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Case Report

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Transient atrioventricular block due to complicated dengue: Case Report

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Images from complementary tests are shown with patient's consent.

ABSTRACT

Dengue's cardiological manifestations are diverse; the virus is able to enter the myocardium and cause acute myocarditis that sometimes may go unnoticed and be asymptomatic, with benign outcomes; while in others, it may produce electrocardiographic rhythm and conduction disturbances or signs of ventricular dysfunction that could lead to severe heart failure. We present the case of a 21-year-old man, a student, previously healthy, who was admitted to the Department of Cardiology with a diagnosis of dengue confirmed by serology and complicated with conduction disorders (2:1 advanced atrioventricular block) related to acute myocarditis due to dengue. This problem can be seen in areas where dengue is an emerging problem. Therefore it is critical to be aware of it in order to design strategies for prevention and treatment of complications.

Keywords: Dengue, Complications, Myocarditis, Atrioventricular block

Bloqueo aurículo-ventricular transitorio por dengue complicado: Presentación de un caso

RESUMEN

Las manifestaciones cardiológicas del dengue son muy variadas, el virus puede penetrar al miocardio y producir una miocarditis aguda que, en ocasiones, puede pasar inadvertida y cursar de manera asintomática, con una evolución benigna; y en otras, puede producir alteraciones electrocardiográficas de trastornos del ritmo y la conducción o signos de disfunción ventricular que pueden llegar a la insuficiencia cardíaca grave. Se presenta el caso de un hombre de 21 años de edad, estudiante, con historia previa de salud, que ingresó en el Servicio de Cardiología con diagnóstico de dengue, confirmado por serología, complicado con un trastorno de la conducción (bloqueo aurículo-ventricular de grado avanzado 2:1) en relación a una miocarditis aguda por dengue. Este problema puede observarse en áreas en las que el dengue constituye un problema emergente, por lo que es de vital importancia su conocimiento para diseñar estrategias de prevención y tratamiento de las complicaciones.

Palabras clave: *Dengue, Complicaciones, Miocarditis, Bloqueo aurículo-ventricular*

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INTRODUCTION

Dengue is an infection caused by a virus transmitted through the bite of infected female mosquitoes belonging to the genus *Aedes*, mainly the *Aedes aegypti*. Dengue virus belongs to the *Flaviviridae* family and there are

four variants: the serotypes DENV 1, DENV 2, DENV 3 and DENV 4. Severe dengue represents a life-threatening complication since it causes plasma extravasation, fluid accumulation, respiratory difficulty, severe hemorrhage and organ failure. The main symptoms are high fever (40°C), myalgia, arthralgia, nausea, vomiting, enlarged lymph nodes, headache and skin rash[1].

Dengue virus infection may be clinically inapparent or cause clinical manifestations of varying intensity, ranging from an undifferentiated febrile syndrome and other varieties associated with body aches to severe shock state and profuse bleeding, since the risk of presenting severe forms of the disease depends on the interaction of individual, epidemiological and viral factors[2].

Finally, there are some other less frequent clinical forms of dengue, characterized by a particularly severe damage to an organ or system: encephalitis, myocarditis, liver disease and renal damage with acute renal failure. As a disease, the characterization of myocarditis has diverse clinical presentations and causes. The myocarditis and the consequent cardiomyopathy that may take place are caused by infectious and non-infectious agents, and even by cardiotoxic drugs. Clinical findings include certain degrees of cardiac dysfunction, ranging from mild subclinical effects to arrhythmias, heart failure, cardiogenic shock, and even sudden death[3,4].

The emergence or reemergence of dengue depend on a combination of micro and macro determining factors, and everything that is related to this arbovirus represents a problem to be solved by the Health Care Sector[5].

CASE REPORT

Personal history and physical examination

A 21-year-old male student, previously healthy, who came to the health care center for presenting headache, general malaise, retroocular pain, myalgia, low fever and skin rash, due to what he was clinically diagnosed with dengue fever that was confirmed through serology.

