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Myocarditis and haemolytic uraemic syndrome

Ishaq Abu-Arafeh, Elizabeth Gray, George Youngson, Ian Auchterlonie, George Russell

Abstract

A 13 year old girl is reported who presented with haemolytic uraemic syndrome (HUS) due to *Escherichia coli* O157:H7 infection. She died during the acute phase of the illness after an episode of unexplained sudden circulatory collapse. Postmortem examination confirmed the diagnosis of HUS and showed histological evidence of myocarditis manifested by the presence of inflammatory cell infiltration in the myocardium and around the conducting system.

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University of Aberdeen, Department of Child Health
I Abu-Arafeh

Department of Pathology
E Gray

Royal Aberdeen Children's Hospital, Department of Paediatric Surgery
G Youngson

Department of Medical Paediatrics
I Auchterlonie
G Russell

Correspondence to:
Dr Ishaq Abu-Arafeh, Department of Child Health, University of Aberdeen, Foresterhill, Aberdeen AB9 2ZD.

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Haemolytic uraemic syndrome (HUS) is characterised by a triad of haemolytic anaemia, thrombocytopenia, and acute renal failure.[1] The incidence is between 1–2 cases per 100 000 children under the age of 16 years,[2 3] with the majority of affected children being under the age of 5 years.[4] Most of the cases are associated with a diarrhoeal prodromal illness[5] caused by *Escherichia coli* O157:H7 (D^+ HUS).

Extrarenal complications of HUS may involve the gastrointestinal tract,[6] the parotid glands,[7] the pancreas,[8] and the central nervous system.[9] Insulin dependent diabetes mellitus,[10] mucocutaneous lesions,[11] rhabdomyolysis,[12] and dilated cardiomyopathy[13] have also been reported. Unexplained death[14] in the acute phase of the disease and cardiomyopathy[13] are recognised complications of HUS. Myocarditis and cardiomyopathy in association with HUS have been reported in two children[15] with coxsackie B virus infection.

In the following case we report on a child who presented with HUS due to *E coli* O157:H7 infection and developed myocarditis as an added complication. The association of myocarditis with HUS due to *E coli* O157:H7 infection has not been reported previously.

Case report

A previously healthy 13 year old girl was admitted to our hospital with a three day history of abdominal pain, headache, and poor sleep and a one day history of anorexia, vomiting, diarrhoea, and rectal bleeding. On admission she was mildly dehydrated, but afebrile and normotensive. Initial investigations are as shown for day 1 in the table. She was treated with intravenous fluids due to poor oral fluid intake. On her third hospital day she had typical features of HUS with a rise in her serum urea and creatinine concentrations and a drop in serum sodium, haemoglobin, and platelet count (day 3; table). Blood film showed fragmented red blood cells and confirmed thrombocytopenia. Stool cultures grew *E coli* O157:H7. On her fifth hospital day she was started on haemodialysis, through a catheter placed in the right atrium via the right subclavian vein. A chest radiograph confirmed the position of the catheter and a normal cardiopulmonary appearance. Her first session of haemodialysis was uneventful except for transient hypotension treated with an infusion of isotonic saline. Urea and electrolytes before and after dialysis are shown in the table (5a and 5b respectively).

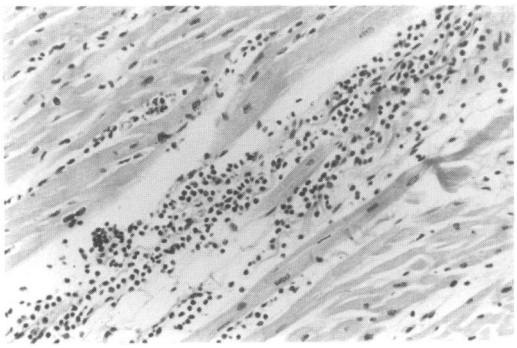
Half an hour after the completion of the haemodialysis she had a bile stained vomit and looked unwell. She was fasted and given an intravenous infusion. An hour later, she had a sudden episode of circulatory collapse, pallor, shallow breathing, bradycardia (50–60/min), and hypotension (60/40 mm Hg). Electrocardiograph (ECG) monitoring confirmed sinus bradycardia and a portable chest radiograph showed normal cardiopulmonary appearance with no change in the position of the central venous catheter. Ventilation was assisted via an Ambu bag and plasma protein solution was infused. She responded within 10 minutes. Arterial blood gases, serum electrolytes, calcium and glucose showed no serious disturbances or metabolic acidosis. An hour later, she had a second similar episode during which the ECG monitor showed bradycardia (30/min) and ectopic ventricular beats. She was resuscitated by intubation, mechanical ventilation, external cardiac massage, intravenous plasma, isotonic saline, bicarbonate, atropine, and adrenaline. Also she was given intracardiac adrenaline and external direct current cardiac shock twice. She died after 35 minutes of active resuscitation.

