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Cardiac findings in children with Crimean-Congo hemorrhagic fever

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Background:

Summary

Crimean-Congo hemorrhagic fever (CCHF) involves the multi-organ systems. The involvement of the heart in adult patients has been described previously. We investigated the electrocardiographic and echocardiographic findings of pediatric patients with CCHF.

Material/Methods:

Patients younger than 16 years of age diagnosed with CCHF were enrolled in the study. The diagnosis of CCHF infection was based upon typical clinical and epidemiological findings and serological tests. All patients underwent a thorough cardiologic evaluation. A standard 12-lead electrocardiography and echocardiography were performed.

Results:

Twenty-three consecutive patients who were hospitalized with diagnosis of CCHF were enrolled in the study (mean age: 12±2 years, 6 female). All electrocardiographic parameters were within normal ranges according to age. Seven patients (30%) had minimal (<1 cm) pericardial effusion. Fifteen (65%) patients had segmental wall motion abnormalities (hypokinesia). A second echocardiography revealed that all wall motion abnormalities had disappeared; the pericardial effusion persisted in only 2 of 7 patients (28%).

Conclusions:

Cardiac involvement appears to be more frequent in children with CCHF disease than in adults, but it is slighter and almost totally reversible; however, the course of the disease in children is milder than it is in adults.

key words:

Crimean-Congo hemorrhagic fever • echocardiography • cardiac involvement

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BACKGROUND

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne disease caused by a Nairovirus of the family Bunyaviridae. The disease involves the multi-organ systems; clinical findings include a rapid progression characterized by hemorrhage, fever, myalgia and liver dysfunction [1]. After first detection of the disease in Turkey in 2002, increasing numbers of patients have been diagnosed with CCHF. By the end of June 2008, a total of 2508 confirmed cases including 133 deaths (5.3%) were reported by the Turkish Ministry of Health [2]. The disease is observed in all age groups (1–92 years). Its prevalence is lower in childhood and infection rarely leads to mortality. The involvement of the heart in adult patients has been described previously in our center [3]. We investigated the electrocardiographic and echocardiographic findings of pediatric patients with CCHF.

MATERIAL AND METHODS

Patients younger than 16 years of age and diagnosed with CCHF were enrolled in the study. The diagnosis of CCHF infection was based upon typical clinical and epidemiological findings and serological tests with ELISA (anti-CCHF IgM and IgG antibodies) or of genomic segments of the CCHF virus by reverse transcription-polymerase chain reaction (RT-PCR) either in the acute and/or convalescent phase of the disease. Serum samples of the patients were sent to the Virology Laboratory of Refik Saydam Hygiene Central Institute, Ankara, Turkey for microbiological testing for CCHF virus infection.

All patients underwent a thorough cardiologic evaluation by a cardiologist after hospitalization. A standard 12-lead electrocardiography was obtained. Following this, within 24 hours of hospitalization, all patients underwent a transthoracic echocardiography examination using an appropriate probe (Vivid 7® GE Medical System, Horten, Norway), performed by an echocardiographer who was blinded to the study. The same echocardiographer measured the ventricular (by modified Simpson's method) and valvular functions, wall motions, and presence of pericardial effusion according to the recommendations of recent guidelines [4]. Echocardiography was repeated on the day of discharge.

All patients were given general supportive therapy including monitoring of vital signs, replacement of fluid and electrolytes and administration of platelets, and fresh frozen plasma and blood transfusion, depending on their hemostasis. Intravenous ribavirin was administered at the dosage recommended by the WHO (30 mg/kg as an initial loading dose, then 15 mg/kg every 6 hours for 4 days, and then 7.5 mg/kg every 8 hours for 6 days). The total duration of treatment was 10 days.

The parametric data are expressed as mean \pm SD and categorical data as percentages. SPSS (version 17) was used to perform statistical procedures.

The local Human Ethics Committee approved the study, and informed consent was obtained from the parents of patients.

