The haemolytic uraemic syndrome and anaesthesia

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The Haemolytic Uraemic Syndrome is the most important cause of renal failure in infancy and childhood. The disease usually consists of a typical triad of renal failure, haemolytic anaemia, thrombocytopenia. It is, however, a multisystem disorder which may also involve the liver as well as cardiovascular, pulmonary and central nervous systems.

We present a case of a female child with Haemolytic Uraemic Syndrome who presented for placement of an arteriovenous shunt to facilitate haemodialysis. The clinical presentation and management of the Haemolytic Uraemic Syndrome is discussed. Anaesthetic management of patients with the Haemolytic Uraemic Syndrome is discussed and recommendations are made.

The Haemolytic Uraemic Syndrome (HUS) is now recognized as the most important cause of acute renal failure in infancy and childhood.[1] Anaesthetists may become involved with patients suffering from HUS for various reasons, including the provision of anaesthesia for surgical procedures such as the creation of AV shunts and fistulae, or as part of the management team during the patient's stay in an Intensive Care Unit. It is therefore important to understand the disease process and its ramifications with respect to anaesthetic practice.

The features of HUS include the prodromal illness, usually gastroenteritis but possibly an upper respiratory infection, followed by the sudden onset of the typical triad of renal failure, haemolytic anaemia and thrombocytopenia.[2] Many viral agents have been implicated in association with HUS, especially Asian influenzae and enteroviruses, particularly the coxsackie groups. Bacterial agents such as Shigella and Salmonella, as well as the Rickettsia-like organism microtatobiote have also been recovered from affected patients.[1] HUS has also occurred in women using oral contraceptives or other oestrogen containing agents.

Key words

ANAESTHESIA: paediatric; BLOOD: haemolysis, anaemia; KIDNEY: uraemia, Haemolytic Uraemic Syndrome.

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Case report

A 28-month-old female was transferred to our hospital with a one week history of vomiting and bloody diarrhoea, accompanied by abdominal cramps. The diarrhoea had begun to resolve with symptomatic treatment when she was noted to be pale and to have progressive oliguria. The child's past history was unremarkable.

Initial examination revealed an alert, frightened 12.4 kg child. Blood pressure was 108 mmHg systolic, heart rate 132 beats/min, respiratory rate 28/min and temperature 36° C. Cardiorespiratory examination was unremarkable but the child was noted to have a distended abdomen and rectal prolapse. There were no petechiae. A chest *x*-ray revealed a slightly enlarged heart with a possible pericardial effusion and a small left sided pleural effusion. Abdominal ultrasound examination revealed the presence of ascites and an ECG was interpreted as normal. Laboratory values are as shown in the Table.

The child was taken to the Operating Room for placement of an arterio-venous shunt to facilitate haemodialysis. On arrival she was lethargic and non-communicative. No premedication had been given. After giving atropine 0.1 mg IV, a rapid-sequence induction, with pre-oxygenation and cricoid pressure, was utilized. Thiopentone 30 mg IV followed by succinylcholine 20 mg IV were administered. A 4.5 mm ID endotracheal tube was placed and anaesthesia was maintained with N20/02 (50:50) and isoflurane.

Three mg of d-tubocurarine was administered shortly after induction to facilitate controlled ventilation. Monitors employed were a pulse oximeter, neuromuscular blockade monitor, end-tidal CO_2 monitor, axillary temperature, precordial stethoscope, ECG and non-invasive blood pressure. Axillary temperature remained 36.2–36.0° C throughout the procedure. A right radial arterial line was established percutaneously and a nasogastric tube was inserted and suctioned for a moderate amount of bilious material. The surgery was uneventful and at the end of the procedure residual neuromuscular block was antagonized by the administration of atropine 0.24 mg and

neostigmine 0.6 mg IV. The patient was extubated when awake, in the Operating Room and transferred to the Intensive Care Unit. Total IV fluids during the two-hour-and-20-minute procedure were 30 ml of Normosol with 5 per cent dextrose in water and 5 ml of 5 per cent dextrose in water with 0.5 N saline.

The child did well in the postoperative period, undergoing haemodialysis and transfusion of fresh frozen plasma. High output renal failure developed but was self-limited and an episode of sepsis was successfully managed with the administration of gentamycin, ampicillin and bacitracin.

