Cardiac tamponade in diarrhoea-positive haemolytic uraemic syndrome

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Abstract
The spectrum of extra-renal involvement secondary to diarrhoeal (D+) haemolytic uraemic syndrome (HUS) includes neurological, gastrointestinal, hepatic, pancreatic and cardiac complications. Among the cardiac complications, myocardial involvement has been more commonly reported with HUS. Literature is scarce on HUS-associated pericardial involvement. We report a HUS-induced significant pericardial effusion that resulted in a cardiac tamponade. We also discuss the diagnostic and therapeutic implications of this complication.

Keywords: HUS; pericardial effusion; troponin-I

Introduction
Among different extra-renal organ manifestations in diarrhoeal (D+) haemolytic uraemic syndrome (HUS), cardiac involvement is an uncommon, but clinically significant complication. Myocardial involvement has been more commonly reported with HUS [1–4]. We report a significant pericardial effusion, leading to cardiac tamponade, in a child with D+ HUS.

Case report
A previously healthy 2-year-old boy presented with a 4-day history of bloody diarrhoea. At presentation, he was unwell, lethargic, afebrile and hypertensive (blood pressure 133/90 mmHg), with no peripheral oedema. The initial abdominal ultrasound revealed diffuse mucosal oedema. Chest X-ray was unremarkable.

Within 24 h of presentation, he developed anuria. His subsequent investigations revealed evidence of haemolysis with a haemoglobin of 70 g/L, lactate dehydrogenase 2522 U/L (normal 176–354 U/L) and haptoglobin 0.31 g/L (0.26–2.26 g/L). His platelets also decreased to 44 × 10^9/L and WBC increased to 67 × 10^9/L. Peripheral blood smear showed fragmented erythrocytes. Serum c-reactive protein (CRP) rose to >380 mg/L (normal <7.5 mg/L). These findings suggested the diagnosis of D+ HUS associated with a significant inflammation. A stool culture confirmed an Escherichia coli O157:H7 infection. The serum lipase of 10 U/L (22–51 U/L), total amylase of 7 U/L (36–128 U/L) and pancreatic amylase of 5 U/L (0–46 U/L) were all normal.

Within 2 days, BUN and serum creatinine rose to 25 mmol/L and 271 µmol/L, respectively. Due to diuretic-unresponsive anuria and rapid BUN and creatinine rise, continuous veno-venous haemodiafiltration (CVVHDF) was instituted. Peritoneal dialysis was withheld because of the panocolitis. Later, CVVHDF was switched to daily intermittent haemodialysis. In view of the significantly elevated WBC and CRP, antibiotic coverage was initially administered, although all cultures subsequently remained negative.

Three days after admission, a protocolized creatinine kinase (CK) and troponin-I increased from initial normal levels to 894 U/L (38–174 U/L) and 0.33 µg/L (<0.08 µg/L), respectively. At this point, his ECG was normal, and the echocardiogram (ECHO) showed an ejection fraction (EF) of 82%, with no evidence of pericardial effusion.

On Day 6 of the hospitalization, he became hypotensive and required inotropic support. A chest X-ray showed a left-sided pleural effusion, pulmonary oedema and an enlarged cardiac silhouette. CK and troponin-I levels also further increased to 1646 U/L and 7.83 µg/L, respectively (Figure 1). Within another 9 h, hypotension worsened, and repeat ECHO showed a significant pericardial effusion, a decreased left ventricular function (EF 56%) and paradoxical movement of right atrium suggesting cardiac tamponade. An immediate pericardiocentesis drained 85 mL of
Fig. 1. Serum troponin-I levels after admission for severe haemolytic uraemic syndrome.

Table 1. Time course of the laboratory profile in the index patient

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>Cardiac tamponade</th>
<th>Resolution of tamponade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/L)</td>
<td>147</td>
<td>76</td>
<td>83</td>
</tr>
<tr>
<td>WBC (10^9/L)</td>
<td>10.9</td>
<td>49.4</td>
<td>19.9</td>
</tr>
<tr>
<td>Platelets (10^9/L)</td>
<td>263</td>
<td>83</td>
<td>380</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>36</td>
<td>281</td>
<td>380</td>
</tr>
<tr>
<td>BUN (mmol/L)</td>
<td>7.2</td>
<td>23.1</td>
<td>19.7</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>139</td>
<td>139</td>
<td>135</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>3.9</td>
<td>3.0</td>
<td>3.5</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>22</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>Troponin-I (µg/L)</td>
<td>&lt;0.03</td>
<td>16.95</td>
<td>0.04</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>1019</td>
<td>1263</td>
<td>235</td>
</tr>
</tbody>
</table>