RESULTS

Fifty-two consecutive patients who were hospitalized with a tentative diagnosis of CCHF were enrolled in the study. The diagnoses of 23 out of 52 consecutive patients with a tentative diagnosis of CCHF were verified. Seven of 23 patients (30%) had CCHF virus-specific IgM antibodies, 5/23 (22%) had a positive RT-PCR test for CCHF virus, and 11/23 (48%) were positive in both tests during the acute and/or convalescent phase of the disease.

Mean age was 12 ± 2 years, 6 patients were female and 17 were male. Demographic, clinical and laboratory data were shown in Table 1. There was no mortality and all were healed and discharged after a mean of 8 (7–10) days. The most common symptom was myalgia and the most common clinical finding was fever. There were no cardiac symptoms or signs. Thrombocytopenia was observed in all patients. On electrocardiography, all patients were on sinus rhythm, mean heart rate was 94 ± 9 bpm, the mean interval of PR was 84 ± 8 msn, the mean of interval of QRS was 90 ± 8 msn, and the mean of interval of QT was 293 ± 22 msn. All electrocardiographic parameters were within normal ranges according to age. There was no change on T wave or ST segments. Electrocardiographic and echocardiographic findings are summarized in Table 2.

Left ventricular ejection fractions (LVEF) measured by echocardiography were within normal ranges $57 \pm 5\%$ (50–66). No global depression on LV systolic function was seen. Seven patients (30%) had minimal (<1 cm) pericardial effusion. Interestingly, 15 patients (65%) had segmental wall motion abnormalities (hypokinesia); 10 on interventricular septum (IVS), 1 on anterior wall of LV, and 4 on both IVS and anterior wall. Second echocardiography revealed that all wall motion abnormalities had disappeared and pericardial effusion persisted in only 2 of 7 (28%) patients. There was no valvular dysfunction in any patient.

DISCUSSION

This study shows that CCHF in children involves the heart. Pericardial effusion and wall motion abnormalities are the major findings defining the cardiac involvement. No valvular lesions or electrocardiographic abnormalities were detected. It is noteworthy that no patient died and no severe complications were observed. The other interesting finding of the study was that almost all cardiac abnormalities were completely reversible.

According to the Turkish Ministry of Health, CCHF most frequently occurs in the 6th decade (17.1%) of life and at a relatively lower frequency in the 1st (3.5%) and 2nd (12.6%) decades [2]. Two prior studies included a total of 52 pediatric patients; 1 patient (2%) died [5,6]. If added to our 23 patients without mortality, the mortality rate of CCHF in children can be considered as 1/75 (1.3%). Given a >5% mortality rate in adults, the clinical course of CCHF among children seems to be milder than in adults. However, our findings suggest that CCHF also involves the heart in children. Its prognostic value could not be evaluated in this study because no mortality was seen and there is no disease classification such as Swanepoel's for pediatric patients [7].

Table 1. Selected demographic, clinical and laboratory data of 23 patients with Crimean-Congo hemorrhagic fever.

Parameters	n, (%)
Mean age, year (range)	12±2 (9–16)
Sex	
Female	6 (26)
Male	17 (74)
History of tick bite	14 (60)
Median days from symptoms to admission (range)	5 (3–7)
Median days of stay in the hospital (range)	8 (7–10)
Most common symptoms	
Myalgia	20 (87)
Fever	18 (78)
Headache	8 (35)
Physical findings	
Fever*	20 (87)
Tonsillopharyngitis	14 (60)
Diarrhea	8 (35)
Hepatomegaly	7 (30)
Conjunctival hyperemia	5 (22)
Rash	3 (13)
Bleeding	3 (13)
Laboratory features	
Thrombocytopenia**	22 (96)
Leucopenia***	20 (87)
Elevated AST [#]	16 (69)
Elevated ALT ^{##}	16 (69)
Long PTT ^{###}	13 (56)
Death	0 (0.0)

* Arm pit, $\geq 38^{\circ}\text{C}$; ** Thrombocytopenia, platelet count $< 150 \times 10^9$; *** Leukopenia, leukocyte count $< 4 \times 10^3$; [#] Aspartate aminotransferase; ^{##} Alanine aminotransferase; ^{###} Partial prothromboplastin time.

