How an Ebstein-Barr Virus May Induce Acute Fulminant Myocarditis in a Young Immunocompetent Adult: A Case Report

A Horovitz, I El Zein, R Valentino, H Medhaoui, J Inamo

INTRODUCTION

Fulminant myocarditis, especially those caused by the Ebstein-Barr virus (EBV) is a rare disease (1). For the first time, we describe a case of fulminant myocarditis caused by EBV in a young, immunocompetent adult, co-infected with parvovirus B19.

Keywords: Ebstein-Barr virus, fulminant myocarditis

CASE REPORT

A 33-year old man was referred to the Emergency Department (ED) with thoracic pain that started two days earlier. His past medical history included dengue fever contracted one year earlier and a 22-pack year smoking history. He reported flu-like symptoms for 10 days with fever. On day two, his general practitioner, suspecting bronchitis, started him on antibiotics (2nd generation cephalosporin) and low dose steroids (20 mg/day).

Forty-eight hours before coming to the ED, he presented with crescendo-type epigastric pain radiating to the back. On admission, the patient was stable haemodynamically without signs of heart failure. The electrocardiogram (ECG) showed anterior ST elevation associated with inferior ST depression along with third-degree AV block (Fig. 1).

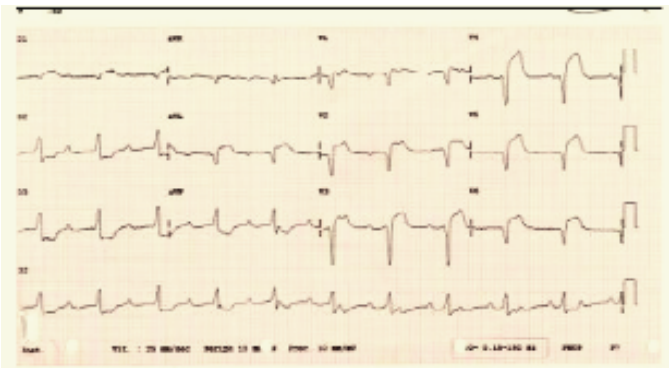

Fig.1: Electrocardiogram, done on the patient's arrival, mimicking anterior infarct.

From: Service de Cardiologie, Centre Hospitalier Universitaire de Fort de France, Martinique.

Correspondence: Dr A Horovitz, Centre Hospitalier Universitaire, Haut Leveque, Service Pr Bonnet, 33600 Pessac, France. E-mail: alicehorovitz@hotmail.com

The initial laboratory tests showed elevated troponin I at 346 ng/dL, C-reactive protein (CRP) at 40 mg/L, a normal platelet count of 193 000 IU, elevated liver enzymes with aspartate aminotransferase (AST) at 1363 IU and alanine aminotransferase (ALT) at 675 IU, lactate dehydrogenase (LDH) at 2.75 and normal creatinine at 75 µmol/l.

The coronary angiography, performed three hours after admission, found normal coronary arteries. Temporary pacing was initiated during the procedure. Dobutamine was introduced at time T+5h at a dose of 5 gamma/kg/min in order to correct the haemodynamic instability.

He stayed three hours in the intensive care unit but then had to be resuscitated in view of a refractory cardiogenic shock at a dose of 10/kg/min of dobutamine. He was intubated, ventilated mechanically after an induction with ethomidate at time T+8h. A peripheral extracorporeal membrane oxygenation (ECMO) was mounted six hours later (time T+14h) with a cardiorespiratory arrest of 50 minutes during the procedure. At day seven, a central Extracorporeal membrane oxygenation (ECMO) was obtained as well as a myocardial biopsy which found major myocardial necrosis of more than 95%. (Figs. 2, 3).

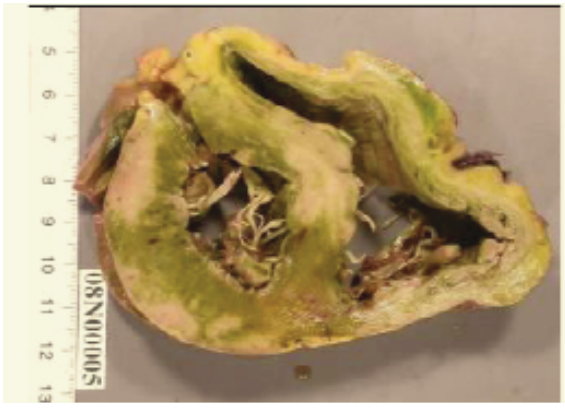

Fig. 2: Histology of the patient's heart with major necrosis.

An exhaustive aetiological investigation was launched (Table 1) with particular focus on an infectious origin. Research of an activation of the autoimmune system turned out to be negative. HIV, hepatitis B virus, hepatitis C virus, adenovirus and the coxsackie virus serologies were equally negative. The only abnormal elements, however, were the

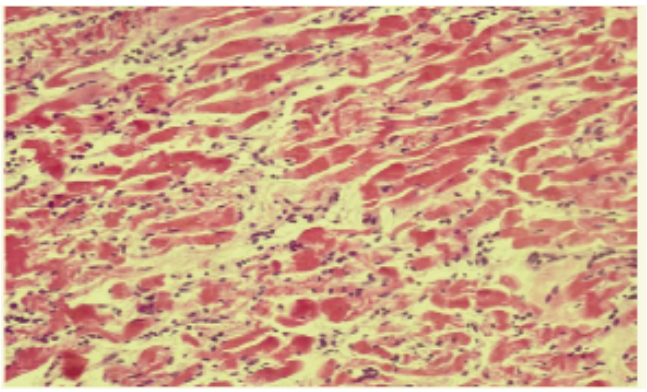

Fig. 3: Macroscopic section of the patient's heart.

