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Case report

Epstein-Barr virus multi-organ attack in a twenty-year-old boy: myocarditis, pneumonia and hepatitis

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SUMMARY

The case of a 20-year-old man who was admitted to our hospital with symptoms of two days, dyspnea, orthopnea, chest pain and fifteen days, cough and fever is presented. The patient was diagnosed with acute Epstein-Barr virus (EBV) infection with liver, lungs and myocardial involvement. He recovered completely within a 20 day period and remains in excellent health with no physical impairment or laboratory abnormalities. We comment on the diagnostic hallmarks of the EBV infection emphasizing physical examination, electrocardiogram, echocardiogram, chest X-ray and serologic tests. Moreover, we discuss clinical prognosis of EBV infection. To our knowledge this is one of the very rare cases of multi-organ EBV infection with myocardial, lungs and liver involvement.

Key words: Epstein-Barr virus, myocarditis, pneumonia, hepatitis, liver.

INTRODUCTION

Epstein-Barr virus is a B-Lymphotropic human herpesvirus with worldwide distribution. Infection in childhood is usually subclinical, but 25-70% of adolescents and adults may develop the clinical syndrome of infectious mononucleosis, which includes the triad of fever, lymphadenopathy and pharyngitis combined with the transient appearance of heterophil antibodies and an atypical lymphocytosis. EBV is also associated with nasopharyngeal carcinoma and certain B-cell lymphomas.[1]

Complications of infectious mononucleosis occur infrequently but may be the predominant manifestation of the illness. Hepatitis is a common component of infectious mononucleosis. Almost 90% of patients have mild liver enzyme elevation. EBV infection may present as an acute hepatitis. Severe or permanent hepatic dysfunction caused by EBV is extremely rare but fatal acute hepatic failure has been described.[2] Pulmonary parenchymal abnormalities are infrequently noted in adults but appear to be more common in children. Cardiac abnormalities are uncommon in infectious mononucleosis but may include pericarditis, myocarditis, coronary artery spasm and electrocardiographic abnormalities.

Herein we present the case of a 20-year-old man diagnosed with myocarditis, pneumonia and hepatitis caused by EBV infection.

CASE REPORT

A 20-year-old man was admitted to our hospital with symptoms of dyspnea, orthopnea and chest pain for the previous two days. He also had a cough and fever up to 39^0C for the previous 15 days.

The patient was a smoker and had no previous hospital admissions. Physical examination revealed a very exhausted and anxious patient with pharyngitis, lymphadenopathy, hepato-splenomegaly, tachycardia up to 130 beats per minute, tachypnea up to 28 breaths per minute,

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fever of 39^{0}C and hypotension (systolic: 90 mmHg, diastolic: 60 mmHg). On auscultation the first heart sound was muffled and there was a protodiastolic third heart sound (S3) with a gallop rhythm. The jugular vein pressure was elevated and rales were heard up to the upper lung fields. The ECG on admission revealed sinus tachycardia, ST – T elevations at leads V_4, V_5, V_6 and ventricular extrasystoles. The echocardiogram showed dilation of the left ventricle with diffuse hypokinesia and a mural thrombus (Figure 1).

Chest X-ray showed increased cardiothoracic index with bilateral bronchoalveolar infiltrations and interstitial pneumonia (Figure 2). Arterial blood gazes were compatible with respiratory alkalosis with pH 7.48, pCO_2 29mmol/lit, PO_2 49mmol/lit, HCO_3 22mmol/lit and saturation 88%. Peripheral blood count revealed hematocrit 48%, white blood cell count 12630/mm^3 with elevated lymphocyte count (with no atypical lymphocytes), ESR 86mm/h, C-reactive protein 123mg/dl, aspartate aminotransferase 50 IU/L, alanine aminotransferase 56IU/L, γ-GT 267IU/L, LDH 583 IU/L, total bilirubin1.9 mg/dl with direct bilirubin 0.85 mg/dl and INR1.4 with aPTT 49 sec (healthy control 31 sec).

