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CLINICAL CASE

Acute Myopericarditis secondary to campylobacter jejuni enterocolitis

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Summary

Myo(peri)carditis is a rare condition that can mimic an acute coronary syndrome. Infective myocarditis is most commonly due to viral infections while bacterial etiology is extremely rare. There are only a few case reports of** Campylobacter jejuni **associated myocarditis. We present a case of previously healthy young adult male who de-

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veloped myopericarditis shortly after infectious gastroenteritis caused by** Campylobacter jejuni**. To our knowledge this is the first reported case of Campylobacter jejuni myopericarditis in Lithuania.

Keywords
Campylobacter, enterocolitis, myocarditis.

Introduction

Myo(peri)carditis is a rare condition that can mimic an acute coronary syndrome. Infective myocarditis is most commonly due to viral infections, while bacterial infection is extremely rare. [1] *C.jejuni* is the most common bacterial cause of enterocolitis in developed countries [2]. There are only a few case reports on *Campylobacter jejuni* associated myocarditis [3, 4]. Patients with C.jejuni associated myo(peri)carditis are usually young and previously healthy adult males. In most cases it ended with no sequel. [5] We present a case of previously healthy 23 year old adult male who developed myopericarditis shortly after infectious gastroenteritis caused by *Campylobacter jejuni*. With aspirin and antibiotics his condition improved within few days.

Case presentation

A 23-year old male, Italian citizen studying in Lithuania, was admitted to the Emergency department of Infectious diseases and tuberculosis hospital on December 1st, 2013, with a history of high fever (38.5 °C) for four days, abdominal pain and profuse watery diarrhea (up to 10 times per day). He did not have any recent travel history, nor contact with other sick people. On examination, patient was haemodynamicaly stable with medium signs of dehydration. After intravenous fluid infusion, the patient was released home with prescription of ciprofloxacin 500 mg BID for 5 days. On December, 5th *Campilobacter jejuni* infection was identified in coproculture analysis. At that point patient had no fever, yet he noticed blood in his stools. Azithromycin 500 mg QD for 3 days was administered. On December, 6th patient developed high fever (38.5 °C), chest pain and difficulty to breathe. After the evaluation at the Emergency department of Infectious diseases hospital patient was referred to the Emergency department of Vilnius University Hospital Santariskiu klinikos. He referred pressure like left chest pain no radiating, increasing with a change of posture and during deep breathing. The chest pain used to subside when sitting upright.

On the admission the patient had high fever (39.1 °C) and was haemodynamicaly stable (blood pressure 116/86 mm Hg, heart rate 96 beats/min.). Palpation of the thorax and abdomen did not show any painful areas and bowel sounds were normal.

Laboratory tests revealed high troponin I (0.993 mkg/l, reference <0.03mkg/l), total white cell count (10.56 $x10^9$/l, reference <9 $x10^9$/l), C-reactive protein (18.3 mg/l, reference <5mg/l) and procalcitonin (0.15 mkg/l, reference <0.05 mkg/l). Potassium level was abnormal (3.7 mmol/l, reference >3.8 mmol/l). CK-CM was normal (2.95 µg/l, reference <5.2 µg/l). Erythrocyte sedimentation rate, haemoglobin level and platelet count were normal.

An electrocardiogram showed sinus rhythm with ST-segment elevation on leads I, II, V4-V6 (Fig. 1).

Echocardiography showed normal myocardial function.

Given the history of recent diarrhea, chest pain, fever, elevated troponin I 0.993 mg/l, CRP 18.3 mg/l, procalcitonin 0.25 mkg/l, ECG changes, the patient was diagnosed with acute perimyocarditis secondary to C*ampylobacter jejuni* infection and was admitted to Department of Cardiology.

He was started on aspirin 100mg QD and amoxicilin with clavulanic acid 1.2g TID i/v. Within the treatment course CRP increased from 18.3 to 107 mg/l, troponin increased from 0.993 to 11.005 mkg/l and CK-MB from 2.95 to 33.78mkg/l. On the 3rd day of hospitalization patient was commenced on Gentamicin 80 mg x TID i/v and clarithromycin 500 mg BID i/v. Urinary and blood cultures were negative.

Colonoscopy showed turgid mucosa of sigmoid intestine. Biopsy revealed chronic active colitis likely of infectious etiology.

