


CASE REPORT

Pancreatitis and myocarditis coexistence due to infection by Coxsackie B1 and B4 viruses

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Introduction

Myocarditis refers to inflammation of the myocardium with a wide range of clinical manifestations. The clinical presentation can vary from mild symptoms of chest pain, fever, sweats, chills, and dyspnea to more severe manifestations such as palpitations, syncope, or sudden cardiac death due to ventricular arrhythmias or atrioventricular block [1, 2]. Specifically, in viral myocarditis, recent history ($\leq 1-2$ weeks) of flu-like symptoms is contributing in the clinical presentation of the patients [3]. Myocarditis can be attributed to infectious agents, drugs and toxics, and immune-mediated mechanisms [4]. According to the current European Society of Cardiology (ESC) guidelines, clinically suspected myocarditis is defined by the presence of \geq one clinical presentation (with or without ancillary findings) and \geq one diagnostic criteria (electrocardiogram/Holter/stress test features, elevated cardiac troponins, functional and structural abnormalities on cardiac imaging, and tissue characterization by cardiac magnetic resonance) [4]. In this case, we report a rare case of acute pancreatitis, which was complicated with viral myocarditis.

Key Clinical Message

Myocarditis can be a rare late manifestation of acute pancreatitis caused by Coxsackie virus infection. Clinicians should be aware of potentially life-threatening myocarditis because immediate recognition and management are the cornerstones in achieving a better outcome.

Keywords

Coxsackie virus, myocarditis, pancreatitis, viral myocarditis.

Clinical History/Examination

A 39-year-old woman was admitted to our hospital complaining of gradual onset of abdominal pain radiating to the back. She has no past medical history and not on any medications. She was a nonsmoker and did not consume alcohol. On admission, she was hemodynamically stable while the physical examination revealed epigastric pain and abdominal tenderness. Electrocardiography revealed regular sinus rhythm at 87 beats/min without ST-T abnormalities. Laboratory tests showed elevated pancreatic enzymes (amylase: 562 U/L), elevated CRP (15 mg/L), and normal lipidemic profile. The management of the patient included nil per os and intravenous administration of fluids and analgesics (pethidine). The patient underwent an abdominal computed tomography scan (CT scan) at the time of admission and magnetic resonance cholangiopancreatography (MRCP) on the fifth day of hospitalization, which revealed swelling of the pancreatic tail, suggesting pancreatitis, without any findings of obstructive lesions. On

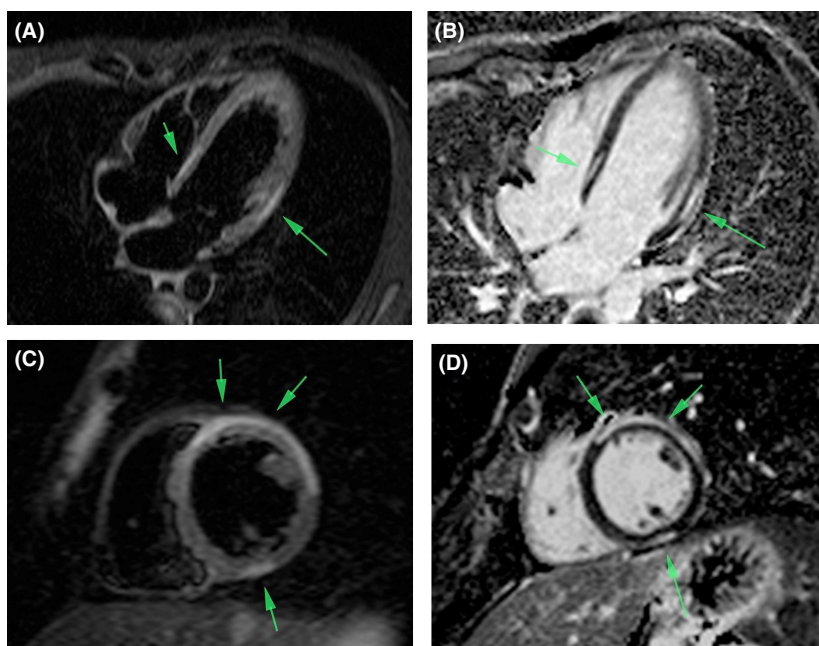


Figure 1. Cardiac MRI images. (A) Four-chamber T2-weighted IR image, showing subepicardial and mid-wall enhancement of the septum and lateral wall. (B) Four-chamber T2-weighted IR image, showing late gadolinium enhancement in the basal segment of the septum and lateral wall. (C) Short-axis T2-weighted IR image, showing subepicardial and mid-wall enhancement of the anterior and posterior wall at the papillary muscle level. (D) Short-axis T2-weighted IR image, showing late gadolinium enhancement in the anterior and posterior wall at the papillary muscle level.

the seventh day of hospitalization, the patient underwent an endoscopic ultrasound followed by fine needle aspiration (EUS/FNA) of inflammatory cells. The biopsy was negative for malignancy. An infectious etiology was suspected following the exclusion of other causes. The clinical course of our patient was stable with an improvement in patient's symptoms, and we started oral feeding.