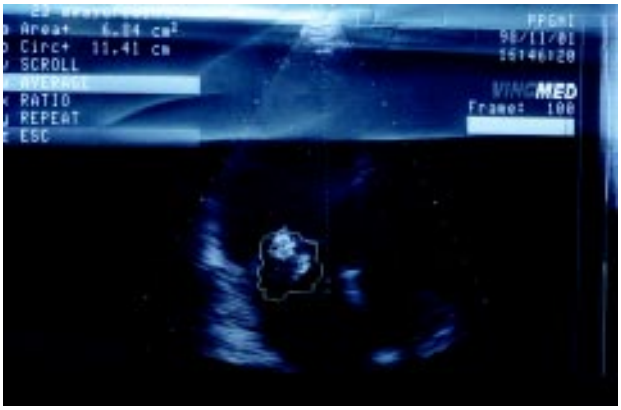

Figure 1. Echocardiogram showing dilation of the left ventricle with diffuse hypokinesia and a mural thrombus.

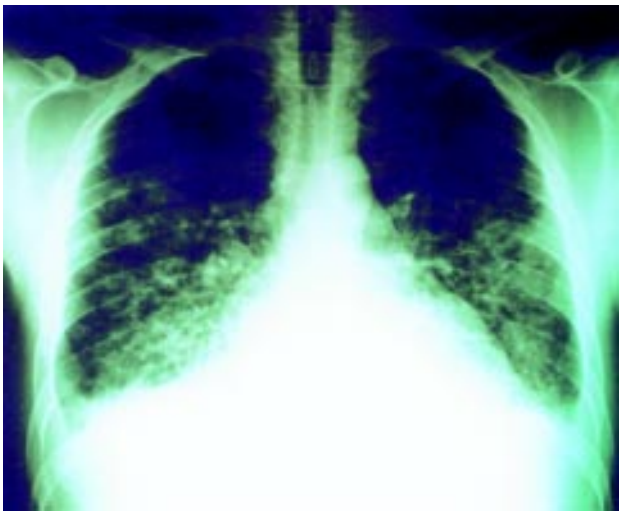

Figure 2. Chest X-ray showing increased cardiothoracic index with bilateral bronchoalveolar infiltrations and interstitial pneumonia

Thyroid function, cholesterol, triglycerides and the remaining biochemical profile were within normal limits. Immunoserologic exam revealed RF (-), ANA (-), ANCA (-), anti-DNA (-), C_3, C_4 and cardiolipins within normal limits.

Further serologic investigation showed a 3-fold increase of IgM title for antibodies against EBV virus capsidic antigen (VCA, ELISA method optical density O.D 1.270 / cut off 0.367) while IgG antibodies to VCA and EBNA-1 proved twice negative at that time. Blood PCR for EBV was negative two times while IgM titles for antibodies against cytomegalovirus, toxoplasma, mycoplasma of pneumonia, leptospira interrogans, borelia burgdoferi, herpes simplex virus, human immunodeficiency virus (HIV), hepatitis A, B, C viruses, Echo and Coxsackie viruses were all negative. Empirical treatment with cefuroxime and clarithromycin was started with no apparent clinical improvement.

On hospital day 5, the EBV antibodies increased at O.D.= 1.687 / cut off 0.367 (4 fold increase) and the patient had signs of congestive heart failure. However, he refused endomyocardial and liver biopsy. He was immediately started on furosemide, digoxin, captopril and heparin with a good response to this treatment. Pharyngeals swabs and stool samples cultured for enteroviruses were negative. On hospital day 12, chest X-ray revealed signs of improvement and on day 14 the cough and fever resolved. On day 17 the patient was discharged in a very good condition with a normal ECG, chest X-ray and echocardiogram (with no evidence of impaired contractility). All laboratory tests on discharge day were within normal limits.

DISCUSSION

Myocarditis has been described during and following a wide variety of viral, ricketsial, bacterial, protozoan and metazoan disease, but the predominant cause of the disease is considered to be the non-poliovirus enteroviruses.