Table 1: Results of viral serology

Serology	IgM	IgG
Coxsaksie	–	–
Dengue, leptospirosis	–	–
Cytomegalovirus	–	+
Ebstein-Barr virus	–	+
Parvovirus B19	–	+
Chlamydia	–	+
Mycoplasma	–	–
Syphilis TPHA VDRL	–	–
Hepatitis A virus	–	–
Measles	–	–
Orthomyxovirus	–	–
Varicella-zoster virus	–	–
Mumps	–	+
Rubella	–	–
Herpes simplex virus 1, 2	–	–
Hepatitis C virus	–	–
Hepatitis B virus	Ag HBS –, Ac anti Hbc +, Ac anti Hbs –	
HIV	–	

presence of IgG antibodies to EBV, parvovirus B19, cytomegalovirus (CMV), chlamydia trachomatis and mumps.

The patient died 16 days later from multi-organ failure: cardiac, renal, haematological and ultimately neurological.

The post-mortem polymerase chain reaction (PCR) analyses revealed presence of EBV in almost all organs (kidneys, heart, lungs and blood). In the lungs, kidneys and liver, parvovirus B19 was also found (Table 2).

Table 2: Results of post-mortem polymerase chain reaction (PCR)

Biopsy/PCR	Blood	Heart	Kidneys	Lungs
Enterovirus	–	–	–	–
Ebstein-Barr virus	+	+	+	+
Cytomegalovirus	–	–	–	–
Parvovirus B19	+	–	+	+
Dengue	–	–	–	–

DISCUSSION

Fulminating myocarditis is rare with a stable incidence (1). Ebstein-Barr virus-induced myocarditis is especially prevalent among newborn and young children (2).

A major issue raised by this case is why an immunocompetent patient developed a fulminating myocarditis, when 90% of the population contracts EBV, and 50% of these have no clinical manifestations (1). One hypothesis might be the reactivation of EBV by parvovirus B19 (3). Parvovirus B19 is known to increase the activation of the autoimmune system, which is a major event occurring in the second phase of fulminating myocarditis (5). The second phase is autoimmune where the specific cellular autoimmune system allows the recycling of viral particles and their pre-sentations to T-specific lymphocytes by the major histocompatibility complex (MHC) inducing the production of cytokines and perforins. Myocardial cell antigens are mistakenly identified as viral antigens and add to the autoimmune activation.

Nevertheless, parvovirus B19 was PCR negative in the heart so intracellular or intratissue coactivation seems to be unlikely and the most likely is inflammatory damage by chemokines and other inflammatory markers. Parvovirus B19 is present in multiple infections (2).

The role of autoimmunity in the development of myocarditis has been well established but its role in the development of acute fulminating myocarditis remains all the more complex (4).

Another possibility is the direct pathogenicity of the EBV (3), the PCR EBV being positive in the heart while that of the parvovirus B19 was negative.

It is to be noted, however, that the myocardial biopsy done on the seventh day allowed confirmation of the diagnosis without affecting the management of the patient. It is also to be noted that the viral cause of the disease had been confirmed only at post-mortem which shows the value of PCRs (7).

The absence of cardiac-MRI at our centre has not been a disadvantage with regards to the diagnosis but could have guided and speeded it up, notably in preventing a coronary angiography and its potential iatrogenic danger. It also could have guided the biopsy; the localization of which allows a better sensitivity knowing that it is the lateral side of the left ventricle which is mostly affected (7).

However, low-dose steroids for 48 hours did not modify immunocompetency even if to date the doses and duration of treatment which entail immunosuppression still remain unclear.

CONCLUSION

To conclude, parvovirus B19 may potentiate EBV infection by a yet unclear mechanism but the role of autoimmunity with amplification of phase 2 may explain the malignant and fatal outcome of a mostly benign infection.

The PCR remains an indispensable tool in aetiology determination even if it indeed leads to late diagnosis.

This case remains unique for the existence of a fulminating myocarditis by Ebstein-Barr virus and co-infection by EBV and parvovirus B19.

REFERENCES

1. MacCarthy R. Long-term outcome of fulminant myocarditis as compared with acute (non fulminant) myocarditis. N Engl J Med 2000; **342:** 690–5.
2. Neil E. Detection of viruses in myocardial tissues by polymerase chain reaction: evidence of adenovirus as a common cause of myocarditis in children and adults. J Am Coll Cardiol 2003; **42:** 466–72.
3. MacSween K. Ebstein Barr virus – recent advances. Lancet Infect Dis 2003; **3:** 131–40.
4. Launardi C. Human parvovirus B19 infection and autoimmunity. Autoimmunity Rev 2008; **8:** 116–20.
5. Cooper LT. Myocarditis. N Engl J Med 2009; **360:** 1526–38.
6. Rose NR. Myocarditis: infection versus autoimmunity. J Clin Immunol 2009; **134:** 80–8.
7. Cooper LT. The role of endomyocardial biopsy in the management of cardiovascular disease. J Am Coll Cardiol 2007; **50:** 1914–31.
8. Baughman KL. Diagnosis of myocaditis. Death of Dallas criteria. Circulation 2006; **113:** 593–5.