



The Brazilian Journal of INFECTIOUS DISEASES

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Case Report

A case of myopericarditis associated to *Campylobacter jejuni* infection in the Southern Hemisphere

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ARTICLE INFO

Article history:

Received 27 November 2011

Accepted 17 February 2012

Keywords:

Campylobacter jejuni

Myocarditis

Infectious diarrheal disease

A B S T R A C T

Myopericarditis is an infrequent complication of acute diarrheal illness due to *Campylobacter jejuni*, and it has been mainly reported in developed nations. The first case detected in Chile – an upper-middle income country –, that is coincidental with the increasing importance of acute gastroenteritis associated to this pathogen, is described. Recognition of this agent in stools requires special laboratory techniques not widely available, and it was suspected when a young patient presented with acute diarrhea, fever, and chest pain combined with electrocardiogram (EKG) abnormalities and elevated myocardial enzymes. *C. jejuni* myopericarditis can easily be suspected but its detection requires dedicated laboratory techniques.

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Introduction

Viral infections are the leading cause of myocarditis and pericarditis in developed countries.¹ On the other hand, parasitic diseases such as acute Chagas disease and endemic viruses such as dengue fever could be important contributory etiologies in developing nations.²⁻⁴ *Campylobacter* sp. is a recognized but infrequent cause of pericarditis or myopericarditis. Its identification requires special microbiological techniques that are not available in impoverished regions. This fact probably explains why case reports are restricted to high or upper-middle income countries from the Northern Hemisphere and Australia.⁵⁻⁸ The first case of *Campylobacter jejuni*-associated-myopericarditis in Chile, which may reveal a wider geographic distribution and relevance for this condition, is reported below.

Case presentation

A 17-year-old adolescent male was admitted to the Hospital Militar de Santiago, in September 2011, with a history of two days of upper abdominal pain, fever (38.5°C), and dysentery. He had no recent history of travel, sexual activity, or contact with animals. On the day of admission, he referred severe anterior chest pain that was relieved by sitting. On examination, the patient presented without respiratory distress or fever, and was hemodynamically stable. Laboratory tests revealed high levels of total creatine kinase (432 U/L; reference 38-174), CK-MB (27.63 ng/mL; reference < 4.99), troponin I (16.8 ng/mL; reference < 0.04), total white cell count of 16.2 10⁹/L (reference < 11.5 10⁹/L, with 87% of polymorphonuclear cells), and C-reactive protein (269 mg/L; reference < 5). A slightly

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increased LDH level (278 U/L; reference 135-225) was also observed. Erythrocyte sedimentation rate, hemoglobin level, and platelet count were normal. An electrocardiogram (EKG) showed ST-segment elevation on V1-V6 leads on the first day, and a negative T wave on the second day. Echocardiography was normal while cardiac magnetic resonance, performed on the third day of evolution, showed patchy focal impregnation of the myocardium on the left ventricle after gadolinium administration (Figs. 1 and 2). Myocardial function was normal. The etiological study included probable viral and bacterial causes. Serological studies for herpes simplex virus types 1 and 2, cytomegalovirus, and Epstein Barr viruses were negative for recent infection. Human immunodeficiency virus (HIV) ELISA testing, VDRL, and IgM for *Chlamydomphila pneumoniae* were also negative. Traditional stool culture on MacConkey and *Salmonella-Shigella* agars grew only normal fecal

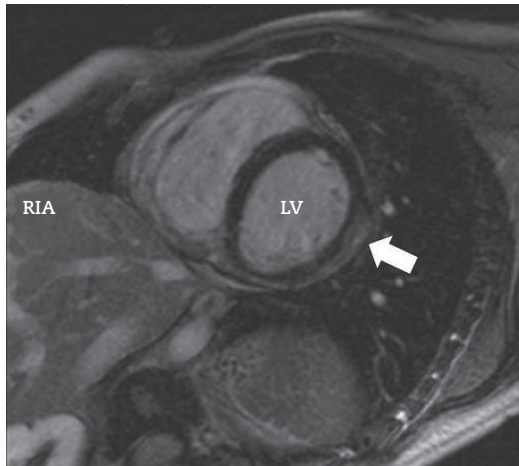


Fig. 1 - Short axis left ventricle (LV) view in T1 signal after gadolinium administration. The white arrow indicates subepicardial myocardium enhancement in the lower-lateral wall of the LV.

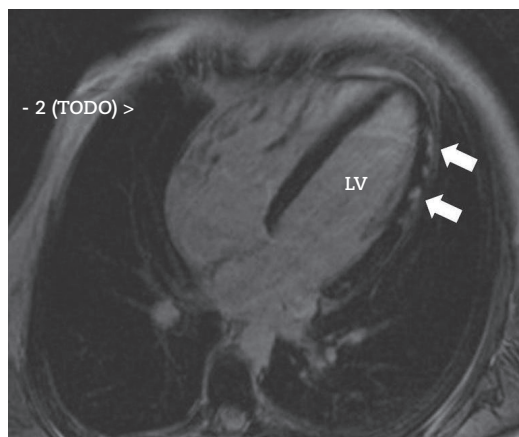


Fig. 2 - Four-chamber view of the left ventricle (LV) in T1 signal after gadolinium administration. Arrowheads indicate patchy focal impregnation in the subepicardium.

microbiota. *Campylobacter* culture on a microaerophilic jar at 42°C grew *Campylobacter jejuni*, but the Hucker stain on stool samples was negative. No antimicrobial susceptibility studies or blood cultures were performed. The patient's evolution was favorable, with rapid decline of diarrhea and chest pain. On the third day post-admission, the EKG was normal and a three-day treatment with azithromycin (500 mg/day) was started. The patient was discharged after five days of hospitalization and had an uneventful recovery.