At the time of discharge the haemoglobin had risen to $84\,g\cdot L^{-1}$, platelets had risen to $397 \times 10^9\cdot L^{-1}$ and urea and creatinine levels had stabilized at $14\,mmol\cdot L^{-1}$ and $41\,\mu mol\cdot L^{-1}$ respectively.

Discussion

HUS usually appears in a previously well child between the ages of one and two years. However, cases have been reported in infants less than six months old and in teenage children and adults.[3] The most common prodrome is an acute infectious haemorrhagic gastroenteritis.[4] This may last approximately one week and apparent recovery will begin, only to be followed shortly thereafter by the onset of anaemia and renal failure. HUS does not involve only kidneys, erythrocytes, and platelets, but is a multisystem disease involving the gut, liver, heart and central nervous system. Mild cases include anaemia, thrombocytopaenia and azotaemia and have an uncomplicated course. Severe cases include anuria lasting for more than 24 hours and, frequently, seizures and hypertension.[2] Myocarditis and congestive heart failure due to circulatory overload have been described,[1] and severe systemic hypertension may also be present.

TABLE Laboratory results

Parameter	*Value*	*Normal values*
Hgb	$78\,g\cdot L^{-1}$	
Hct	0.223	
WBC	$1.4 \times 10^9\cdot L^{-1}$	
Platelets	$29 \times 10^9\cdot L^{-1}$	
PT	24 sec	(10–12)
PTT	24 sec	(25–36)
Thrombin clotting time	10 sec	(7–11)
Fibrin split products	$64–128\,\mu g\cdot dl^{-1}$	<10
Fibrinogen	117 mg%	(200–400)
Glucose	$10.6\,mmol\cdot L^{-1}$	(3.3–5.6)
Sodium	$126\,mmol\cdot L^{-1}$	(135–145)
Potassium	$4.8\,mmol\cdot L^{-1}$	(3.6–5.2)
Urea	$25.9\,mmol\cdot L^{-1}$	(2–7)
Creatinine	$400\,\mu mol\cdot L^{-1}$	(35–130)
Calcium (total)	$2.7\,mmol\cdot L^{-1}$	(2.1–2.7)
Aspartate transaminase	$69\,u\cdot L^{-1}$	(9–29)
Alanine transaminase	$53\,u\cdot L^{-1}$	(3–25)
Lactate dehydrogenase	$1515\,u\cdot L^{-1}$	(111–269)
Total bilirubin	$26\,\mu mol\cdot L^{-1}$	(0–17)
Indirect bilirubin	$21\,\mu mol\cdot L^{-1}$	(0–10)
Total proteins	$45\,g\cdot L^{-1}$	(62–78)
Albumin	$26\,g\cdot L^{-1}$	(36–49)

Neurologic and complications include drowsiness, seizures, hemiparesis and coma.[2] Severe pulmonary insufficiency requiring mechanical ventilation and oxygenation can occur. This appears to be unrelated to volume overload, pulmonary oedema or congestive heart failure, and does not respond to dialysis.[5]

Hepatosplenomegaly occurs in many cases and there is also biochemical evidence of hepatitis in some individuals.[6] Acute renal failure is associated with well known pathophysiologic changes, including acid base and electrolyte disturbances.

Haemolysis occurs rapidly, with haemoglobin levels falling to as low as $4\,g\cdot L^{-1}$. Thrombocytopenia is present in almost every patient, and lasts 7–14 days. Peripheral destruction is the most likely aetiology. Of the disturbances in the coagulation profile, thrombocytopenia is the most common, but a wide variety of abnormalities may be found. These include functional platelet defects, prolonged bleeding times and prothrombin times. Factors II, VII, and X have been found to be moderately decreased. However, other changes occur suggesting a hypercoagulable state.[7] These include increased factor VIII and a shortened PTT.

The most consistent renal finding is a glomerular capillary endothelial cell injury.[8] Clinically, patients have proteinuria, haematuria and oliguria which may progress to anuria.

Severe infections are common during the acute phase. Peritonitis may develop, caused by pseudomonas, candida or staphylococcus. Meningitis and osteomyelitis may occur.[4]

Treatment and recovery

Blood transfusion, control of electrolyte and fluid imbalances, control of blood pressure and early institution of dialysis lead to considerable success in the acute phase.[2] Transfusion with red cell suspensions may be necessary. Transfusion is best accomplished during dialysis, should this become necessary. Early and repeated peritoneal haemodialysis has reduced the mortality in the acute phase.

