

Campylobacter jejuni myocarditis: A journey from the gut to the heart

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Abstract

Objectives: *Campylobacter jejuni* is an unusual cause of myocarditis and could easily be missed.

Methods: We describe a case of a 25 year old man, who presented with 3 day history of vomiting and diarrhoea, followed by chest pain and significant high sensitive troponin rise.

Results: The patient's profuse diarrhoea was accompanied by raised inflammatory markers, electrocardiogram changes and evidence of cardiomyopathy on transthoracic echocardiogram. Various aetiological viral serologies which were tested for came back negative. However, stool culture was positive for the bacteria, *Campylobacter jejuni*. He was successfully treated with antibiotics and made an uneventful recovery.

Conclusions: *Campylobacter jejuni* gastroenteritis has a worldwide prevalence. Therefore, prompt diagnosis and treatment is crucial when this organism is implicated in myocarditis.

Keywords

Cardiovascular, infectious diseases, epidemiology/public health, *Campylobacter jejuni*, cardiomyopathy

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Introduction

Myocarditis is defined as the inflammation of the heart muscle.¹ It has a broad range of causes including infectious organisms and also non-infective insults to the myocardium involving chemicals, toxins, and drugs and a diverse group of collagen vascular disorders such as lupus, scleroderma and dermatomyositis.² By far, the most putative aetiological pathogens are viruses, and in this regard, Coxsackie Virus A and B, Adenoviruses, Enteroviruses, Parechovirus, Hepatitis B and C, and Human Immunodeficiency Viruses have all been implicated.² Parvovirus B19 and Human Herpesvirus-6 are most commonly recovered from endomyocardial biopsy.³ Other infectious causes are protozoa, helminth infections, fungi, spirochaetes, rickettsia and some bacteria.^{1,3} The bacteria often cited are *Legionella*, *Mycobacterium*, *Streptococci* and *Staphylococci*;^{1,3} *Salmonella* and *Shigella* have been mentioned in some case reports.⁴ Only, very infrequently, *Campylobacter jejuni* has been reported in association with myocarditis.⁵ This is a case demonstrating an unusual link between diarrhoeal disease and acute myocarditis.

chest tightness worsened by deep inspiration and relieved by sitting forward. He gave 3 days history of vomiting and watery diarrhoea prior to the onset of chest pain. The patient could not recall ingesting any specific food or drink that could have precipitated his diarrhoeal symptoms. He was not on any regular medication, and there was no history of recreational drug use.

On examination, he was afebrile (36.7°C), with a heart rate of 80 beats/min: the blood pressure was 122/74, his respiratory rate was 17 cycles/min and oxygen saturation was 95% on room air. Cardio-respiratory and abdominal examinations were unremarkable.

Laboratory examination revealed normal renal and liver function tests. Haemoglobin and platelets were normal, but white cell count was slightly raised at $11.4 \times 10^9/L$ (normal: 4–11) with neutrophilia. C-reactive protein (CRP) was also elevated at 104 mg/L (normal: <15). High-sensitive troponin (fifth generation Troponin T) was significantly raised at 1963 ng/L (normal: <14). Electrocardiogram (ECG) on

Case report

A 25-year-old previously healthy man, with no cardiac risk factors for coronary artery disease, presented to the Accident and Emergency Department of Aintree University Hospital NHS Foundation Trust, Liverpool, with central

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admission showed sinus rhythm with ventricular rate of 80 beats/min and ST depression in anteroseptal lead.

He was transferred from Accident and Emergency Department to Coronary Care Unit. Transthoracic echocardiography was carried out and demonstrated normal left ventricular wall thickness and mildly impaired left ventricular systolic function. The basal to mid inferior septum and posterolateral wall appeared hypokinetic. There was no pericardial effusion.

The patient's watery diarrhoea lasted for a total of 12 days, with loose stool frequency as much as 10 times on some days. Stool samples taken on third, fifth and sixth days of active diarrhoea came back positive for *Campylobacter jejuni* on three occasions. They were negative for *Salmonella* and *Shigella* species, *Escherichia coli* 0157, *Cryptosporidium* and *Clostridium difficile* toxin. Blood cultures done on three occasions were sterile.

The patient was initially commenced on intravenous Meropenem 1 g 8 hourly, based on the advice of the microbiology department. Routine disc-testing done by microbiology laboratory demonstrated sensitivity to Ciprofloxacin and Erythromycin, so his antibiotics were switched to oral Ciprofloxacin 750 mg 12 hourly, after 48 h of intravenous Meropenem. He completed 5 days of antibiotics therapy in total.

A repeat echocardiogram 1 week later showed improvement in left ventricular systolic function. He remained well, the diarrhoea settled and he was allowed home after 11 days of in-hospital stay.

He returned to the cardiology outpatient department 6 months later, wholly asymptomatic, having made a full recovery and was discharged. Coronary angiogram was not done due to the fact that his age, lack of risk factors for coronary artery disease, history, clinical presentation and laboratory investigations favoured an alternative diagnosis to acute coronary syndrome. A cardiac magnetic resonance imaging (MRI) was not carried out, since the patient made a rapid recovery.

