Case Report

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Dilated Cardiomyopathy Several Months after Hemolytic Uremic Syndrome

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Nasrin Esfandiar,[1]
Fariba Alaei,[2*]
Mostafa Sharifian,[1]
Mastaneh Alaei,[3]
Reza Dalirani,[1]
Mohammad Reza Khalilian[2]

1Pediatric Nephrology Research Center, Faculty of Medicine, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2 Pediatric Cardiology Department, Faculty of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3Assistant Professor of Pathology, Blood Transfusion Research Center, High Institute for Research and Education in Transfusion, Tehran, Iran.

***Corresponding Author**
Fariba Alaei MD,
Assistant Professor of Pediatric Cardiology, Faculty of Medicine, Mofid Children's Hospital,
Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: +98 9123362474
E-mail: alaeifariba@yahoo.com

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This is a report of a 44-month-old baby girl diagnosed as a case of atypical hemolytic uremic syndrome (aHUS) presenting with hematuria, periorbital edema, anemia, thrombocytopenia, and hypertension lacking any history of previous bloody diarrhea. She was treated with plasma infusion followed by plasmapheresis and peritoneal dialysis. After two months, she was discharged in remission undergoing periodic plasmapheresis. Four months later, she was visited for fatigue, tachypnea, and palpitation. Cardiac evaluation revealed dilated cardiomyopathy with an ejection fraction of 15-20%. She was hospitalized and treated with inotropes and diuretics; one week later, she was discharged in a favorable condition. After six months follow-up, she showed an acceptable renal and cardiac state. It seems that cardiomyopathy can occur as a late and rare complication of HUS. We recommend cardiac evaluation for all patients with HUS at its presentation and in later follow-ups.

Keywords: Cardiomyopathy; Hemolytic Uremic Syndrome; Child.

Running Title: Dilated Cardiomyopathy in Hemolytic Uremic Syndrome

Introduction

Hemolytic uremic syndrome (HUS) is traditionally diagnosed by the triad of "microangiopathic hemolytic anemia, thrombocytopenia, and acute renal injury" [1]. In recent years, researchers have found new causes as the pathophysiology of atypical HUS (aHUS) [2-5].

An international consensus about the definition, diagnosis and management of aHUS, was made between nephrologists and hematologists in 2015 [6]. Based on this agreement, a diagnosis of aHUS was made after excluding the deficiency of ADAMTS13 (A Disintegrin And Metalloproteinase with a ThromboSpondin type 1 motif, member 13) activity in cases such as thrombotic thrombocytopenia purpura (TTP), shiga-toxin producing Escherichia Coli (STEC-HUS), and coexisting conditions (e.g. transplant, drug related diseases, autoimmune diseases, malignancies, HIV or pneumococcal infections, and cobalamine C deficiency) which are mostly induced as a result of dysregulations in the alternative complement pathway [6-7].

Cardiac involvement can occur as myocarditis and myocardial hemorrhage during the course of HUS due to volume overload, electrolyte abnormalities, or hypertension [8-10]. We report a child with

dilated cardiomyopathy several months after the remission of aHUS.

Case report

A 44-month-old otherwise healthy baby girl presented with cola-colored urine, preorbital edema, hypertension, anemia with a hemoglobin level of 5.8 gr/dl, thrombocytopenia with a platelet count of 43000/mm3, schistocytes in the peripheral blood smear, and increased blood creatinine to 1.53gr/dl.

She was admitted to the nephrology ward with the impression of hemolytic uremic syndrome. Laboratory evaluation showed rather normal range complement factors (C3, CD46, I, B and H). ADAMTS13 activity and anti-ADAMTS antibody showed normal values. Table 1 demonstrates the laboratory findings during her admission.

Treatment was started with plasma infusion followed by plasmapheresis. Peritoneal dialysis was performed due to a significant volume overload and the uremic state. She also received multiple packed cell infusions because of her severe anemia and active hemolysis.

Echocardiographic evaluation showed the normal size of the heart chambers and an ejection fraction of 70% during the course of admission.

Renal function improved and peritoneal dialysis was discontinued after two months. She was discharged on oral nifedipine and plasmapheresis twice weekly.

Two weeks later, she was admitted again with fever and chills because of the catheter site infection. Treatment was started with intravenous antibiotics and the catheter was withdrawn. The treatment was continued with plasma infusion twice weekly which was tapered gradually every three weeks.

Almost 6 months after her first admission, she was visited due to nausea, fatigue, palpitation, and dyspnea. Hypertension, tachycardia, tachypnea, and respiratory distress were also detected on physical examination. There was no detectable anemia or thrombocytopenia. Renal function tests were within normal limits. Chest x-ray showed cardiomegaly and increased pulmonary vascular marking. Electrocardiogram showed sinus tachycardia, left atrial enlargement, and left ventricular hypertrophy. Echocardiogram revealed marked left atrial and ventricular enlargement, reduced global activity with an ejection fraction of 15-20%, and a slightly increased pulmonary arterial pressure.

