

Epstein Barr Virus Infection Induced Suspected Acute Myocarditis in COVID-19 Pandemic

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Abstract

Background: Epstein Barr Virus infection (EBV) could be associated with cardiovascular disease, including myocarditis. We informed a case of EBV infection presenting initially as myocarditis, followed 5 days later by the typical symptoms of infectious mononucleosis. **Case Presentation:** A 19-year-old man with persistent retrosternal chest pain was admitted to the emergency department. On physical examination, the patient had sub-febrile fever (37.2°C) and palpable cervical lymphadenopathy, with no hepatosplenomegaly. Initial ECG has repolarization abnormalities in leads II, aVF and III. Laboratory testing revealed elevated cardiac enzymes and liver enzymes (high sensitive troponin I levels 3000 ng/mL, aspartate transaminase 158 U/L, alanine transaminase 100 U/L). Blood white cells were 10,500 μ L, platelet level were low 98,000 (thrombocytopenia), and lenfo-monocytosis in complete blood count. We hospitalized the patients the intensive coronary unit (ICU) because of high troponin levels. We recognized hypokinesia of the posterolateral wall of the left ventricle with mild impaired systolic function and increased perimyocardial brightness by echocardiography. Antibody serology tests showed that the anti-EBV capsid antigen IgM (EBV-VCA) was positive, EBV-VCA) IgG was negative. Other etiologies were excluded. Therefore, the patient was referred to cardiac positron emission tomography due to technic problems of magnetic resonance imaging device. We documented in positron emission tomography imaging that increased ¹⁸F-FDG uptake on posterior and posterolateral walls of left ventricle (indicating a large jeopardized area). We diagnosed suspected diagnosis of myocarditis without associated pericarditis. We monitored the patient and gave beta blocker, and aldosterone anta-

gonists. Complications in the intensive care unit not occurred. We discharged patients after one week. After three weeks, we re-evaluated the patient. We not observed wall segment motion abnormality on echocardiography and liver tests were near normal. **Conclusion:** In suspected EBV myocarditis, ^{18}F -FDG PET-CT cardiac positron emission tomography imaging represents an interesting noninvasive imaging technique to identify inflammatory processes in acute myocarditis and can be considered in patients with contraindications/unavailable to cardiac magnetic resonance.

Keywords

Epstein Barr Virus, Myocarditis, ^{18}F -FDG PET/CT

1. Introduction

The incidence of myocarditis in children and adolescents is 1 to 2 per 100,000. Viral infectious etiologies are most common [1]. Viral myocarditis is associated with a variety of presentations ranging from subclinical to severe cardiac dysfunction. Viruses, coronavirus 2 (SARS-CoV-2) can also cause a clinical picture as acute viral myocarditis. Similarly, Epstein-Barr virus (EBV) infection or reactivation could be associated with cardiovascular disease, including myocarditis [2]. EBV is the most common cause of infectious mononucleosis and has a triad of pharyngitis, lymphadenopathy and fever [3]. EBV infection has a viral prodrome period preceding any cardiac signs or symptoms [1].

Here we informed a case of EBV infection presenting initially as myocarditis, followed 5 days later by the typical symptoms of infectious mononucleosis in COVID-19 Pandemic.

2. Case Summary

19-year-old man with persistent retrosternal chest pain was admitted to emergency department. Before 5 days, he had described slight discomfort in the upper chest, bilaterally near the collarbone, and back pain. He had informed mild cough and throat pain. The patient had generalized weakness and reduced appetite. He reported that he was active in sports before 5 days. The patient had higher social classes and no history any before health problems.

On physical examination, the patient had sub-febrile fever (37.2°C) and palpable cervical lymphadenopathy, no hepatosplenomegaly. Repolarization abnormalities were present leads II, aVF and III on initial ECG (Figure 1). Laboratory testing revealed elevated cardiac enzymes and liver enzymes (high sensitive troponin I levels 3000 ng/mL, aspartate transaminase 158 U/L, alanine transaminase 100 U/L. Blood white cells were 10,500 μL , platelet levels were low 98,000 (thrombocytopenia), and lenfo-monocytosis in complete blood count (Table 1).

