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Campylobacter jejuni Pericarditis: A Case Report

Pericardite por *Campylobacter jejuni*: Um Caso Clínico

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Acta Med Port 2022 Dec;35(12):912-914 ▪ https://doi.org/10.20344/amp.17251

ABSTRACT

Campylobacter jejuni is one of the most common causes of enteritis. In rare cases, extraintestinal infection can occur, with a handful of cases of cardiac involvement, of which the pathophysiological mechanism is unclear. We report a case of pericarditis in a patient with X-linked agammaglobulinemia presenting with chronic diarrhea and chest pain who evolved to cardiac tamponade, requiring a pericardial window and a long course of broad-spectrum antibiotics. To the best of our knowledge, this is the third case of pericarditis caused by *Campylobacter jejuni* reported in the literature, the second in a patient with X-linked agammaglobulinemia. Despite its rarity, this case serves as a reminder of *Campylobacter* as a potential cause of cardiac inflammation for clinicians treating pericarditis/myocarditis, especially in patients with a history of diarrhea or immunosuppression.
Keywords: Agammaglobulinemia; Campylobacter Infections; Campylobacter jejuni; Pericarditis

RESUMO

A *Campylobacter jejuni* é uma das causas mais comuns de enterite. A infeção extraintestinal pode ocorrer raramente, estando reportados alguns casos de atingimento cardíaco, de mecanismo fisiopatológico incerto. Reportamos um caso de pericardite num doente com agamaglobulinemia ligada ao X, que se apresentou como diarreia crónica e dor torácica, evoluindo para tamponamento cardíaco com necessidade de confeção de janela pericárdica e tratamento prolongado com antibióticos de largo espectro. Este é, tanto quanto é do nosso conhecimento, o terceiro caso de pericardite por *Campylobacter jejuni* reportado na literatura, o segundo em doente com agamaglobulinemia ligada ao X. Apesar da sua raridade, este caso serve para reforçar a importância do género *Campylobacter* como causa de inflamação cardíaca para médicos que tratem pericardite/miocardite, especialmente em doentes com história de diarreia ou imunossupressão.
Palavras-chave: Agamaglobulinemia; Campylobacter jejuni; Infecções por Campylobacter; Pericardite

INTRODUCTION

Campylobacter spp. are one of the most common pathogens associated with human enteritis, and represent a zoonosis with a worldwide distribution.[1] Two species account for the majority of infections, with *Campylobacter jejuni* (*C. jejuni*) being the prototype for intestinal infection and *C. fetus* more associated with extraintestinal manifestations, usually as an opportunistic infection. These can be protean, with well documented descriptions of persistent bacteremia, cholangitis/cholecystitis, central nervous system infection, septic arthritis, osteomyelitis, septic abortion, mycotic aneurysms, endocarditis and myopericarditis.[1] The diagnosis requires a high degree of clinical suspicion, due to the relative rarity of these manifestations and frequently absent gastrointestinal symptoms. Compounding this extensive spectrum of clinical expressions, antimicrobial resistance is a growing problem especially in developing countries, with a significant number of isolates being resistant to macrolides and quinolones in particular.[2,3]

Furthermore, *C. jejuni* has been associated with several immunological sequelae, such as reactive arthritis, Guillain-Barré syndrome, hemolytic-uremic syndrome and small intestinal MALT (mucosal associated lymphoid tissue) lymphoma.[1]

CASE REPORT

A 34-year-old male with a history of X-linked agammaglobulinemia treated with monthly subcutaneous immunoglobulin and bronchiectasis presented to the emergency department with a seven-month history of non-bloody diarrhea and intermittent fever, chest pain and orthopnea.

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Recebido/*Received*: 30/09/2021 - **Aceite/*Accepted*:** 16/03/2022 - **Publicado *Online*/*Published Online*:** 28/04/2022 - **Publicado/*Published*:** 02/12/2022

There was a history of consumption of undercooked poultry and several cases of diarrhea several months before in his area of residence. There was no recent travel history. He had received two courses of antibiotics (amoxicillin/clavulanate) and had two negative stool cultures (collected on two occasions, namely four months and one month prior to hospital admission). On physical examination there was fever, tachycardia, hypotension, medium volume ascites and hepatomegaly. There was hyperlactatemia, elevation of markers of systemic inflammation and cholestasis, with normal hepatic and renal function. A chest radiography showed an enlarged bottle-shaped heart and echocardiography showed a large volume pericardial effusion. The electrocardiogram and cardiac enzymes were normal.

