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Case Report

Dilated cardiomyopathy: A rare and late complication of the hemolytic-uremic syndrome

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ABSTRACT

Hemolytic uremic syndrome (HUS) is a non-exceptional, progressive complication of acute gastroenteritis in children, especially secondary to *Escherichia coli* infection. It is responsible for significant morbidity and significant mortality (10% of deaths) because of acute renal failure which often complicates it. Dilated cardiomyopathy is a rare but critical extra renal manifestation of the HUS. This article highlights the importance of considering the diagnosis of associated cardiomyopathy in the acute phase of HUS and the following months.

A five-year-old boy presented with HUS with acute renal failure requiring peritoneal dialysis for 24 days. No cardiac signs appeared during the acute phase of the disease. After dialysis and normalization of blood pressure, fluid, and electrolyte disturbance, severe dilated cardiomyopathy with cardiac failure appeared three months later without definite etiology.

A review of the literature confirmed the rare and severe nature of cardiac lesions occurring in HUS. Dilated cardiomyopathy is a rare but important extra renal manifestation of the HUS and is best demonstrated by echocardiography. A cardiac manifestation should also be screened for in the acute phase of HUS and several months later.

<**Learning objective:** The main message to draw from this case is that despite the rarity of cardiac complications, routine echocardiographic screening of children with hemolytic uremic syndrome should be performed both in the acute phase and during subsequent follow-up even in the absence of clinical signs because of severe prognosis of this complication, and it is therefore the investigation of choice.>

Introduction

Hemolytic uremic syndrome (HUS) is defined by a triad combining non-autoimmune hemolytic anemia with schistocytes, thrombocytopenia, and acute renal failure. The disease is most commonly triggered by gastroenteritis due to *Escherichia coli*. This condition affects mainly infants and young children, aged from 16 months to 5 years according to many studies [1–3].

HUS is considered as one of the thrombotic micro-angiopathies. Histologically, these affections are characterized by thrombosis of blood vessels (arterioles and capillaries). The thrombotic lesions affect mainly the kidney; however, other organs may also be affected (gut, brain, heart, . . .) and the vascular lesions observed are the same, regardless of the organ.

The extra-renal manifestations of HUS are increasingly recognized and are responsible for significant morbidity and mortality [4]. The occurrence of cardiac complications, especially cardiomyopathy, is a rare manifestation of HUS [5]. The following case establishes that severe dilated cardiomyopathy can be a late complication of HUS.

Case report

A five-year-old boy, without specific pathological history, was admitted to the pediatric department for sudden anemic and

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edemato-ascitic syndrome after seven days of acute gastroenteritis. On clinical examination, we noticed an intense paleness, palpebral edema, edemas, and ecchymotic spots on the lower limbs and abdominal distension. His body temperature was 36.8°; his heart rate was 112 beats/min, his blood pressure was 130/90 mmHg, and he had moderate proteinuria.

The diagnosis of HUS was based on the following criteria: microangiopathic anemia at 4.7 g/dl with the presence of schistocytes (2/1000), thrombocytopenia 79 000/mm^3, and anuric renal failure (plasma creatinine 71.2 mg/l) with hyperkalemia 6.8 mmol/l. Peritoneal dialysis was necessary, it was initiated on the second day and continued for the following 24 days. Table 1 demonstrates the laboratory findings during patient admission.

The histological examination of a renal biopsy specimen revealed lesions compatible with thrombotic microangiopathy.

On the fourth day, he presented generalized tonicoclonic seizures complicated by a state of epilepticus as a result of hypertensive encephalopathy; blood pressure was 160/90 mmHg. Treatment with calcium inhibitor was given intravenously with a favorable neurological outcome. The patient was discharged after improvement in his renal function and was referred to the outpatient clinic for follow-up.