We hospitalized the patients to intensive coronary unit (ICU) because of high troponin levels. We realized hypokinesia of the posterolateral wall of the left

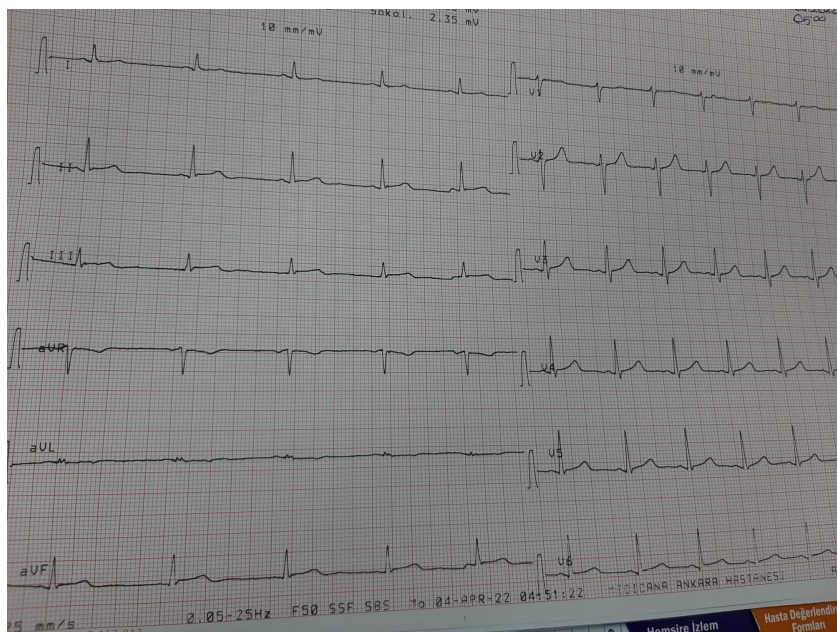


Figure 1. ECG shows repolarization abnormalities leads II, aVF and III.

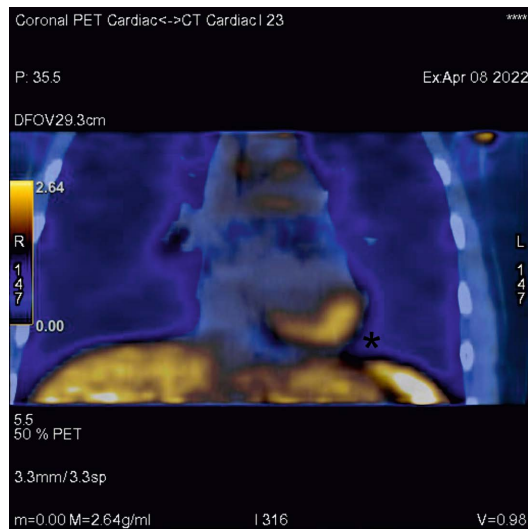
Table 1. Patient's laboratory results at presentation.

LABORATORY TESTS	RESULTS
TROPONIN I	3000 ng/L (normal < 34 ng/L)
Alanine aminotransferase	100 U/L (normal < 34 U/L)
Aspartate aminotransferase	158 U/L (normal < 34 U/L)
White Blood Count	10,500 μ L, (normal; 4000 to 11,000 per microliter of blood), lenfo-monocytosis
Platelet Count	98,000 (normal; 150,000 to 400,000 per microliter of blood)
Anti-EBV capsid antigen IgM (EBV-VCA)	positive

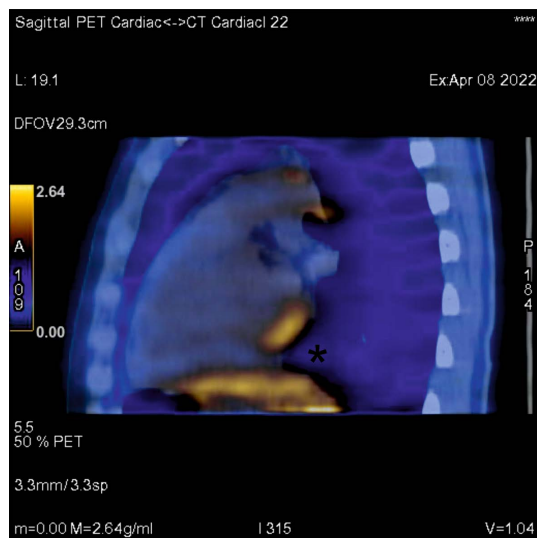
ventricle with mild impaired systolic function and increased perimyocardial brightness by echocardiography [4].

Due to triad of clinical signs, we suspected EBV infection associated with myocarditis and hepatitis. Antibody serology tests showed that the anti-EBV capsid antigen IgM (EBV-VCA) was positive, EBV-VCA IgG was negative. Other etiologies were excluded by PCRs, serologies, cultures, and viral tests including COVID-19 and hepatitis.