Upon intravenous hydration he developed signs of pulmonary edema, with serial echocardiography showing signs of imminent tamponade with right ventricle dysfunction, requiring pericardiocentesis on the first and second day and window pericardiectomy on the third day. The analysis of the pericardial fluid and biopsy revealed pyogenic inflammation (86 585/µL leukocytes, 79 577/µL neutrophiles and 7008/µL mononucleated cells) with elevated ADA (adenine deaminase), with a negative Gram examination and culture, no granulomas and a negative flow cytometry for lymphoma.

Due to the insidious clinical presentation, he was empirically treated for pericardial tuberculosis with systemic glucocorticoid therapy and an alternative drug regimen due to significant hepatic cholestasis, comprising ethambutol, levofloxacin and amikacin for 10 days. This course of treatment was abandoned after all the biologic samples (four sputum, three pericardial fluid samples and the pericardial biopsy sample) were negative for granulomata, alcohol-acid resistant bacilli and *Mycobacterium tuberculosis* by polymerase chain reaction.

Ten days after hospital admission, the blood cultures became positive for *C. jejuni*, and the diagnosis of invasive campylobacteriosis was made. The patient was thus started on imipenem and an antibiotic susceptibility test later confirmed susceptibility to carbapenems and aminoglycosides and resistance to quinolones, macrolides, beta-lactam/beta-lactamase inhibitor and tetracyclines.

After six weeks of treatment there was complete recovery, with echocardiography showing no residual effusion and normal systolic function of both ventricles.

DISCUSSION

Campylobacter species are commensal microorganisms in the digestive tract of several species, including fowl, dogs, swine, sheep and cattle. Human infection by *C. jejuni* starts one to seven days after consumption of contaminated meat, milk or water, leading to a febrile illness followed by non-characteristic diarrhea and abdominal pain, usually resolving in one week even without antibiotic treatment.[1,4] Portal and even systemic bacteremia seem to be a common occurrence, with spontaneous clearance in the immunocompetent host. In patients with immunoglobulin deficits, this species has been documented to cause chronic infection.[5] Due to the presence of a proteinaceous capsule that protects it from the opsonizing (coating by the C3b fragment of complement that signals for phagocytosis by macrophages) and lytic effects of complement, *C. fetus* has a much greater tendency to evade the immune system, resulting in a more protracted clinical course, persistent bacteremia and seeding of distant organs.[6]

Several cases of cardiac involvement have been described (pericarditis, myopericarditis and myocarditis), by both *C. fetus* and *C. jejuni* but while the former has almost always been isolated from blood or pericardial fluid samples, it is seldom the case with the latter.[7–10] This has led some scientists to question whether the pathophysiological mechanism behind cardiac inflammation could differ between both species, with *C. fetus* being related with direct bacterial/bacterial toxin mediated damage and *C. jejuni* resulting from a type 2 hypersensitivity reaction to bacterial antigens.[7] The latter has been supported by the well-documented role played by this species in the development of reactive arthritis and Guillain-Barré syndrome. However, our case may disprove this hypothesis: on the one hand, *C. jejuni* was isolated from blood cultures, indicating at least a potential for direct cardiac invasion even if not identified in pericardial fluid cultures (bearing in mind that these were obtained when the patient was already being treated with an aminoglycoside); on the other hand, the coexistence of X-linked agammaglobulinemia might be 'protective' against immune pericarditis by a type 2 hypersensitivity reaction, since the production of antibodies is severely decreased. However, this does not exclude other immune mechanisms, such as T-cell mediated tissue damage. To the best of our knowledge there are only two other cases of exclusive pericardial involvement by *C. jejuni* reported in the literature,[11,12] one of them in a patient suffering from X-linked agammaglobulinemia,[12] akin to our patient.

Our case serves as a highlight to remind clinicians treating patients with pericarditis or myocarditis of the possibility of infection by *Campylobacter*. This may be especially important when gastrointestinal symptoms or immunosuppression coexist, with the diagnosis being made by non-invasive tests such as blood and stool cultures or even serology, where available. As this case underscores, a negative stool culture does not exclude the diagnosis, and when possible, several samples plus blood cultures should be taken. Awareness of this manifestation of *Campylobacter* infection may avoid unnecessary invasive procedures, such as coronary catheterization, and improve outcomes by prompt treatment with antimicrobials which must be adapted to local antibiotic susceptibility.

AUTHOR CONTRIBUTIONS

JNM: Literature review, draft of the manuscript.
CG, AM, RA: Critical review of the manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical

Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PATIENT CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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