During his evolution, electrocardiographic alterations were detected, so he was admitted to the Department of Cardiology with general malaise, but without cardiovascular symptoms. Physical examination revealed bradyarrhythmic heart sounds of good intensity, without third heart sound or heart murmurs; absence of thermal gradient or edema in the lower limbs; heart rate of 47 beats per minute and blood pressure of 110/80 mmHg. In the respiratory system the vesicular murmur was audible in both lung fields and there were no rales. The rest of the physical examination was normal.

The electrocardiographic monitoring revealed a 2:1 advanced atrioventricular conduction disorder (**Figure**) that was transient, without requiring pacemaker, that disappeared subsequently, with the restoration of sinus rhythm on the eighth day after the acute phase, which was interpreted as an acute myocarditis due to dengue complicated with an atrioventricular conduction disorder.

Complementary tests

- Blood analysis: normal blood count, coagulation with slightly decreased platelets, normal renal profile, ions and liver enzymes. Creatinphosphokinase (CPK) at the moment of the admission: 356 units.
- Dengue serology: positive for IgM on the sixth day.
- 12-lead electrocardiogram: the described conduction disorder is observed, in the form of 2:1 advanced atrioventricular block (**Figure**).
- Chest X-ray: cardiac silhouette within normality, absence of congestive pattern and no pleural effusion.
- Transthoracic echocardiography at the moment of the admission: evidence of slight pericardial effusion and decreased systolic thickening of the left ventricle anterior wall segments, with preserved global systolic function and structurally

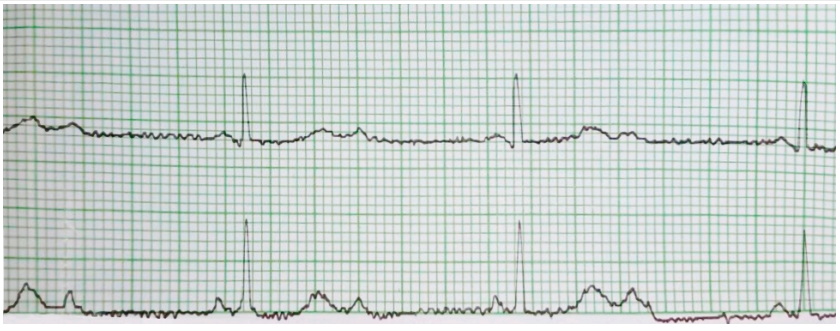

Figure. Electrocardiographic segment showing atrioventricular block secondary to a myocarditis due to dengue.

normal valve apparatus. No other disturbances of interest.

The patient had a favorable evolution and he was discharged in sinus rhythm, with the conduction disorder completely solved. At the 30-day follow-up medical appointment he was asymptomatic and the electrocardiogram was normal.

COMMENTS

The dengue virus is cardiotropic and it can damage the cardiovascular system. Cardiac damage can range from mild, without any clinical repercussions, to severe state with significant viral myocarditis, in which inflammatory cytokines due to complement activation, tumor necrosis factor-alpha and oxygen free radicals are involved in its pathogenesis[6]. Shock takes place four to five times more frequently at the moment of fever reduction or in the first 24 hours after its disappearance, in relation to the febrile stage, and when it develops, it is manifested through significant capillary leakage, in prolonged or recurrent infections, where most patients die due to direct or secondary to complications causes (massive hemorrhage, disseminated intravascular coagulation, non-cardiogenic pulmonary edema and multiple organ failure), as a sign of the hypoperfusion and reperfusion syndromes that characterize cases of severe dengue[7].

Patients with myocardial damage due to the dengue virus may have alterations in the electrocardiogram as well as decreased ejection fraction with global hypokinesia, but most of them have benign outcomes, with disappearance of all changes after some weeks, although on some other cases heart failure is refractory and leads to the patient´s death[8].