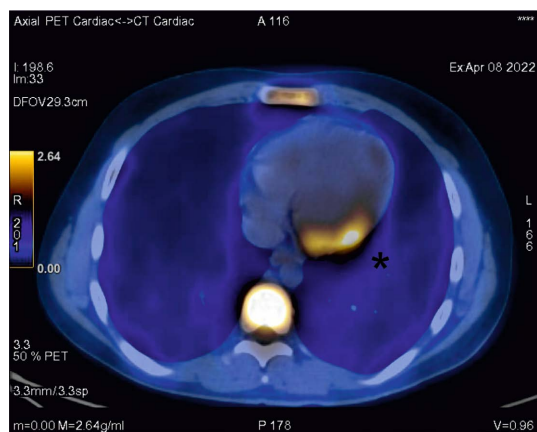
The patient not underwent magnetic resonance imaging (CMR), due to technical problems of CMR device. Therefore, the patient referred to cardiac positron emission tomography (PET-CT). We recognized in PET imaging that increased 18 F-FDG uptake on posterior and posterolateral walls of left ventricle (indicating large jeopardized area) (**Figures 2(a)-(c)**). Coronary angiography was not performed. We diagnosed suspected diagnosis of myocarditis without associated pericarditis [5] [6].



(a)



(b)



(c)

Figure 2. PET-¹⁸F-FDG uptake at posterolateral wall of the left ventricle on corresponding coronal, sagittal and axial appearance on PET-CT images, respectively. (*) indicate large jeopardized area.

In treatment, we monitored the patient and gave beta blocker, and aldosterone antagonists. In following time, malignant arrhythmias, hemodynamic instability not occurred. We discharged patients after one week when serum troponin levels returned to normal levels. After three weeks, we re-evaluated the patient in control. Left ventricular systolic function in echocardiography was found as normal. We not observed wall segment motion abnormality on echocardiography and perimyocardial brightness. Moreover, liver tests were near normal.

3. Discussion

In patients with suspected acute myocarditis, endomyocardial biopsy is currently considered the gold standard. However, the definition of clinically suspected myocarditis encompasses one or more of the clinical presentations and one or more abnormalities from different diagnostic categories, including electrocardiogram, troponin levels, noninvasive cardiac imaging according to the 2013 European Society of Cardiology (ESC) consensus paper [5].

EBV (Human Herpes Virus-4) is one of the lymphotropic viruses with lifelong persistence that belong to the Herpesviridae family. EBV was found to induce a severe, chronic active infection of CD8+ T cells in the myocardium in a patient with ongoing perimyocarditis [7] [8].

Myocarditis can be the first symptom of EBV infection with manifestations ranging from asymptomatic electrocardiographic changes to fulminant heart failure, cardiac arrhythmias, or even sudden death [9].

2018 consensus guidelines about cardiovascular magnetic resonance in non-ischemic myocardial inflammation suggested the addition of T2-weighted cardiac MRI to the pre-existing Lake Louise criteria (LLC) for the diagnosis of myocarditis. Furthermore, 2018 LLC presented better diagnostic performance than the original criteria owing to increased sensitivity [6].

FDG-PET imaging is noninvasive imaging technique to identify inflammatory processes in acute myocarditis and would be used in patients with contraindications to cardiac MRI. Moreover, integrated PET-MRI systems can be combined for the identification of lesions and the high sensitivity of FDG for the detection of inflammatory processes [10].

Increased glucose metabolism is a hallmark of inflammation, because of over-expression of glucose transporters and overproduction of glycolytic enzymes in inflammatory cells [11]. Inflammation can be visualized effectively using the glucose analog ^{18}F -FDG and PET. We thought that ^{18}F -FDG PET-CT could represents an interesting alternative imaging technique in this patient. ^{18}F -FDG accumulates in cells with high metabolic activity such as activated inflammatory cells. Using prolonged fasting protocol, the physiological uptake of ^{18}F -FDG of the myocardium was be completely suppressed whereas FDG uptake into inflammatory cells was clearly localized to myocarditis affected areas in our patient.

ECG findings in myocarditis include ST- and T-wave changes. Echocardi-

graphy is useful to rule-out valve diseases and to monitor myocarditis progression and response to therapy. Global ventricular dysfunction, regional motion abnormalities, and increased perimyocardial brightness could occur in myocarditis.

Treatment regimens for patients with virus-negative or autoimmune inflammatory cardiomyopathy include steroid-based treatment combined with subsequent intravenous immunoglobulin (IVIG) therapy [12].

4. Conclusion

EBV infection in young adults may appear as myocarditis with the classic features of pharyngitis, lymphadenopathy, and fever. ¹⁸F-FDG PET imaging represents an interesting noninvasive imaging technique to identify inflammatory processes in acute myocarditis and can be considered in patients with contraindications/unavailable to cardiac MRI.

Informed Consent

The case was reviewed by the Institutional Review Board and informed consent was obtained from the patient.

Conflicts of Interest

All authors declared no any conflicts of interest.

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Abbreviations

EBV: Epstein Barr virus.

ECG: Electrocardiogram.