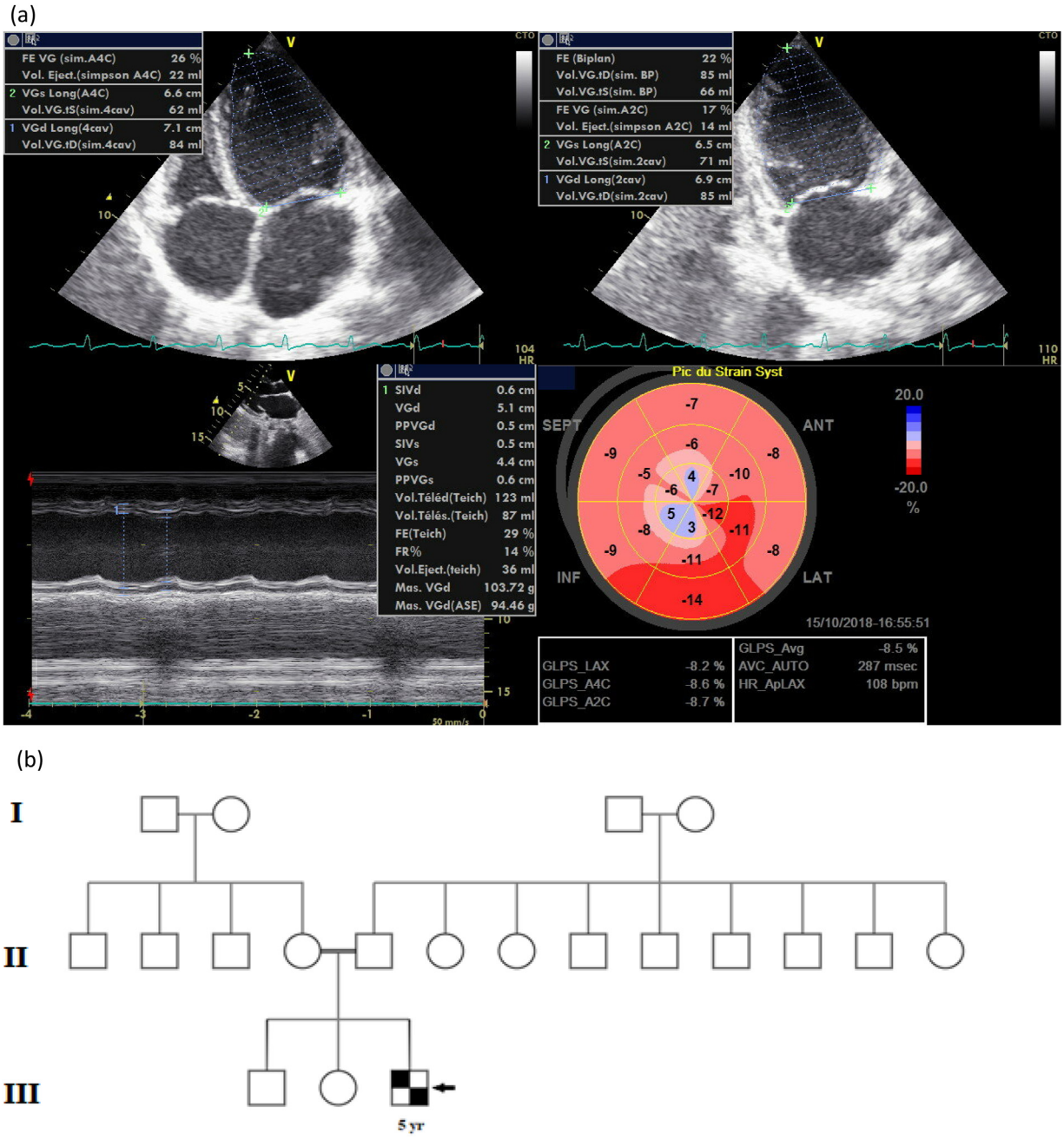

Fig. 1. Familial tree and echocardiographic findings in the index patient: (a) Patient echocardiographic images showing the importance of dilatation and left ventricular dysfunction with alteration of left ventricular ejection fraction measured by Simpson and Teicholz methods, and alteration of global longitudinal strain. (b) The pedigree. Women are represented by circles and males by squares. Consanguineous individuals are indicated by double lines between symbols. Affected individuals are shown with solid symbols. The age of disease onset is indicated.

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

Days after admission Biologic parameters	1 day	3 days	12 days	14 days	18 days	25 days	30 days
Creatinine (mg/l)	71.2	60.4	72.1	50.1	32.7	9.5	5.5
Kalemia (mEq/l)	6.8	5.7	5	5.6	6	5.7	5.1
Calcium (mg/l)	81	96	91	91	106	91	98
Indirect bilirubin (mg/l)	3.9						
Uric acid (mg/l)	122.7						
Haptoglobin (g/l)			<0.10				
Hemoglobin (g/dl)	4.7	9.2	10	7.9	8.1	8.2	10.2
Platelets (/mm^3)	79000	177000		391000	579000	458000	441000
LDH (IU/L)	2042	1292	483	244	427		
CPK (IU/L)	753	132					
	⬆						
Initiation of peritoneal dialysis on the second day							

mg/l: milligram per liter; mEq/l: milliequivalent per liter; g/l: gram per liter; g/dl: gram per deciliter; IU/l: international unit per liter; mm^3: cubic millimeter LDH: lactate dehydrogenase ;CPK: creatine phosphokinase.

Table 2 Previous literature for cardiac involvement complicating hemolytic uremic syndrome.

