congestion, haemorrhage	Myocarditis
31/ Female	Pleural effusion Hypotension Tachycardia	Heart - interstitial oedema, inflammatory cells (lymphocytes), necrosis of myocardial fibers	Myocarditis

Results

A total of 319 patients were presented to the hospital during the considered period and the highest incidence was observed in June. Of the total, 166 (52%) had complications (Table 2). Of them 90% of patients had secondary dengue infection and in 5 patients, DEN-1 was identified as the causative serotype.

During this period 11 patients died, of them 6 were admitted to the ICU in a state of shock. The complications were multiple. Multiple system involvement with thrombocytopenia predominated whilst a significant number had cardiovascular complications such as hypotension and myocarditis. Those who had myocarditis and effusions simultaneously were extremely unstable and needed close monitoring.

The histopathological findings are shown in table 1. Four patients had evidence of florid myocarditis. There were interstitial oedema with inflammatory cell infiltration, necrosis of myocardial fibers and also one had evidence of pericarditis. Further there were pulmonary abnormalities denoted by septal congestion, pulmonary haemorrhage and diffuse alveolar damage.

Discussion and Conclusion

We observed an abrupt rise in the incidence of dengue infection with very high morbidity and mortality during May to July 2009. Compared to published literature, more than 50% of patients had complications (Kularatne, 2007; Malavige, 2004). The multiple complications developing simultaneously led to staggering recovery whilst unprecedented number succumbed to illness. The management of patients became difficult as the current management guidelines failed to cover all these aspects of complications (Kularatne *et al.*, 2006). We were able to identify that a significant number of patients had both effusions (pleural and ascites) and myocarditis together causing hypotension leading to shock. We observed that those who died had tachycardia and effusions suggesting extravasations of plasma causing dengue haemorrhagic fever – grade 4. But they failed to respond to prompt fluid replacement. This fact arose the suspicion that the possibility of coexistence of primary cardiac failure due to myocarditis in these patients. Subsequent histopathological evidence proved the presence of florid myocarditis in these patients and contributed for death. This was the very first study that brought histopathological evidence by autopsy studies, to prove myocarditis in dengue infection.

Table 2. Identified complications

Complication	**Number of cases**
Thrombocytopenia (< 50)	94
Bleeding	47
Hypotension (SBP < 100mmHg)	56
Myocarditis	45 (27%)
Pleural effusion	41
Myocarditis + pleural effusion	21 (13%)
Ascites	29
Acute renal failure	6
Acute liver failure	34

References

Buan, W.H. and Ton, G. (1967). Cardiac involvement in haemorrhagic fever. Journal of Singapore Paediatric Society, 9: 26 - 28.

Guidelines on clinical management of dengue fever/ dengue haemorrhagic fever. (2005). Epidemiological Unit, Ministry of Health.

Kularatne, S.A.M., *et al.* (2007). Cardiac complications of a dengue fever outbreak in Sri Lanka, 2005. Transaction of the Royal Society of tropical medicine and Hygiene, 101: 804 - 808.

Kulatatne, S.A.M. *et al.* (2006) Synopsis of findings from recent studies on Dengue in Sri Lanka. Dengue Bulletin, 30: 80 - 85.

Malavige, G.N. *et al.* (2004). Dengue viral infection. Postgrad. Med. Journal, 80: 588 - 607.