WBC, white blood cell; LDH, lactate dehydrogenase; BUN, blood urea nitrogen.

over the course of next 3 days, an in situ pericardial drain removed 132 mL of fluid, and CK and troponin-I levels began to fall (Figure 1 and Table 1). With improved blood pressure, inotropes were weaned over 3 days, and the pericardial drain was removed after 4 days. The pericardial fluid analysis revealed an exudative profile (protein 39 g/L, glucose 9.6 mmol/L and nucleated cells 0.480 \times 10^9/L, with 94% neutrophils) and grew no organisms. After removal of the pericardial drain, a repeat ECHO showed no residual pericardial effusion and an improved EF of 80%. Troponin-I levels normalized by Day 26 of the hospitalization.

Discussion

The reported cardiac complications in HUS have been predominantly in the form of myocardial involvement [3–5]. The clinical manifestations from myocardial injury can vary from an asymptomatic decrease in ventricular function [2] and mild ECG changes [4] to fulminant heart failure, significant arrhythmias [6] and death [6,7]. Reports are scarce on pericardial involvement in HUS. Tobias [5] reported a 9-month-old child with an incidental pericardial effusion, followed by spontaneous resolution. In contrast, Birk et al. reported a 6-year-old girl with cardiac tamponade as the terminal event [7]. Although not related to the HUS disease process, Oakes et al. have reported a fatal iatrogenic cardiac tamponade in a HUS patient [8]. In a case series on haematopoietic stem cell transplantation for various malignancies, 10 of 193 children developed HUS and 60% (6 of 10) of the HUS patients developed pericardial effusion [9]. We examined the findings in our patient to establish aetiology of the pericardial effusion. Early initiation of regular dialysis suggested against a uraemic origin of the effusion.

Throughout the course, the patient’s neurological and pancreatic status remained unaffected. A mild transaminitis during the course subsided unremarkably. After an improvement in his pancolitis, the patient was switched to peritoneal dialysis (PD) on Day 21 of the hospitalization. PD was weaned once his renal functions improved. During the follow-up, further complications ensued. Three months after his initial presentation, the patient required a sigmoid colon resection and an end-to-end anastomosis for an intestinal obstruction. Histopathological findings confirmed a radial stricture with extensive haemorrhagic mucosal infarction, granulation tissue and fibrosis. During this episode, he again required dialytic support in the form of haemodialysis. At 4 months’ follow-up, his cystatin C-based glomerular filtration rate was 20/mL/1.73 m², and the urinary microalbumin-to-creatinine ratio was 1402 mg/mmol. He has been on enalapril 0.35 mg/kg/day and losartan 1.56 mg/kg/day for microalbuminuria and blood pressure control.
Imaging did not reveal a major vessel interruption. The culture from the drained pericardial fluid remained sterile. The absence of pericardial effusion on initial echocardiography excluded a pre-existing pericardial pathology. A detailed viral, bacterial, autoimmune and thyroid function screen was also negative. In view of elevated troponin-I levels, a temporal relationship of HUS onset with effusion development, the absence of an alternative aetiology and a recognized potential of cardiac injury from HUS [1–4], the pericardial effusion in our patient appears likely to be secondary to HUS.

The mechanism of pericardial effusion in HUS is not well defined. Our case, and also the two HUS patients described by Tobias and Birk et al., had associated myocardial involvement [5,7]. Traditionally, myocardial injury is believed to be secondary to thrombotic microangiopathy [10,11], although a fatal, histologically proven myocarditis has also been reported in a 13-year-old girl [6]. Also, in the patient reported by Birk et al., massive cardiac tamponade had an associated significant myocarditis without any autopsy evidence of microthrombi [7]. With coexisting myocardial involvement, we speculate that pericardial effusion is more likely a reactive response from the adjoining myocardial inflammation. An exudative nature of pericardial fluid in our patient further supports this hypothesis.

The role of troponin-I as a screening tool to detect cardiac injury in HUS can be debated, as the troponin-I level can also increase from concomitant renal failure. In a small case series, Thayu et al. reported normal troponin-I levels in eight HUS children with unaffected cardiac parameters despite coexisting renal failure, whereas one child with cardiac involvement had an elevated troponin-I level [3]. Moreover, Askiti et al. described a temporal relationship of troponin-I rise with significant myocardial injury in HUS [12]. Our patient also demonstrated a troponin-I rise that preceded the cardiac tamponade and subsided after its resolution, despite persistent renal failure during this period.

In summary, our patient highlights the potential of therapeutically significant pericardial effusion in HUS. The role of troponin-I as a screening tool for cardiac injury in HUS needs evaluation.

Conflict of interest statement. None declared.

References

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