Author	Patient numbers	Âge	Gender	Time of onset of cardiac involvement after admission	Type of cardiac event	Evolution under treatment
Poulton et al. [6]	2	21 month- old	Girl	56 days	DCM with global functional impairment	At 1-year follow-up the left ventricular diastolic dimension returned to normal but left ventricular function remained abnormal and mural thickness continued to be above the normal range
		8 year- old	Boy	21 days	DCM with considerable reduction in ventricular function	Left ventricular contractility returned to normal after 4 months
Walker et al. [10]	1	2 year- old	Girl	4 months	DCM, LVEF = 14%	Residual thickening of the LV wall, LVEF = 59%; 4 months after the onset of CHF, she was clinically well 22 months later
Eckart et al. [5]	3	21 month- old	Boy	10 days	Myocardial infarction	Favorable evolution with persistence of antero apical residual necrosis
		24 month- old	Girl	4 days	DCM, LVFS = 21%	Favorable evolution 5 days after stopping dialysis LVFS = 42%
		25 month- old	Girl	3 months	DCM, LVFS = 17%	Favorable after evolution 1 month and 1/2 of digitalis treatment
Kim and Kim [11]	1	10 month- old	Boy	10 days	DCM, LVEF = 39%	Favorable after 34 days, normal heart
Esfandiar et al. [12]	1	44 month- old	Girl	6 months later	DCM, LVEF = 15-20%	Favorable after 6 months: reduction in the size of the cardiac chambers, LVEF = 40-45%
Palanca Arias et al. [13]	1	21 month- old	Boy	4 days later	DCM, LVEF = 27% segmental kinetic disorder	Favorable after 15 days: return of normal ventricular function

DCM, dilated cardiomyopathy; LVEF, left ventricular ejection fraction; LVSF, left ventricular fractional shortening; CHF, cardiac heart failure.

Three months later, the child was readmitted to pediatric emergencies for afebrile respiratory distress; he developed shortness of breath, tachycardia, and crackles, his blood pressure was 110/60 mmHg. A chest radiograph revealed marked enlargement of the cardiac silhouette and bilateral interstitial pulmonary markings consistent with pulmonary edema, an electrocardiogram was performed and showed voltage changes consistent with left ventricular hypertrophy.

Echocardiography revealed a severe bi-ventricular enlargement with diffusely diminished contractility and a resting ejection fraction of 22% by Simpson method (Fig. 1a). The rest of the biological assessments showed normal serum calcium, plasma creatinine, and thyroid-stimulating hormone.

The patient was put on a digitalis–diuretic and angiotensin-converting enzyme inhibitor treatment with anticoagulant therapy due to the presence of a spontaneous left intra-ventricular contrast.

An evaluation of his medical pedigree revealed that there is no family history of HUS nor dilated cardiomyopathy. Although he has no history of genetic disease, a thorough family history revealed that he has an uncle with special needs. Further investigation revealed no other family medical issues. This case is referred to as sporadic (Fig. 1b).

Discussion

Cardiac complications have been described during HUS with varying delays, either during or after the onset of the syndrome. It is generally related to volume overload, to hypertension, to electrolyte disorders within the metabolic consequences of acute renal failure, or anemia [5].

Dilated cardiomyopathy may be seen early in the acute phase of the syndrome, or exceptionally after several weeks to a few months

[6,7]. It cannot be induced by the hemodynamic or biological disorders mentioned.

Several hypotheses have been put forward concerning the pathophysiology of this cardiomyopathy:

- 1/lesions of the micro vascularization of the cardiac muscle caused by the presence of micro thrombi. These latter are formed from an activation of platelet aggregation by modification of the vascular endothelium, disruption of the endothelium-platelet relation as well as localized intravascular coagulation [8], provoking a necrosis which is quite extended, associated or not to left ventricular hemorrhagic lesions, which can be confirmed by postmortem histological findings [9].
- 2/infectious myocarditis is also a raised hypothesis. Several pathogenic agents have been detected, including *Shigella dysenteriae* and *E. coli* 0:157 producers of verotoxins and lipopolysaccharidic endotoxin carriers: derived from bacterial walls; after overcoming the intestinal barrier, these verotoxins are thought to be responsible for vascular endothelial lesions [5]. Myocarditis has been described in two children with HUS, which seemed to be induced by coxsackie B infection [6].

Regarding our patient, the temporal relation with the HUS suggests that this disease was a more probable cause. The accountability of dilated cardiomyopathy to one or other of the two hypotheses cannot be tested.

It appears from this report that severe dilated cardiomyopathy may occur several weeks or months after the resolution of the blood film abnormalities.

Table 2 shows different cases of cardiac involvement particularly dilated cardiomyopathy complicating HUS, their time of onset after admission, as well as their evolution.

The main message to draw from this case is that despite the rarity of cardiac complications, routine echocardiographic screening of children with HUS should be performed both in the acute phase and during subsequent follow-up even in the absence of clinical signs because of severe prognosis of this complication, and it is therefore the investigation of choice.

Conflict of interest

Authors declare that they have no conflict of interest.

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