

# Fulminant myocarditis treated with high doses of steroids

Efekt steroidoterapii w zapaleniu mięśnia serca o piorunującym przebiegu

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## Abstract

We present the case of a 4.5-year-old girl suffering from a fulminant type of myocarditis who was admitted to our clinic in a very poor condition due to cardiogenic shock. After treating her by invasive methods and very aggressive pharmacotherapy (catecholamines, high doses of steroids, human immunoglobulin), she fully recovered.

**Key words:** myocarditis, heart failure, steroids

## Streszczenie

Zapalenie mięśnia sercowego jest częstym powikłaniem infekcji wirusowych, może mieć przebieg dramatyczny i stanowić zagrożenie dla życia dziecka. Przedstawiono przypadek 4,5-letniej dziewczynki, u której schorzenie to miało piorunujący przebieg, przekazanej w stanie ciężkim, z objawami wstrząsu kardiogenego do ośrodka autorów. Po zastosowaniu leczenia inwazyjnego (elektroda endokawitarna) oraz agresywnego leczenia farmakologicznego (aminy katecholowe, duże dawki steroidów, immunoglobulina ludzka) uzyskano pełny powrót do zdrowia.

**Słowa kluczowe:** zapalenie mięśnia sercowego, niewydolność serca, steroidy

## Introduction

Myocarditis may complicate common viral infections in children. It may have a dramatic course and be life-threatening to children. Fulminant myocarditis includes symptoms of severe left ventricular (LV) dysfunction, conduction abnormalities and arrhythmias which can quite often lead to cardiogenic shock. For that reason this situation requires urgent diagnosis, which is often based only on medical history and clinical picture. Despite the application of intensive forms of therapy including mechanical support, mortality in the acute phase of fulminant myocarditis reaches 50%. The use of steroids may be life saving for some patients. We presented the case that illustrates this situation.

## Case report

The 4.5-year-old girl was urgently admitted to the hospital because of symptoms of cardiogenic shock. The

girl suffered from symptoms of mild upper respiratory tract infection 2 weeks before admission. On the twelfth day there was a decrease of the child's activity accompanied by unwillingness to eat. On the next day she suffered from a few minutes of unconsciousness with body contractions, involuntary urination and defecation. The child was transferred to the Intensive Care Unit. During transport, several incidents of loss of consciousness caused by bradycardia were observed – episodes of Morgagni-Adams-Stokes (MAS) attacks. Because of the worsening clinical condition of the child, with persistent bradycardia despite administration of atropine and continuous infusion of dopamine (10 g/kg bw/min), the patient was transferred to our Ward for further treatment.

On admission the girl was conscious, but in poor general condition. Symptoms of a cardiogenic shock were present: diaphoresis, pale-gray skin, cold extremities, weak peripheral pulse, bradycardia 36-40/min and hypotension

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70/40 mm Hg. On the basis of electrocardiogram (ECG), diagnosis of a complete atrioventricular block with frequency of 36 beats per minutes (bpm) was made.

Initial echocardiographic examination showed marked depression of left ventricular contractility (LVEF = 35%) affecting mainly the interventricular septum (IVS) with its marked thickening (IVS diameter [IVSd] 11-12 mm). Results of the laboratory findings: white blood cells (WBC) 15 000, C-reactive protein (CRP) 30.8 mg/l, pH 7.3, BE (-) 7, lactate level 5.5 mmol/l, troponin 4.06 ng/ml, NT pro-BNP 30486 pg/ml.

The patient received an infusion of milrinone at a dose of 0.5 µg/kg bw/min. Dopamine infusion was continued. In the first hour of hospitalization, the child was electively intubated and an endocavitary electrode was inserted through the puncture of the internal jugular vein. External stimulation of the right ventricle (VVI) was started (100 bpm).

Given the clinical picture, morphology and degree of LV dysfunction on echocardiography, and 3<sup>rd</sup> degree atrioventricular block, fulminant myocarditis with interstitial edema was considered.

In that situation it was decided to start treatment with high doses of steroids (hydrocortisonum) initially at the dose of 200 mg *i.v.*, i.e. 13.3 mg/kg bw, and then at the dose of 200 mg/day in four doses. Additionally human immunoglobulin at the dose of 15 g *i.v.*, i.e. 1 g/kg bw, was used (Intraglobin F, Biotest, Germany).

The pharmacological treatment (dopamine, milrinone, hydrocortisonum) was modified by addition of drugs acting to prevent brain edema (20% mannitol and furosemide). Because of the LV hypokinesia, continuous infusion with unfractionated heparin (5 U/kg bw/h) was started. The general clinical condition of the child improved during the next few hours of observation. Left ventricular function (LVEF) determined with echocardiography dramatically improved to 60-65% after approximately 16 h.