Postmortem examination showed typical changes of HUS in the bowel (haemorrhagic colitis and focal mucosal ulceration) and the kidneys (intravascular microangiopathic thrombosis). The brain, lungs, liver, spleen, pancreas, and thymus were all normal. Gross examination of the heart showed no cardiomegaly or dilatation, but the tip of the

Results of renal function tests and blood counts during hospital days

Day	*Sodium (mmol/l)*	*Potassium (mmol/l)*	*Urea (mmol/l)*	*Creatinine (μmol/l)*	*Haemoglobin (g/l)*	*Platelet count ($\times 10^9$/l)*
1	137	4·7	7·1	59	156	354
3	122	3·3	18·3	191	111	46
5a	120	3·2	28·6	451	92	59
5b	123	4·1	22·5	395	–	–
5c	125	3·3	20·4	329	–	–
Normal values	135–144	3·4–4·9	<6·5	<95	115–135	150–400

5a: Before dialysis, 5b: after dialysis, 5c: after first episode of collapse.



Focal inflammatory cell infiltration of the myocardium with myocytolysis of muscle fibres (haematoxylin and eosin ×250).

central venous catheter was displaced into the wall of the right ventricle. Histological examination of the myocardium, including serial sections taken from the region of the conducting tissues, showed an inflammatory cell infiltration mainly of monocytes and lymphocytes, but with occasional eosinophils and myeloid cells (figure). In the absence of frozen tissue a full profile of lymphocyte subsets was not possible. The majority of the lymphocytes carried T cell antigens, the remainders were negative for both T and B cell markers. Myocytolysis was also detectable. No positive labelling for coxsackievirus was seen by in situ hybridisation using a digoxygenin labelled coxsackie B2 derived probe.

Discussion

Sudden death is a rare complication during the acute phase of HUS, but when it occurs, it is usually due to metabolic disturbances such as hyperkalaemia or congestive cardiac failure secondary to hypertension or fluid overload. Unexplained sudden death during the acute phase of HUS is also a rare recognised complication.[14]

Clinical evidence of myocarditis in association with HUS has been reported in the past, secondary to coxsackie B virus infection,[15] in two children, but that was long before the association between HUS and *E coli* O157:H7 was established. Dilated cardiomyopathy,[13] possibly as a result of myocarditis, has also been reported in two other children secondary to HUS several weeks after the onset of the disease.

In our patient the two episodes of collapse are clinically suggestive of acute cardiac rhythm disorder especially in the absence of any significant metabolic disturbance involving serum electrolytes and the absence of any evidence of heart failure or hypoxia to account for the sudden deterioration. The presentation with bradycardia, hypotension, and ventricular arrhythmia in the second episode are consistent with the postmortem histological findings of myocarditis manifested by active non-specific inflammatory process within the myocardium and in close proximity to the conducting system.

The catheter displacement is believed to have occurred during the second episode of collapse due to active cardiopulmonary resuscitation, as chest radiography after the first episode of collapse showed no change in the position of the tip of the central venous catheter from the time of insertion and also it continued to be in good working order throughout haemodialysis and resuscitation. The displaced catheter did not cause the inflammatory process in the myocardium which was present in both cardiac chambers and probably of several days duration.

In view of the histological evidence of myocarditis and in the absence of evidence of another infective cause of the cardiac inflammatory process, we conclude that myocarditis occurred secondary to HUS due to *E coli* O157:H7. The mode of death was an arrhythmia triggered by the inflammatory process. Although the association between HUS and myocarditis has been suspected in the past, this is the first report to provide the histological evidence.

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