Histological imaging of acute myocarditis due to dengue has demonstrated the severe myocardial damage caused by this virus, with destruction of cardiac myofilaments and intense interstitial edema that causes separation and disruption of myocardial fibers, and it is angiocardiographically manifested by an image of peculiar striation of the myocardium (waffling), which is a sign of myocardial necrosis[8].

Focal spots with mononuclear cell infiltrates are evident in the heart and certain degree of cardiac myocytes degeneration is observed, with absence of their nucleus and loss of striae, as a result of interstitial edema, suggesting myocarditis. These findings suggest that direct infection of the virus in cardiac myocytes may be responsible, at least partially, for the dysfunction. However, in addition to the direct cytotoxic effect of the virus on the cardiac myocytes, the exacerbation of the host immune response leads to an increased expression of cytokines, which may contribute to the observed tissue damage. The lesions also seem to produce apoptosis, with the presence of pyknotic nuclei in myocytes and the loss of the mitochondrial integrity[9].

An important clinical consideration is the pathophysiology of myocarditis in COVID-19 which also has a viral origin. It is possible that there is a direct viral invasion or that the disease corresponds to an immune disorder[10]. Irabien-Ortiz *et al.*[11] describe the case of a patient with COVID-19 and note that her clinical condition was consistent with acute myocarditis, without initial respiratory symptoms, with a rapid progression to cardiogenic shock and the need for venoarterial extracorporeal membrane oxygenation (ECMO).

But the effect of myocarditis is not only limited to the mechanical heart functioning, it can also alter its electrical conduction[12]. This myocardial inflammation predisposes to arrhythmias through three mechanisms: a) inflammatory processes of myocytes and interstitium can lead to disturbances in the membrane potential, b) changes in the parameters of ventricular dynamics, the highest wall stress and the increase in oxygen consumption of the myocardium also increase the potential for arrhythmias, and finally c) secondary fibrosis and atrophy of the myocardial cell can favor the development of ectopic pacemaker sites. Probably the first two mechanisms play a predominant role in the arrhythmias associated to myocarditis due to dengue, as an acute and reversible disorder[13].

Lee *et al.*[14] found, in patients with myocarditis due to dengue, that bradyarrhythmias were more frequent (9/11 patients) compared to tachycardia (2/11 patients), which is the most frequent form of presentation of the rest of viral myocarditis. Some other disturbances of cardiac rhythm have been observed in children and adults with dengue infection such as sinus bradycardia, premature ventricular contractions, atrial fibrillation and Mobitz type I first and second degree atrioventricular block (Wenckebach)[15]. Some of these are described as atypical within the cardiac manifestations of dengue, which also include myocarditis itself, paroxysmal supraventricular tachycardia, and pericardial effusion[16]. Most patients have a spontaneous resolution of

these cardiac manifestations with symptomatic treatment. The association between cardiac rhythm disturbances and dengue is attributed to the presence of myocarditis[16].

Indications for permanent cardiac stimulation should continue to be based on clinical practice guidelines. As described by Bertomeu-González *et al.*[17], in patients with active SARS-CoV-2 infection, it should be taken into account that the implantation of a permanent cardiac stimulation device is contraindicated in any patient with active infection and fever. If it is considered that this stimulation cannot be delayed or temporarily replaced by drugs, a temporary pacemaker should be implanted until the patient is stable and afebrile for at least 48 hours, with negative blood cultures and C-reactive protein.

The patient that is presented did not require pacemaker implantation nor other treatments because the atrioventricular block was transient, which is described as remitting spontaneously after the acute phase or within some weeks.

Personnel of all health care services should be trained in all aspects for dengue prevention and care, and be aware that this disease −which generally evolves favorably in few days− may have serious implications. Another unresolved question, for which further studies are needed[3], is whether there is any genetic mutation of the virus that may have increased its cardiac pathogenicity.

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