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Myocarditis in Dengue Fever

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Abstract

There is a wide variation in the reported incidence of cardiac involvement in dengue due to the difference in the criteria used to identify cardiac involvement. Most common cardiac rhythm abnormality noted was sinus bradycardia, which was often self limited. Fulminant and fatal myocarditis have been documented in a few cases; though in general, most cases with cardiac manifestations improve with supportive care. Only about one tenth of patients with biomarker elevation had evidence of depressed left ventricular systolic function on echocardiography. Higher incidence of depressed left ventricular ejection fraction was noted in dengue shock syndrome.

Keywords: dengue fever, dengue hemorrhagic fever, dengue shock syndrome, expanded dengue syndrome, myocarditis

Dengue fever is a viral infection transmitted by mosquito vector *Aedes aegypti*. It has a wide spectrum of manifestation ranging from very mild disease to life threatening dengue shock syndrome (DSS) [1]. Dengue fever patients having cardiac manifestations come under the category of expanded dengue syndrome (EDS), which may have involvement of other systems like nervous system or gastrointestinal system as well.

In a recent single centre report from North India, only 1 out of 115 cases had evidence of myocarditis [1]. This patient had an initial ejection fraction of 40% which rose to 56% at hospital discharge. Clinical presentation was with fever and breathlessness. Features of congestive heart failure were noted on physical examination. There was sinus tachycardia on ECG; X-ray showed bilateral pleural effusion, echocardiography revealed mild pericardial effusion and global left ventricular hypokinesia. Decongestive therapy, inotropic support and platet transfusions were given and there were no long term sequelae on follow up.

Dengue myocarditis may not respond well to management in all cases. Fatal dengue myocarditis despite support with extracorporeal membrane oxygenator (ECMO) has been documented by Yee-Huang Ku et al [2]. This patient was hemodynamically unstable, had ST-T changes on ECG and rising Troponin I levels. Echocardiography had shown hypokinesia of anteroseptal region of the left ventricle with ejection fraction of 34%. Coronary angiography showed patent coronary arteries. Arterial blood gas analysis showed severe metabolic acidosis and high lactate levels. Intra aortic

balloon pump (IABP) and ECMO were used as there was poor response to three vasopressors. Ejection fraction deteriorated to 10% and severe pulmonary edema occurred. Patient died on 6th day in spite of all supportive measures. Another case of fulminant dengue myocarditis with shock and fatal outcome despite IABP support was reported by Lin TC et al [3].

A study of 100 cases of dengue from South India specifically looking at cardiac manifestations could not document any case with echocardiographic evidence of myocarditis [4]. At the same time 32 of them had sinus bradycardia, which was noted to be the commonest rhythm abnormality in their series. This is also the observation at author's institution during a recent epidemic of dengue (unpublished observation). Ventricular bigeminy, ventricular trigeminy and ventricular tachycardia were noted in one patient each. AV dissociation with sinus node dysfunction was noted in another. All these changes reverted within 24 hours. Abnormalities of ST segment and T waves were noted in 11 patients.

In another study from South India involving 120 patients, cardiac manifestations were noted in 44 [5]. But this study had a broad definition of cardiac manifestations, including rhythm disturbances, changes in heart rate, raised cardiac enzymes, abnormal ECG and echocardiogram. In sharp contrast with the previous study, sinus bradycardia was noted only in 10 (8.77%). ST-T changes were noted in 4, first degree AV block in 4 and right bundle branch block in 2. All these abnormalities were transient. 28 patients had both CK-MB and troponin I elevation; 12 had isolated CK-MB elevation and 4 had isolated troponin I elevation. But the cut off value for CK-MB was taken as 25 and that for troponin I as 0.04, both being just the upper limit of normal. None of the patients in this study had significant echocardiographic abnormalities.

Twenty percent incidence of myocarditis among 300 cases of dengue was reported from Eastern India [6]. Other studies from different parts of India have also reported myocarditis as part of EDS [7, 8]. A report from Sri Lanka stated that there were 35000 cases of dengue during an out break in the country, of which 340 died. This study focussed on the 15 cases of dengue which occurred during pregnancy, of which one had myocarditis, but recovered with supportive measures [9]. Only one case of myocarditis was noted among 560 dengue patients at Martinique (Caribbean Island) [10]. In another report, 10.7% of 102 pediatric patients from Colombia with dengue hemorrhagic fever had myocarditis [11]. So it can be seen that the reported incidence of myocarditis varies widely between geographic regions and different studies.

Troponin I and N terminal fragment of B-type natriuretic peptide (NT-proBNP) were checked in 81 dengue patients by Miranda CH et al from Brazil [12]. 12 were found to have elevated cardiac biomarker levels. Ten of them underwent echocardiography and left ventricular dysfunction was noted in one, while 2 had regional wall motion abnormalities of the left ventricle and another had pericardial effusion with tamponade. Tamponade resolved after pericardiocentesis. Evidence for cardiac involvement was further confirmed by cardiac magnetic resonance imaging in these 4 patients. Two patients died before imaging could be obtained, but had necropsy findings were compatible with myocarditis. Dense staining of mononuclear cells were noted on immunochemistry for dengue virus in the myocardial specimens. Eight of the 12 patients had presented with clinical manifestations suggestive of cardiac involvement: 4 with heart failure, 3 with chest pain and 3 with hypotension and shock.

Radionuclide ventriculography in addition to ECG and echocardiography has been used to evaluate cardiac function in dengue [13]. Eight of the 17 patients studied had DSS while the rest had dengue hemorrhagic fever. Seven patients had left ventricular ejection fraction below 40% and 12 had global left ventricular hypokinesia. 99m Tc-pyrophosphate imaging was done in 4 patients initially, but no myocardial necrosis was demonstrated and further such imaging was discontinued. Five of the 8 patients with DSS had ejection fraction below 40%. ECG changes and left ventricular function reverted to normal within 3 weeks in this study.

One of the largest published studies on dengue myocarditis was from the outbreak which occurred in China in 2014 [14]. Of the total 1782 cases admitted at a single centre, 201 were diagnosed with myocarditis (11.28%). Diagnosis of myocarditis was made according to 2013 European Society of Cardiology position statement for myocarditis [14]. It is heartening to note that there were only 2 deaths in this large study. One of them was a sudden death while another died of severe heart failure.

In conclusion, cardiac involvement in dengue can vary from just biomarker elevation to severe fulminant fatal myocarditis. Whether sinus bradycardia which is the most common cardiac manifestation in dengue, can be taken as a feature of myocarditis is debatable. Most cases of dengue myocarditis make a good recovery with supportive intensive care, while an occasional patient can succumb to the illness.

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