It included mainly the IVS, whose end-diastolic diameter decreased to 7-8 mm. In that situation the child was awoken and extubated. At the same time, the sinus rhythm (90-110 bpm) with normal atrioventricular conduction returned. External stimulation was not required. Catecholamine doses were reduced and they were discontinued on the 2<sup>nd</sup> day of treatment.

Oral pharmacotherapy with captopril, spironolactone and carvedilol was initiated. Subsequent NT-proBNP sampling showed improvement of the LV function: day 2 – 21 000 pg/ml, day 7 – 1094 pg/ml.

The results of serological studies (CMV, Coxsackie type B, Parvovirus B19) were negative. The endocavitary electrode was removed on day 7. The patient was discharged home on day 11 of hospitalization in a good general condition. Ambulatory control on week 2 after discharge showed normal LV function (LVEF = 76%) and NT-proBNP concentration of 128 pg/ml. Steroid therapy was ended,

maintaining only the oral treatment with captopril, spironolactone and carvedilol.

## Discussion

Around 20 years ago during one of her lectures Professor Wanda Wyszacka-Aleksandrow said that failure to give steroids in the case of a patient with fulminant myocarditis may lead to the patient's death. Several years later we hospitalized a 16-year-old patient with symptoms of cardiogenic shock in the course of a viral infection.

Echocardiography demonstrated diffuse LV myocardial thickening: intraventricular septum (IVS) 19 mm, left ventricular posterior wall (LVPW) 20 mm with diffuse LV hypokinesia (LVEF 35-40%). In the 1<sup>st</sup> hour of hospitalization cardiac arrest caused by asystole occurred. Despite prolonged reanimation life functions were not restored. Given the clinical picture and results of the echocardiography at that time we suspected myocardial edema in the course of fulminant myocarditis. Autopsy confirmed interstitial myocardial edema with lymphocytic infiltration. In the presented case the echocardiographic picture was similar – massive thickening of the IVS and diffuse LV hypokinesia. We were convinced that in this case we were dealing with interstitial myocardial edema, which was responsible for both the LV dysfunction and third-degree atrioventricular block. This led us to apply high doses of steroids. The spectacular response to treatment and the time in which the remission of conduction abnormalities and improvement of LV function were obtained suggests that myocardial interstitial edema determines the expression of symptoms in the acute phase of fulminant myocarditis.

For about 20 years we have observed in the literature reports indicating LV myocardial thickening in the acute phase of myocarditis [1-3]. It can be located both in the IVS and in the LV free wall. Analysis of the material obtained during biopsy showed that this condition is a result of an interstitial edema. Hiramitsu *et al.*, who on the basis of a careful histological analysis of biopsies demonstrated that myocardial cells do not undergo edema, also confirm this. The authors did not observe any changes of the longitudinal and transverse dimensions of the myocytes and emphasized that the edema is located only in the parenchymal cells [3]. The highest severity of edema is observed in the first three days of myocarditis and it undergoes gradual regression during the next eight days. Myocardial biopsies obtained after 30 days from the beginning of myocarditis do not show any characteristics of interstitial edema [3, 4].

Myocardial edema is responsible for systolic and diastolic LV dysfunction. Morimoto *et al.* [5] and Felker *et al.* [6] stated that edema results in reduction of the LV end-diastolic volume and finally in the reduction of cardiac output.

Myocardial thickening and conduction abnormalities seem typical for fulminant forms of myocarditis. Other clinical factors suggesting this course of myocarditis include increased levels of CRP, CK, troponin, LV hypokinesia and QRS widening [7]. Fulminant form of myocarditis may be also suggested by the echocardiographic picture: myocardial thickening, hypokinesia, no signs of LV dilation. Left ventricle dilation, on the other hand, is typical for acute myocarditis [6]. It is worth noting that despite the high mortality of up to 50% in the acute phase of fulminant myocarditis, patients who survive experience complete regression of the observed morphological changes and, recovery of LV. In the case of acute myocarditis, on the other hand, due to progressive LV dysfunction the long-term prognosis is worse. In effect, a large proportion of patients with dilated cardiomyopathy are observed in this group of patients.

Immunosuppression, including steroids, in the treatment of myocarditis is still controversial. Some authors question the therapeutic value of this method [8-10]. Others, however, emphasize the potential benefits of this form of treatment [11, 12]. In view of the treatment effect we obtained in our patient, we believe that in the case of fulminant myocarditis with myocardial thickening, LV hypokinesia and conduction abnormalities, the use of high doses of steroids to reduce the degree of interstitial edema may be the treatment of choice and could save the patient's life.

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