Within the course of antibacterial treatment the patient's condition improved. His temperature settled and inflammatory markers decreased. He was discharged on 7th day of the hospitalization.

Discussion

Myocarditis is an inflammatory disease of cardiac muscle. The exact prevalence of the myocarditis is not known, though evidence of myocardial inflammation is foud in 5% of post mortem examinations.[6] Infective myocarditis is most commonly due to viral infections – coxsackie A and B viruses, echovirus and adenovirus. Myocarditis due to a bacterial infection is

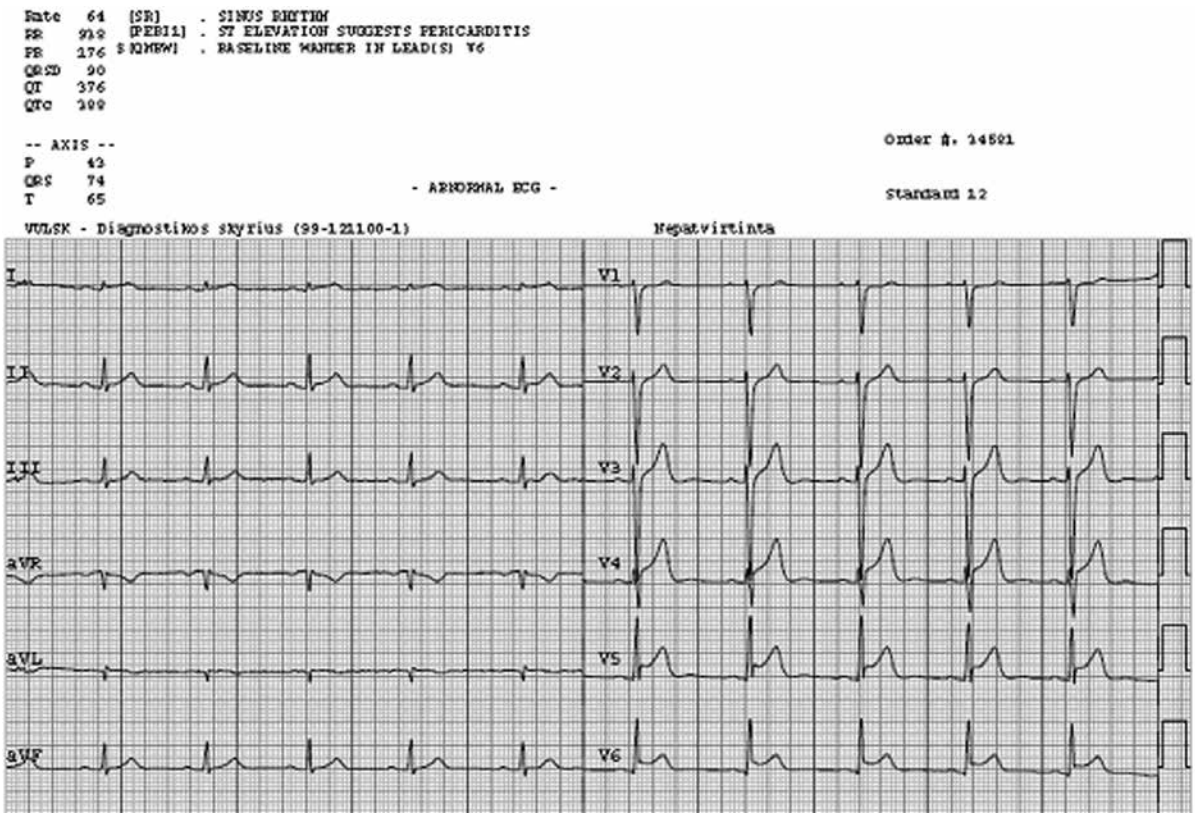

Fig. 1. ECG showed ST-segment elevation on leads I, II, V4-V6

rare. Bacterial pathogens associated with myocarditis include Streptococci, Staphylococci, Pneumococci, Neisseria, Legionella, Coxiella, Pneumophilus, Mycobacterium tuberculosis.[7] Enteric pathogens cause myocarditis in extremely rare cases, with most of them associated with Salmonella and Shigella. To this day only a few cases of C.jejuni associated myocarditis have been reported in the literature, most of them being young adult males.[5, 8-13] Myocarditis can progress to a chronic cardiomyopathy and is a leading cause if sudden death in adults under 40 years old [14].