Discussion

Culture of *Campylobacter jejuni* requires a microaerophilic environment and an incubation temperature of 42°C. These conditions are not routinely available in clinical microbiology laboratories in developing nations. Unfortunately, the screening strategy using the Hucker stain lacks sensitivity, as is underscored by this case.⁹ This is an important limitation because the diagnosis of *Campylobacter*-associated-myopericarditis can only be achieved by the finding of *C. jejuni* in stools coupled with clinical manifestations. Thus, *C. jejuni*-associated-myopericarditis or pericarditis could be missed. The rate of positive *Campylobacter* spp. stool cultures in this hospital has steadily increased from less than 0.5% in 2004 to 2% during 2010, suggesting that the present report could be the tip of the iceberg of an endemic problem that is not included in the list of notifiable diseases in Chile.¹⁰ Moreover, this case is coincidental with a recent report of high levels of food industry contamination by *Campylobacter* sp. in this country.¹¹ Epidemiological data from Denmark suggest that myocarditis is ten times more frequent in the population with *Campylobacter*-associated diarrhea than in the population without this condition, but with no significant differences.⁶ Enterovirus was not included in the etiological study of myopericarditis because laboratory diagnosis was not possible. Nevertheless, the close temporal relationship between the occurrence of diarrhea, *C. jejuni* isolation in stools, and cardiac manifestations suggests that this bacterial agent was the most probable cause.

The clinical features observed in this patient are in full accordance with those reported in the literature for *Campylobacter*-associated myocarditis. That is, a condition that affects predominately young adults or adolescents, usually has a benign course, and is suspected when a patient presents with chest pain shortly after or during diarrheal episodes.^{5-8,12,13} Of the 16 cases summarized by Hannu et al., up to the year 2005, 93% were male patients with a mean age of 32.4 years (range 23-54), and had a four-day average period (range 0-14) between diarrhea and the onset of cardiac manifestations.⁷ Full recovery was observed in 78.6%, and only 21.4% developed chronic sequelae such as arrhythmia or left ventricular dysfunction. None of these patients died.⁷

Elevated cardiac enzymes coupled with transient EKG ST-segment elevations or T wave inversions are important to recognize heart disease.⁵ Some cases evolve with hypotension, congestive cardiac failure, and/or arrhythmia.^{8,13} A normal PR interval and a sinus rhythm are usually observed,¹³ in contrast with EKG conduction abnormalities present in acute Chagas disease.^{2,3}

C. jejuni-associated cardiac involvement is different from that of *C. fetus* subsp. *fetus*. The former has negative blood or pericardial cultures, in contrast with the microbiological yield observed during *C. fetus* disease.¹⁴ On the other hand, *C. fetus* cardiac disease is usually observed in older or immunocompromised patients and has a worse prognosis.¹⁴ Polymorphonuclear infiltration with focal myocytolysis and negative *C. jejuni* PCR in cardiac tissue have been reported in fatal cases of *C. jejuni* myocarditis.¹⁵ These findings suggest a toxin-mediated mechanism rather than direct microbial invasion as the probable cause of myopericarditis. Furthermore, the short period of time elapsed between diarrhea and cardiac manifestations makes an autoimmune disease unlikely.

Sometimes, differential diagnosis is complicated by the presence of underlying risk factors. In these cases, early coronary angiography and thrombolysis may be necessary.⁵ Prompt suspicion of this cause is important to avoid unnecessary invasive procedures, even if the patient has cardiovascular risk factors.

Cardiac magnetic resonance has rarely been used in these cases and shows a diffuse enhancement of the myocardium after gadolinium administration.^{12,16} In this patient, patchy focal irregularities similar to those described during the first days of well-documented cases of viral myocarditis were observed.¹⁷ Cardiac magnetic resonance was more sensitive than echocardiography in this patient.

The clinical efficacy of antimicrobial treatment for this rare complication is unknown, and most cases have been treated during the recovery phase, predominately with quinolones or macrolides. Azithromycin was chosen in this case because of the increased reports of ciprofloxacin resistance among *C. jejuni* isolates in Chile.¹⁸

In summary, despite being a rare complication, *C. jejuni*-associated-myopericarditis should be suspected when chest pain appears shortly after an episode of diarrhea and fever. This condition usually affects young adult male patients and has a favorable prognosis. Cardiac enzymes are initially elevated but decline promptly. ST-segment elevations and/or T wave changes are concurrently observed, but they rapidly normalize. Cardiac magnetic resonance can be more sensitive and helpful than echocardiography, showing focal enhancement with gadolinium during the first days of evolution. Identification of *C. jejuni* in stools requires special culture media. The efficacy of antimicrobial therapy still lacks evidence.

Conflict of interest

All authors declare to have no conflict of interest.

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