Acute Myocarditis with Positive Enterovirus 71 IgM in a Young Adult

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In 1998, an epidemic of enterovirus 71 resulted in hand-foot-and-mouth disease and herpangina among thousands of people in all regions of Taiwan. Most of the patients involved in this infectious outbreak were infants or children who were five years old or younger. The severe condition was uncommon among adults. We report herein on an 18-year-old male patient who suffered from myocarditis, and who had a positive serum enterovirus 71 IgM titer and also respiratory failure post endotracheal intubation. This patient received intra-aortic balloon pumping and was administered dopamine for his heart failure. Intravenous immunoglobulin was also prescribed. The patient was discharged uneventfully. Echocardiography performed five months later revealed adequate left ventricular global performance without chamber dilatation.

Key words: myocarditis, enterovirus 71 IgM

Introduction

Myocarditis is defined clinically as inflammation of the heart muscle\(^1\). Although the specific cause of myocarditis for any given patient may often be unknown, a number of different conditions/events have been associated with the development of this disease, including a large variety of systemic infections, a number of systemic diseases, the administration of various drugs and the impact of a variety of toxins\(^1\). The symptoms of myocarditis may be both fulminant and rapidly progressing, and previous viral infections would appear to play an important role in the etiology of myocarditis. In a recent study, it was reported that researchers were able to detect the presence of enteroviruses in endomyocardial biopsies and cases of pericardial effusion from dilated cardiomyopathy and myocarditis\(^2\). In addition, in 1998, an epidemic of enterovirus 71 infection resulted in widespread hand-foot-and-mouth disease and herpangina among thousands of people in all regions of Taiwan, and some of them had a clinical complication of myocarditis\(^3\). Most affected individuals in this outbreak were infants or children; most of the severest cases were children five years old or younger. Enterovirus 71-related myocarditis was uncommon in adults. Most adult patients were asymptomatic or only suffered upper respiratory tract infections. The complication of enterovirus 71-related myocarditis is rare in adults\(^4\). Here, we report on an 18-year-old male suffering from myocarditis and featuring a positive serum enterovirus 71 IgM titer.

Case Report

An 18-year-old male presented at our institution with a sport-related injury. He reported that his father had suffered from cough and
rhinorrhea for approximately one week prior to our patient’s admission. The patient had suffered chest contusions while playing basketball four days prior to his admission; nausea with mild vomiting and left chest pain followed one day subsequently. Our patient reported that he had no symptoms such as fever, sore throat or diarrhea associated with his presenting at our hospital. As the patient’s symptoms appeared to have been progressive subsequent to initial injury and feelings of being unwell, he initially visited a local hospital for help. At this time a medical examination was performed and he was informed of abnormal test results for cardiac enzymes, following which he was transferred to our emergency room. The laboratory date revealed CK-total (1,817 IU/L), CK-MB (85 IU/L) and Troponin I (39.6 ng/mL). The patient’s first electrocardiogram (EKG) revealed left bundle branch block. Body temperature was 36.1°C, pulse 94 beats/min, respiration rate 20 breaths/min and blood pressure 104/45 mmHg. However, blood pressure dropped to 90/51 mmHg 1.5 hours later and dopamine was then given. Six hours later, unfortunately, acute respiratory failure developed and we performed endotracheal intubation. The first chest X-ray film at arrival revealed no obvious abnormality. Nevertheless, subsequent chest X-ray (Figure 1) indicated frank pulmonary edema. A follow-up EKG (Figure 2) revealed left bundle branch block. Echocardiography revealed impaired left ventricle global performance without chamber dilatation or pericardial effusion. Left ventricular internal diameter in diastole (LVIDd) was 4.68 cm and ejection fraction was 0.44. Physical examination revealed an ulcer on his lip but no obvious skin rash on his hands or feet. Severe pink foamy sputum was also noted. Cardiac catheterization performed the day after admission revealed left ventricular global hypokinesis (ejection fraction = 32%, left ventricle end-diastolic pressure = 20 mmHg) and normal coronary arteries. However, hypoxia was noted (SaO₂ 80-85%) under ventilation of FiO₂.

Fig. 1 Chest X-ray taken six hours after the patient arrived at our emergency room. Severe pulmonary edema can be seen, as well as the inserted endotracheal tube.
Blood pressure dropped to 69/40 mmHg under high dose of dopamine. Hence, intra-aortic balloon pumping was undertaken immediately in order to deal with severe heart failure and the patient’s rather unstable hemodynamic status. After the intra-aortic balloon pump was inserted, the vital signs became stable. Furthermore, a Swan-Ganz catheter was also inserted several hours later in order to monitor the patient’s hemodynamic status and the first data revealed cardiac output 5.5, cardiac index 3.2 L/min/m², systemic resistant 973, central venous pressure 7 mmHg and pulmonary capillary wedge pressure 8 mmHg. At this stage, we evaluated the risk factors and causes of myocarditis for our patient, including review of virus titer, evidence of any autoimmune disease and former drug history. The patient’s enterovirus 71 IgM titer proved positive. Hence, intravenous immunoglobulin (200 mg/kg) and hydrocortisone (100 mg q12h) were prescribed soon after the intra-aortic balloon pump was inserted. Immunological testing including Mycoplasma pneumonia Ab, Legionella pneumonophilia IgM, Adenovirus IgM, EBV-CA IgM, CMV IgM, Toxoplasma IgM, Anti-HIV, HSV-1 IgM, HSV-2 IgM and Coxsackie B1-B6 were all negative. In addition, perindopril 2 mg once daily was prescribed after the blood pressure became stable. As a high fever was noted in this patient in the intensive-care unit, an antibiotic regimen including ceftriaxone and minocycline were prescribed for suspected pneumonia. The clinical condition stabilized soon after this series of treatments. The follow-up EKG revealed disappearance of left bundle branch block on Day 3 (Figure 3). The Swan-Ganz catheter and intra-aortic balloon pump were removed on Day 6. The endotracheal tube was removed on Day 8 and the patient was discharged uneventfully on Day 13. Echocardiography performed five months later revealed adequate left ventricular global performance without chamber dilatation.
Discussion