She was hospitalized in the cardiology ward with a clinical impression of dilated cardiomyopathy. Metabolic tests were within normal limits. Evaluations for Influenza, Enterovirus, and Adenovirus infections were negative. Intravenous milrinone, dobutamine, furosemide, and oral spironolactone were prescribed. The patient's symptoms gradually resolved and she was discharged one week later with oral digoxin, captopril, spironolactone, and carvedilol.

Follow-up evaluations for the next 6 months showed favorable conditions with a reduction in the size of the cardiac chambers; ejection fraction increased to 40-45%, and a normal pulmonary arterial pressure was observed in echocardiography.

Cardiac problems appeared approximately six months after the onset of HUS while hematologic and renal tests were normal during plasma infusion. There was no evidence of volume overload or electrolyte imbalance and the blood pressure was controlled by antihypertensive drugs.

Discussion

Hemolytic uremic syndrome can lead to volume overload and hypertension because of renal impairment. Myocarditis, myocardial hemorrhage, and myocardial infarction are also reported during its course [8-10].

NJ Thomas and colleagues reported 2 cases of cardiac failure requiring extracorporeal membrane oxygenation and suggested considering cardiac involvement during the course of hemolytic uremic syndrome [11].

Walker and his colleagues reported a 2-year-old girl presenting with edema 4 months after the onset of typical hemolytic uremic syndrome who revealed dilated cardiomyopathy with an ejection fraction of 15% on echocardiographic evaluation [12].

J Poulton et al reported 2 children with dilated cardiomyopathy and left ventricular thickening during the course of hemolytic uremic syndrome with improved systolic function but persistent wall thickening after several months [13].

Taylor and colleagues evaluated 35 children with hemolytic uremic syndrome during 1982-3 and reported cardiomyopathy 4 weeks after the onset of HUS in one child.

The left ventricular function improved after 1 year follow-up but did not return to its normal value [14].

Table 1. Laboratory results of the patient based on time of admission

Days after admission	1d	3d	12d	14d	18d	25d	30d
BUN (mg/dl)	102	108	100	101	102	29	23
Cr (mg/dl)	2.5	2.2	3.2	3.1	3.7	1.2	0.8
Na (mEq/L)	134	131			131	135	133
K (mEq/L)	2.6	3.1			3.3	4.7	4
Ca (mg/dl)	9.1	8.6			7.9	9.4	9.1
P (mg/dl)	5	5.5			4.6	4.9	4.6
Uric acid	7.3		8.4			4.7	
Hgb	9.3	8.2	5.8	6.2	9.9		10.1
Plt	147000	110000	45000	28000	30000		121000
LDH	2828	2640	2235	1028	1496	495	310
	↑	↑					
	PI*	**PE** & PD*** **					

*PI=plasma infusion, **PE= Plasma exchange, ***PD= Peritoneal dialysis

Cosami and colleges described a 34-week pregnant woman with thrombotic thrombocytopenic purpura who was treated with plasma exchange and plasma infusion after pregnancy termination. She developed cardiomyopathy with an ejection fraction of 25% on the seventh day of her treatment. Thrombotic thrombocytopenic purpura and CMP improved after treatment [15].

Alexopoulou and his colleges reported a 47-year-old woman with typical hemolytic uremic syndrome 15 days after acute gastroenteritis who developed heart failure 11 days after her admission. Subsequent echocardiographic evaluation showed dilated cardiomyopathy with an ejection fraction of 20%. Treatment was performed by plasma exchange and hemodialysis. The left ventricular function improved months later [16].

Eckart et al reported 3 patients with hemolytic uremic syndrome and cardiac involvement. One showed myocardial infarction, the other showed dilated cardiomyopathy during the course of hemolytic uremic syndrome, and the third showed dilated cardiomyopathy 3 months after treatment, all with good outcomes [8].

Leray et al evaluated a 24-year-old post-partum woman with hemolytic uremic syndrome who developed dilated cardiomyopathy 3 months later. The cardiac outcome was reported favorable thereafter [17].

Our patient's cardiac involvement appeared about 6 months after the onset of hemolytic uremic syndrome with no evidence of renal impairment, electrolyte imbalance, or sign of volume overload at that time. The cardiac function gradually improved within months although it did not become completely normal, similar to other rare case reports of cardiomyopathy occurring after HUS.

Conclusion

Cardiomyopathy in our patient developed several months after admission for HUS and was controlled by appropriate treatment, showing an improved cardiac function during follow-up. We suggest that cardiomyopathy is a late and rare complication of HUS, not a consequence of renal dysfunction.

We recommend careful evaluation of the cardiac function in patients with HUS at the onset of disease and during its follow-up.

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