Discussion

Campylobacter jejuni is a major cause of gastroenteritis worldwide, with increase in both incidence and prevalence over the past decade.⁶ The diarrhoea often results from ingestion of contaminated water and dairy products.⁶ *Campylobacter*-related myocarditis is relatively uncommon. A Danish study⁷ which matched 6204 *Campylobacter* stool-positive patients against 62,040 control subjects found an incidence rate of 16.1 (95% confidence interval (CI)=2.3–114.4) per 100,000 person-years in the *Campylobacter* group as against 1.6 (95% CI=0.2–11.4) per 100,000 person-years in the control cohort. Importantly, the study failed to demonstrate significant difference in the incidence of myocarditis between the two sampled populations.⁷ A major limitation of this research, however, is its statistical imprecision due to the rare occurrence of myocarditis in the study population.

From the first reported case in 1980,⁴ there has been an increasing awareness of *Campylobacter jejuni*-associated myocarditis pathogenicity, especially in the developed world.⁵ A recent up-to-date review of this rare clinical entity by Hessulf et al.⁵ provided the distinct features of the previously published cases in literature, with suggestion of further studies to elucidate its pathology.

To a disproportionate degree, mainly young, immunocompetent males have been shown to be afflicted in the published literature similar to this index case.⁵ In studies relating to viral myocarditis, the common occurrence of infection noted in the male sex has been postulated to be due to the influence of sex hormones; oestrogen was shown to protect against viraemia and viral infectivity in the cardiac muscle cells of female mice, while testosterone demonstrated the exact opposite, through prevention of anti-inflammatory responses in male mice.¹ It would seem reasonable to extrapolate this finding to bacterial myocarditis as well.

Although the clinical course is usually benign, in one of very few reported cases of *Campylobacter jejuni* myocarditis from the United Kingdom,⁸ cardiac MRI demonstrated a severe left ventricular systolic dysfunction.⁸ Up to 30% of patients could eventually develop dilated cardiomyopathy.⁹ In some patients, the disease is completely asymptomatic,^{2,3} while in others, mild chest discomfort or a very severe chest pain mimicking myocardial infarction could occur.³ Others could present with arrhythmias and cardiogenic shock leading to sudden cardiac death.¹⁰

Troponin T and I, creatinine kinase and brain natriuretic peptide (BNP) are often elevated, as well as inflammatory markers, CRP.⁹ Although a normal cardiac enzyme level does not rule out the diagnosis,^{3,9} higher levels of troponin T confers poor prognosis.² Echocardiography is a valuable tool in identifying myocardial dysfunction or pericardial effusions which could occur in myocarditis.⁹ Cardiac MRI with gadolinium enhancement has come into its own as an important non-invasive investigative modality.⁹ For good measure, it could help in differentiating myocarditis from myocardial infarction, an important differential diagnosis.^{11,12}

Endomyocardial biopsy, which is regarded as the gold standard for diagnosis of myocarditis, is not routinely used in clinical practice.^{6,9,11} Based on American and European standard guidelines,¹³ endomyocardial biopsy is reserved for fulminant and giant cell myocarditis or acute heart failure resistant to conventional treatment.¹³

Although the precise pathogenic mechanism has not been conclusively elucidated,⁵ the observed short interval between the onset of enteric infection and development of cardiac symptoms has led to the suggestion that this probably involves a direct attack of the bacteria on the myocardium or toxin-mediated mechanism.^{5,14} This is in contrast to immunological-mediated phenomenon as seen in Guillain-Barré syndrome, where the same organism causes symptoms about 2–3 weeks after the initial gastroenteritis.^{5,14}

Similar to other reported cases, where bowel symptoms usually precede chest pain for about 2–4 days,^{7,9} our patient developed chest pain 3 days after the onset of diarrhoea. Moreover, his blood culture was sterile as often noted in other previously reported cases.⁵ Becker et al. raised the possibility of viral co-infection as an aetiological factor in the cause of myocarditis hitherto ascribed to *Campylobacter jejuni*, and highlighted the lack of assessment of viral agents, in the previously cited cases.⁷ However, the viral serologies done in this case were negative. The viruses tested for were as follows: Cytomegalovirus IgM and IgG, Epstein–Barr Virus IgG and IgM, Parvovirus IgG and IgM, Hepatitis A IgG and IgM, Enterovirus RNA, Parechovirus PCR and Human Immunodeficiency Virus antigen and antibody, which were all negative.

The treatment of acute myocarditis is largely supportive.³ Antibiotics are given for gastroenteritis-associated myocarditis,⁵ and for patients who develop significant heart failure, treatment with beta blockers and angiotensin-converting-enzyme (ACE) inhibitors along standard international guidelines is advocated.^{2,3} Acute myocarditis remains a vastly under-diagnosed disease.³ With the increase in cases of *Campylobacter jejuni* infection worldwide⁶ and the possibility of progression to dilated cardiomyopathy,^{1,9} prompt diagnosis and effective management are of paramount importance.

Declaration of conflicting interests

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Ethical approval

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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