The specific mechanisms underlying the pathogenesis of CCHF infection have not been clearly explained [7–9]. Mononuclear phagocytes, hepatocytes, and endothelial cells are major targets of the CCHF virus [10]. Infection of the endothelium has an important role in CCHF pathogenesis. Endothelial damage contributes to hemostatic failure by stimulating platelet aggregation and degranulation, and, consequently, activation of the intrinsic coagulation cascade [7,8,10]. Myocarditis and cardiomyopathy can be caused by several viruses; hemorrhagic fever viruses can also cause cardiac involvement [11–15]. There is insufficient data about cardiac involvement in CCHF from postmortem studies, and little is known about the effect of CCHF virus on the heart. Endomyocardial biopsy can be fatal due to the low platelet count in CCHF patients. The observation of cardiac congestion and edema in a fatal CCHF case may support cardiac involvement [10]. The wall motion abnormalities of our patients might have been due to involvement of the myocardium by the CCHF virus and/or myocardial endothelial injury [8,9,12,16,17]. The underlying mechanism of the pericardial effusion may be capillary leakage and hemorrhage.

Table 2. Electrocardiographic and Echocardiographic findings.

Parameters	
Electrocardiographic findings	
Heart rate	94±9 bpm
PR interval	84±8 msn
QRS interval	90±8 msn
QT interval	293±22 msn
Echocardiographic findings	
Left ventricular ejection fraction	57±5% (50–66)
Global depression on LV systolic function	0
Pericardial effusion	7 (30%)
Segmental wall motion abnormalities (hypokinesia)	15 (65%)
Interventricular septum (IVS)	10
Anterior wall of LV	1
On both IVS and anterior wall	4
Valvular dysfunction	0

A case report of a patient with CCHF and pleural effusion defined the fluid as being of a hemorrhagic nature [18].

Echocardiographic examination may be helpful in detecting myocardial involvement [12,19,20]. A recent study by Engin et al showed that CCHF virus impairs cardiac functions in adult patients [3]. They investigated 44 patients with CCHF, but did not report the electrocardiographic findings of the patients. On echocardiography, they found that 8 (18%) patients had wall motion abnormality (3 global and 5 anterior wall) and 19 patients (43%) had pericardial effusion. They classified cases as severe and non-severe. Pericardial effusion was more frequently seen in severe cases and those in whom LVEF was more reduced. In that study, the characteristics of patients who died were compared to surviving patients and it was found that pericardial effusion, reduced LVEF and wall motion abnormalities were more frequent in fatal cases. Wall motion abnormality was observed in 65% of our patients and pericardial effusion in 30%. Pericardial effusion was observed in 14% the non-fatal cases by Engin et al. These findings suggest that cardiac involvement is seen more frequently, but more mildly, in children with CCHF than in adults. Engin et al did not report whether the cardiac findings were reversible. In all of our patients except 2, all cardiac abnormalities were resolved at discharge. The higher rate of wall motion abnormality and pericardial effusion (compared to non-fatal cases) in children could not be explained. The possible higher rate of recovery also needs a documentary explanation. For example, although similar data are not available for children, complete recovery is more likely in adults with fulminant compared to acute viral myocarditis [21]. Further studies are needed to determine the pathogenesis of myocardial involvement in CCHF. Electrocardiographies of our patients revealed no abnormality, suggesting that CCHF does not involve the conduction system of children's hearts.

CONCLUSIONS

Cardiac involvement appears to be more frequent in children with CCHF disease than in adults, but it is milder and almost completely reversible. However, the course of the disease in children is milder than it is in adults.

Conflict of interest

None declared.

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