In general, the symptoms of myocarditis may be quite variable and can include an asymptomatic state, clinical heart failure or even be fulminatory. Endomyocardial biopsy has typically been cited as the gold standard for the diagnosis of myocarditis but its sensitivity and specificity would appear to be somewhat limited\(^1\). A correct diagnosis of myocarditis is mostly dependent upon the clinical course\(^1\). Although the cause of myocarditis for any given patient often remains largely unknown, a large variety of infections, certain systemic diseases, some drugs and certain toxins have been associated with the development of myocarditis\(^1\). An enteroviral genome was detected in 27.3% of patients suffering from myocarditis or dilated cardiomyopathy\(^5\). In addition, enterovirus-related myocarditis has been noted among certain children in Taiwan\(^3\).

In 1998, thousands of children in Taiwan suffered from an epidemic of enterovirus 71 infection and some suffered the complication of myocarditis. Enterovirus 71-related myocarditis among adults is relatively uncommon. The detection of enterovirus RNA in the myocardium of patients with heart-muscle disease at the time of initial investigation is typically associated with an adverse prognosis\(^6\). The standard diagnostic method for enterovirus 71 infection is to isolate the virus from the patient and subsequently pursue its identification by a neutralization test or immunofluorescent assay. Such a method is time-consuming, however, and relies heavily upon the availability of anti-sera or commercial monoclonal antibodies. It would appear that IgM for enterovirus 71 infection is a rapid serological assay, the technique having been reported to feature a sensitivity and specificity of 91.5% and 93.1%, respectively\(^7\).

Supportive care for such an afflicted patient needs to be immediate. For cases of fulminate myocarditis, aggressive hemodynamic support is clearly warranted\(^8\). The implantation of various circulatory-support systems (e.g. intra-aortic balloon pumping or extracorporeal membrane oxygenation) may improve the poor prognosis for cases of

Fig. 3 Electrocardiogram after recovery; the left bundle branch block has disappeared.
fulminate myocarditis. Further, such treatments allow for some level of myocardial recovery and/or may be used to provide some sort of bridging to the time of heart transplantation\textsuperscript{(6)}. In addition, the administration of high-dose intravenous immunoglobulin for the treatment of acute myocarditis is associated with the improved extent and rate of recovery of left ventricular function, with a tendency toward better survival during the first year\textsuperscript{(10)}. For our patient, we prescribed a dose of intravenous immunoglobulin (200 mg/kg) for the treatment of his acute myocarditis. The previous report revealed higher doses of intravenous immunoglobulin were used. As a consequence of our patient’s significantly improved state following a series of treatments, we felt that we did not need to give any further doses of such intravenous immunoglobulin.

Assessment of the titer for enterovirus 71 IgM is a rapid and effective test for the presence of myocarditis. For our patient, a positive response to enterovirus 71 IgM testing was noted two to three hours after blood sampling. Thus, we were able to prescribe intravenous immunoglobulin as soon as possible to do our best to improve the patient’s clinical condition.

In conclusion, enterovirus-related myocarditis is typically associated with an adverse prognosis, although enterovirus 71-related myocarditis would appear to be rather uncommon among adults. In order to effectively deal with sufferers of this malady, mechanical circulatory support may be necessary. On the other hand, fulminant myocarditis is a distinct clinical entity and features an excellent long-term prognosis\textsuperscript{(8)}.

References

年輕男性罹患心肌炎合併腸病毒71型IgM
陽性反應之個案報告

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在1998年，台灣全島各地71型腸病毒肆虐，造成數以千計的民眾感染手足口病和皰疹性咽峡炎(herpangina)。此次感染腸病毒的病患多為五歲或五歲以下的孩童及嬰兒，至於成年人嚴重感染的情形則較為罕見。本文報告一位18歲男性病患罹患心肌炎、血清檢驗亦呈現腸病毒71 IgM陽性反應的特徵，這位患者一度出現呼吸衰竭現象而接受氣管插管治療。我們為這位患者施予intra-aortic balloon pumping，並且給予dopamine用以治療患者的心臟衰竭，還給予血清免疫蛋白(intra-venous immunoglobulin)之處方。這位病患終於痊癒出院，出院五個月後再回院作心臟超音波追蹤檢查，我們發現這位病患整個左心室功能恢復正常，心房心室亦無擴張跡象，健康情況良好。

關鍵詞：心肌炎，腸病毒71型IgM