Epidemiological studies showed that Campylobacter was the cause of diarrheal illness more than 2-7 times as frequent as infections with Salmonella, Sheila species or Escherichia coli O157:H7. Extraintestinal manifestations of Campylobacter infection are quite rare and may include meningitis, endocarditis, septic arthritis, osteomyelitis and neonatal sepsis. The most common postinfectious complication of C.jejuni infection is the Guillain –Barre syndrome. People with the HLA-27 histocompatibility antigen are prone to the development of reactive arthritis several weeks after infection with Campylobacter. Other postinfectious complications are rare and include uveitis, hemolytic anemia, hemolytic uremic syndrome encephalopathy and myocarditis [15].

The pathophysiologic mechanism by which Campylobacter causes myo(peri)carditis remains uncertain. It may be caused by direct bacterial invasion of cardiac tissue, bacterial toxins, circulating immune complexes, or cytotoxic T-cells. Direct bacterial involvement is documented in Campylobacter fetus cases, were pathogen was isolated from blood in almost all cases. But in C.jejuni associated cases the organism was isolated only in one case. PCR studies were negative when performed with myocardial tissues in one fatal case of C.jejuni associated myocarditis in USA – thus supporting toxin induced myocardial injury theory.[10] Although C.jejuni is known to produce a variety of exotoxines with cytotoxic, haemolytic and hepatotoxic effects, but none is known to cause cardiotoxicity. [16] There were few reports on patients with longer interval between enterocolitis and cardiac complications and arthritis, both occurring at the same time. These cases suggest immunological involvement.

Diagnosis of myo(peri)carditis is primary clinical. Clinical features observed in this patient are as reported in the literature. Elevated cardiac biomarkers and acute phase reactants can be detected. Troponin I has high specificity (89%) but limited sensitivity (34%) in the diagnosis of myocarditis (elevated in a minority of patients with acute myocarditis) that coupled

with transient ECG ST-segment elevations or T wave inversions are important to recognize heart disease. Cardiac enzymes are initially elevated but decline promptly as right medication are given even though the efficacy of antimicrobial therapy still lacks evidence. [17, 18] The 12 lead ECG may mimic the changes of an ACS or it may show tachy or bradyarrhythmias. In patients presenting with chest pain, ECG abnormalities and a raised cardiac biomarker, diagnostic coronary angiography needs to be performed to exclude obstructive coronary artery disease. There is no clear relationship between the clinical, laboratory and ECG findings in patients with myocarditis and no validated diagnostic criteria are used in daily clinical practice.

Gold standard for diagnosing myocarditis is endomyocardial biopsy (EMB). EBM usually shows inflammatory cellular infiltration with or without necrosis. However, these criteria are unreliable due to possible infiltration tissue sampling error, therefore cell-specific immunoperoxidase stains for surface antigens, such as anti-CD3, anti-CD4, anti-CD20, anti-CD68, and anti–human leukocyte antigen should be performed and may have prognostic value. Due to lack of sensitivity and the invasive nature of the procedure it is not commonly performed at many medical centers. [19, 20]

Noninvasive methods are primarily used for diagnosis of myocarditis. Recent studies have shown that cardiac magnetic resonance with gadolinium enhancement provides an accuracy of 78%. [21] Gadolinium accumulates in areas of inflammation so that the hyperintense areas observed on T2-weighted images are due to increase in myocardial free water content due to lymphocytic infiltration and myocytolysis. [8] Cardiac MRI is more sensitive than echocardiography. [22]

The clinical efficacy of antimicrobial treatment for C.jejuni associated myo(peri)carditis is unknown. Treatment of myocarditis is usually supportive. Patients with heart failure should be started on diuretics and angiotensin-converting-enzyme inhibitors. Once stabilized, beta-blockers should also be initiated in patients with left ventricular systolic dysfunction.[23] Aspirin may be given if concomitant pericarditis is suspected, however, other nonsteroidal anti-inflammatory agents, including ibuprofen and indometacin, have been shown to worsen myocarditis in animal studies.[7]

Conclusion

In summary, despite being a rare complication, *C. jejuni* associated myopericarditis should be suspected when chest pain appears shortly after or during 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 though efficacy of antimicrobial therapy still lacks evidence.

Conflict of interest statement

The authors of this case report that have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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