

Case Report

Open Access, Volume 2

Myocarditis caused by salmonella enteritidis in a healthy 19-year-old male

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Received: Apr 20, 2021

Accepted: May 21, 2021

Published: May 25, 2021

Archived: www.jcimcr.org

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Introduction

Myocarditis is defined histologically as an inflammation of the heart muscle with a large variety of infectious and non-infectious etiologies and an incidence of approximately 1.5 million cases in 2013 worldwide [1,2]. The diagnosis of myocarditis is usually based on clinical presentation, laboratory testing, electrocardiographic and echocardiographic findings and, in selected patients, other cardiac imaging tools like coronary angiography and Cardiovascular Magnetic Resonance (CMR). A definitive diagnosis can only be established by Endomyocardial Biopsy (EMB), although most of the patients do not undergo this invasive procedure [3,4].

Nontyphoidal salmonellae are a major cause for diarrhea worldwide with about 94 million cases and 155.000 deaths yearly [5]. The main reservoirs of these gram-negative bacteria represent animals and agricultural products [6]. Nontyphoidal salmonella gastroenteritis is usually self-limited and bacteremia or septic courses are very rare in immunocompetent individuals [5].

Abstract

Myocarditis caused by nontyphoidal salmonellae is very rare in immunocompetent individuals. We present a case of a previous healthy 19-year-old male suffering from chest pain. Laboratory findings, ECG, echocardiogram and blood cultures led to the diagnosis of salmonella myocarditis. Cardiovascular magnetic resonance is a promising non-invasive diagnostic tool which is useful for follow-up and might help to confirm diagnosis. In patients with diarrhea and symptoms of angina pectoris, microbiological testing should include Salmonella enteritidis as possible cause for myocarditis.

Keywords: Cardiovascular magnetic resonance; endomyocardial biopsy; myocarditis; salmonella enteritidis.

Case presentation

A 19-year-old man presented to our emergency department with an undulating, 1-week lasting fever, night sweats and abdominal pain. He complained about watery diarrhea and suffered from severe chest pain since the day before presentation. Two weeks earlier, he had returned from a travel to Cuba. His medical history was unremarkable. Physical examination of heart, lung and abdomen showed no abnormalities except for mild tachycardia of 103 bpm. Laboratory testing upon admission revealed an elevated WBC (11.2/nl, normal < 10.0/nl) and C-reactive protein (4.43 mg/dl, normal < 0.5 mg/dl). Heart enzymes were high (CK 487 U/l, normal < 190 U/l, CK-MB 57 U/l, normal < 25 U/l, high-sensitive troponin t 1017 pg/ml, normal < 14 pg/ml, NT-proBNP 1344 pg/ml, normal < 62,9 pg/ml). ECG showed sinus tachycardia and elevated ST-segments in I, aVL and V2-6 as well as negative T-wave in III (Figure 1). Left-ventricular function in echocardiogram was moderately reduced showing anterolateral hypokinesia. Suspecting myocarditis, the patient was transferred to our cardiology department. He was

started on ibuprofen and acetaminophen as well as a heart failure treatment with ramipril, bisoprolol and ivabradine. Eventually, blood and stool cultures returned positive for *Salmonella enteritidis*. The initial empiric antibiotic therapy with piperacillin/tazobactam and azithromycin was changed to ciprofloxacin. The patient's condition improved quickly. On day 3 of therapy the echocardiogram showed an improved left-ventricular function with mild inferior hypokinesia. Heart enzymes and inflammatory laboratory parameters normalized within 6 days. Immunoglobulin assay was normal, HIV test was negative. The patient was discharged on day 9 in good clinical condition. He received a 14-day course of ciprofloxacin and heart failure medication was continued until the last follow-up at 3 months. 3 months after hospitalization CMR revealed an almost normal left ventricular ejection fraction (53%), mild Dilated Cardiomyopathy (DCM) and no signs for an active or chronic myocarditis.

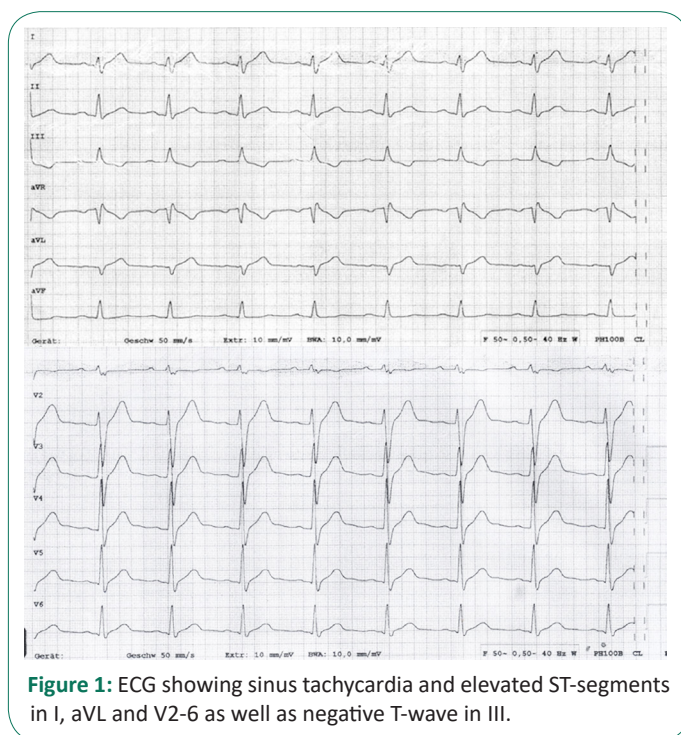


Figure 1: ECG showing sinus tachycardia and elevated ST-segments in I, aVL and V2-6 as well as negative T-wave in III.