Infectious agents may cause myocardial damage through three mechanisms; myocardium invasion, production of a myocardial toxin and immunologically mediated myocardial damage.

Clinical expression of myocarditis ranges from the asymptomatic state, secondary to focal inflammation to fulminant congestive heart failure. Tachycardia is the rule, the first heart sound is often muffled and a protodiastolic fallow may be present. A transit apical systolic murmur may appear but diastolic murmurs are rare. The most common changes in electrocardiogram (ECG) are abnormalities of the ST segment and T wave as seen in this patient. Approximately two dozen different viruses have been associated with myocarditis which characteristically develops several weeks after the initial systemic infection.[3]

Myocarditis caused by EBV infection may become fatal in young patients, especially in children. EBV can cause one single episode or repetitive myocarditis resulting either in congestive heart failure[4] or in complete heart block.[5] A case of EBV-induced myocarditis with substernal chest pain, hypotension, ECG changes and left ventricle hypokinesia simulating myocardial infarction has been reported.[6] Endomyocardial biopsy usually reveals myocyte necrosis and mononuclear cell infiltration consisting entirely of T-cells. Evident cardiac involvement in infectious mononucleosis is extremely rare although non-specific ST-T segment and T wave abnormalities may be seen. In rare cases, EBV myocarditis is accompanied by pericarditis, which was not found in this patient.

Myocarditis is diagnosed by endomyocardial biopsy according to the Dallas histopathological criteria.[7] Lieberman et al classified myocarditis[8] as either fulminant or acute (non-fulminant) according to clinicopathological criteria. Fulminant myocarditis is characterized by a rapid onset with hemodynamic compromise requiring high doses of vasopressors, accompanied by fever, symptoms of heart failure, edema during the last few days and a history of viral illness within the two weeks prior to hospitalization. On the other hand, non-fulminant myocarditis is characterized by an indistinct onset of symptoms of heart failure without the features of fulminant myocarditis. According to McCarthy et al,[9] patients with fulminant attack of myocarditis have a better prognosis, and reserve more chances of recovering completely after the initial attack.

Pulmonary parenchymal abnormalities during EBV infection appear to be more common in children. Upper airway obstruction by pharyngeal or paratracheal adenopathy may occur, and may require surgical intervention, although it is usually sensitive to glucocorticoid therapy. Autoimmune hemolytic anemia, thrombocytopenia, spleenic rupture, encephalitis and cranial nerve palsies represent some further complications of infectious mononucleosis which were not evident in this patient.

Final diagnosis is established by viral serology showing a 3 to 4 fold titer increase in EBV specific anti-VCA antibodies and by detection of the EBV genome with polymerase chain reaction (PCR) on heart and liver biopsy[4] which could confirm the diagnosis of EBV hepatitis. Positive IgM antibodies to EBV in the absence of VCA-IgG and EBNA-1 antibodies are compatible with primary EBV infection, which fit the clinical case, presented here. Non-poliovirus enteroviruses are considered to be the predominant cause of myocarditis and should always be excluded.[10]

Experimental infection with herpes simplex virus produces clinical and histopathologic changes in its natural host, the cottontail rabbit (Sylvilagus froridanus), similar to those observed in humans acutely infected by EBV. More severe histopathologic changes were seen in virus-infected juvenile rabbits than in adult rabbits; these changes included myocarditis, interstitial pneumonia, lymphocytic myositis, hepatitis and lymphocytic depletion of spleen and lymph nodes.[11] Our case could be considered as a human model of EBV multi-organ infection; heart, liver and lungs. In addition, we reconfirmed the usually good prognosis of EBV multi-organ infection in adult patients.

In summary, in cases with infectious mononucleosis, the possibility of developing myocarditis or pneumonia should be kept in mind and the patients should be instructed to consul their physician immediately in case of dyspnea, edema or cough. The prognosis of EBV myocarditis is usually good, but complications or even dilated cardiomyopathy may develop. The EBV induced hepatitis is a more common manifestation but it is usually subclinical and does not lead to chronic liver disease.

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