On the 18th day of hospitalization, the patient complained thoracic pain which irradiated to the neck. Electrocardiography showed sinus rhythm with ventricular extrasystoles and without ST-T abnormalities. Cardiac ultrasound revealed regional hypokinesia of the middle segment of anterior and interventricular septal wall with preserved ejection fraction. Blood tests showed a marked elevation of troponin I (524 ng/mL). Twenty four-hour Holter ECG monitoring recorded two thousand ventricular extrasystoles. A coronary angiography was performed at the next day, which revealed normal coronary vessels. On the 24th day of hospitalization, we performed cardiac MRI, which showed edema of the basal and middle segment of anterior, interventricular, posterior, and lateral wall; and in late gadolinium enhancement, a distinctive pattern of subepicardial and mid-wall enhancement with nonischemic distribution (Fig. 1). The left ventricular ejection fraction was calculated at

57% in the MRI. These findings suggested a diagnosis of myocarditis. We initiated a β -blocker (Carvedilol 6.25 mg bid) and an angiotensin-converting enzyme inhibitor (Ramipril 2.5 mg od) while we advised our patient to avoid exercise for at least 6 months. Serological tests detected a high antibody titer (IgM) against Coxsackie viruses B1 and B4. The patient's clinical course was uncomplicated, and she completely recovered with normalization of pancreatic and myocardial enzymes on the 28th day of hospitalization.

Discussion

In this paper, we reported a rare case of pancreatitis complicated by myocarditis due to infection by Coxsackie viruses. Coxsackie virus B is a member of the Picornaviridae family (a nonenveloped single-stranded RNA virus) associated with human diseases including myocarditis and pancreatitis [5]. Viral myocarditis is important because as it can cause both mechanical dysfunction and electrical abnormalities leading to ventricular arrhythmias that are potentially life-threatening. To the best of our knowledge, there are three previously reported cases of adult patients with myocarditis and pancreatitis attributable to Coxsackie virus infection with serotypes A4, B2, B4, and B5 being implicated [6–8]. An interesting finding in

experimental models was the etiologic link between group B Coxsackie-induced pancreatic and heart disease [9]. Moreover, selective depletion of T lymphocyte subpopulations indicated that CD4 cells were either completely or partially responsible for cell damage in both organs in mice inoculated with coxsackie virus B3 [10]. Other infectious agents that have been associated with acute myocarditis and pancreatitis are leptospirosis, hepatitis E, enterovirus, West Nile virus, EBV, and mumps [11–18].

Cardiac angiography is often indicated to rule out coronary ischemia as a cause of chest pain and elevated troponin levels. However, CT angiography can be an alternative noninvasive approach for excluding coronary artery disease. Furthermore, CT angiography can help in the diagnosis of myocarditis. Particularly, Brett *et al.* showed that in patients with acute myocarditis as confirmed by CMR, edema was demonstrated on arterial phase CT coronary angiography [19]. Regarding echocardiography, the ejection fraction was within normal range in our patient. Pinamonti *et al.* reported that left ventricular dysfunction was common (69%), particularly in patients with congestive heart failure [20]. On the other hand, cardiac MRI revealed three features that made myocarditis more likely according to the Lake Louise consensus criteria. These criteria were an increased regional signal on T2-weighted images, increased early gadolinium enhancement ratio, and focal lesions of late gadolinium enhancement without an ischemic distribution. This was the main reason that we did not perform an endomyocardial biopsy (EMB) directly. EMB is the criterion standard for the diagnosis of myocarditis, although it has limited sensitivity and specificity. The risk of complications is low if it is performed by experienced teams (0–0.8%) [4]. Epidemiologic results from the European Study on the Epidemiology and Treatment of Cardiac Inflammatory Disease (ESETCID) database found that only 11.8% (enterovirus 2.2%) of patients with suspected acute or chronic myocarditis and reduced ejection fractions had detectable viral genomes in biopsy sample [21].

In regard to myocarditis management, patients with hemodynamically stable heart failure should be treated with diuretics, angiotensin-converting enzyme inhibitor, or angiotensin receptor blockade and beta-adrenergic blockade [4]. Antiviral therapies are still not recommended for the treatment of enteroviral infections [4]. On the other hand, steroid therapy is indicated in cardiac sarcoidosis and in some forms of infection-negative eosinophilic or toxic myocarditis with heart failure and/or arrhythmia [4].

A limitation of our study was that it is well known that there is a lack of correlation between serology and EMB findings. Indeed, in a relevant study, only in 4% of the

patients was serological evidence of an infection with the same virus that was detected by EMB [22].

Conclusions

We presented a rare case of coexistence of acute pancreatitis and myocarditis caused by Coxsackie virus infection. Clinicians should be aware of potentially life-threatening myocarditis that needs to be monitored closely to achieve better outcomes.

Conflict of Interest

None declared.

Authorship

KL, AK and TI: involved in management of the patient, major revision, and approval of the final manuscript. GB: wrote the first draft, involved in major revision, and in approval of the final manuscript. GT and AS: involved in major revision and in approval of the final manuscript.

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