Discussion

Myocarditis can be a challenging diagnosis due to the wide spectrum of clinical manifestations, ranging from subclinical disease to acute coronary syndrome-like symptoms or overt heart failure that can in some individuals progress to life-threatening conditions, including arrhythmias and cardiogenic shock [1]. As an example, among 45 patients with suspected acute myocardial infarction and normal coronary angiograms, 35 patients had scintigraphic patterns of diffuse or focal myocarditis [7]. Similarly, in autopsy studies myocarditis was reported in up to 44 % of young persons after sudden cardiac death [8].

Most asymptomatic patients or patients with only mild symptoms and preserved left ventricular function have a good prognosis with low risk of complications [1]. In contrast, worse outcomes have been reported in patients with left ventricular ejection fraction < 50%, ventricular arrhythmias or low cardiac output syndrome upon presentation [9]. Prognosis in myocarditis also varies among different etiologies [10].

Viral infections are presumably the most common cause; nonetheless, bacterial infections range from 0.2 to 1.5 % and should always be considered [11]. Moreover, infections due to parasites and noninfectious causes like cardiotoxins (e.g. alcohol, anthracyclines or cocaine), hypersensitivity reactions, systemic disorders (e.g. celiac disease, sarcoidosis or thyrotoxicosis) and radiation should be taken into account [1,4].

Electrocardiogram, echocardiogram, laboratory testing and in some cases coronary angiography and CMR can establish diagnosis [3,4]. CMR is considered the most accurate noninvasive imaging tool for assessment of suspected acute myocarditis based on visualization of pathophysiological changes in myocardial tissue, including edema, hyperemia and myocyte necrosis or fibrosis defined in the Lake Louise Criteria (LLC) [12]. Novel quantitative CMR techniques like T1 and T2 mapping are a promising add-on which allow a more objective tissue characterization and might be able to overcome some of the previous limitations of the LLC [13]. The combination of clinical presentation and noninvasive cardiac imaging affirms diagnosis in most myocarditis cases. Nevertheless, EMB remains the gold-standard in myocarditis applying Dallas Criteria and immunohistochemical criteria. Considering the risks of this invasive technique and concerns about the diagnostic accuracy only selected patients receive EMB [14]. EMB is recommended for patients with unexplained fulminant heart failure, heart failure within 2 weeks to 3 months combined with dilated LV and/or higher grade arrhythmia or persistent heart failure despite usual care over 2 weeks [15]. Indication for EMB should consider likelihood that histological results would change therapy [3]. Myocarditis treatment comprises heart failure therapy in accordance to clinical presentation, mechanical circulatory support or heart transplantation in cases of severe and persistent heart failure, therapy for arrhythmia if needed and anticoagulation in case of atrial fibrillation, embolism or thrombus [1]. Nonsteroidal anti-inflammatory drugs should not generally be used in patients with heart failure [16]. Moreover, alcohol restriction is recommended [17]. Physical exercise might not be performed during acute phase of myocarditis and heart failure. A return to competitive sports is possible after 3 to 6 months in case of normalized holter monitor, stress testing and electrocardiogram [18].

Nontyphoidal salmonellae are a major reason for diarrhea worldwide and cause about 94 million cases and 155.000 deaths per year. This food associated infection is usually self-limited [5]. Less than 5% of individuals with nontyphoidal salmonella gastroenteritis develop bacteremia what may be owed to an unappreciated immunological dysfunction like a HIV infection. Bacteremia can cause various complications like endocarditis, pericarditis, vascular infections or osteomyelitis [15,19]. The primary cardiovascular involvement is endocarditis, especially in patients with pre-existing atherosclerosis [20]. For salmonella bacteremia, a 14- day-course of fluoroquinolones or third-generation cephalosporin is recommended.

Ingested infectious dose determines frequency and rapidity of salmonella infection. Infectious threshold might be lower during antibiotic use or with impaired acidic barrier. Acidic environment of the stomach and normal intestinal microbial flora are protective host factors [21-25]. Adherence to and subsequent invasion through GI tract is complex and regulated by multiple genes. Salmonellae can survive within macrophages and spread

into circulation [26]. Innate, cell mediated as well as humoral immune response are important to overcome infection. Impaired immunocompetence of different etiology like HIV, sickle cell disease, malaria, glucocorticoid use or B-cell disorders are associated with an aggravated course of disease [27-31].

There are only a few case reports about patients suffering from myocarditis due to nontyphoidal salmonella infection [32-34].

In our case report, the patient was a young man with no risk factors for coronary heart disease and no identifiable immunodeficiency. Elevated heart enzymes and inflammatory parameters in combination with the ECG findings and the echocardiogram led to the diagnosis which was reassured after finding *S. enteritidis* in the blood culture. Anti-infective, anti-inflammatory and heart-failure therapy worked well and the patient recovered quickly. Therefore, we did not perform CMR or EMB to prove diagnosis during initial hospital stay. Outpatient CMR 3 months later confirmed a mild DCM.

In patients with diarrhea and symptoms of angina pectoris, *S. enteritidis* should be considered as possible germ causing myocarditis. As *S. enteritidis* bacteremia is more likely in patients with immunodeficiency, a screening for immunological dysfunction seems to be sensible. CMR as a non-invasive imaging modality is an important part of the diagnostic approach to myocarditis which is not only useful for follow-up examination but can also confirm diagnosis. Further research is needed to evaluate the clinical utility of novel quantitative mapping techniques in CMR and to integrate them into clinical workflows. Apart from that, there is no case of *S. enteritidis* myocarditis undergoing EMB procedure to our knowledge.

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