Treatment of neurologic problems is symptomatic. Many anticonvulsant drugs are useful, and their dosage must be modified accordingly. Diazepam and clonazepam are the drugs of choice. Severe cerebral involvement may lead to the need for assisted or controlled ventilation.[4]

The haemolytic crisis seldom lasts more than two

weeks, but anaemia continues for months. Haemoglobin levels may return to normal after approximately three months.[4] Thrombocytopenia and coagulation disorders are not evident after the acute stage. Renal function may recover completely or the child may require permanent dialysis. Neurologic abnormalities may persist and range from mild defects, including hearing loss, to evidence of complete decortication.[4]

Anaesthetic management

The anaesthetic implications of HUS are numerous. As described in our case report, the anaesthetist may be confronted with a somnolent, profoundly anaemic paediatric patient with a coagulation disorder who is in urgent need of dialysis. In association with problems more specific to the paediatric age group such as temperature regulation and active autonomic reflexes, one may also encounter a patient in congestive heart failure with or without associated myocarditis, haemorrhagic gastritis and associated "full stomach" problems and altered hepatic function. Where it might seem that the placement of the peripheral AV shunts would be best accomplished using local infiltrative anaesthesia, IV or regional block techniques, we feel that none of these is an acceptable choice in this instance, in light of the young age of most of these patients, their mental status and the potential or actual presence of coagulation disorders. Therefore, a general anaesthetic was chosen as the optimal technique.

In the immediate preoperative period our patient was lethargic and non-communicative and therefore no sedative pre-medication was administered. There was no clinical evidence of cardiorespiratory distress and her mental status was felt to be secondary to progressive renal failure and uraemia. Preoperative chest *x*-ray revealed evidence of a small pleural effusion and a small pericardial effusion. Some myocardial depression and volume overload was probably present. Evidence of a sub-clinical coagulopathy was provided by noting elevation of fibrin split products as well as a somewhat reduced fibrinogen level despite normal coagulation times. Elevation of serum bilirubin was probably secondary to ongoing haemolysis; however, hepatic dysfunction was also present.

The presence of clinical or laboratory evidence of hepatitis and hepatic dysfunction (as demonstrated in our patient) suggests that the clinician should avoid anaesthetic agents which may be associated with hepatotoxicity and every effort should be made to maintain adequate oxygenation and perfusion pressures. If a potent inhalational agent is desired, isoflurane appears to be the best choice, due to its reduced myocardial depressant activity, of importance in a patient with fluid overload and possible myocardial dysfunction.

A rapid-sequence induction with pre-oxygenation and cricoid pressure was employed due to the likelihood of a "full stomach." A reduced dose of thiopentone was employed since it has been shown that less than 50 per cent of a dose of thiopentone is protein bound in patients with hepatic disease and decreased serum albumin.[9] Normally 65–75 per cent of thiopentone is protein bound.

Our utilization of muscle relaxants requires comment. Succinylcholine, in our opinion, remains the best choice for obtaining a rapid and profound muscle relaxation required during a rapid sequence induction and we had no hesitation in using it in this instance. For prolonged neuromuscular blockade d-tubocurarine was chosen, due to familiarity with its clinical effects. A markedly reduced dose was employed, due to anticipation of a prolonged duration of action in the presence of renal failure. Indeed this was the case. Relaxation was evident, both clinically and during train-of-four stimulation with a peripheral nerve stimulator, for the entire case. Although train-of-four fade was evident two hours following administration of 3 mg of d-tubocurarine, antagonism was readily obtained using a standard dose of neostigmine. Muscle relaxants, if used at all, should be carefully titrated to effect and those agents dependent almost entirely on renal excretion should be avoided. Atracurium would appear to be an ideal choice in the circumstance since termination of action is independent of changes in hepatic or renal function.

The problems of profound anaemia need not be elaborated upon here. Disturbances in acid base status and electrolyte changes such as the hyponatremia carry with them the potential for significant problems in the perioperative period.

It should be noted that patients with the HUS may present for more than one anaesthetic during their hospital stay and further problems may become evident. These include concerns regarding a patient undergoing haemodialysis as well as the possibility of occult or clinically obvious sepsis.

In summary, we suggest the following steps in the anaesthetic management of a patient suffering from haemolytic uraemic syndrome.

1 Thorough preoperative evaluation with specific focus on possible cardiorespiratory dysfunction, the severity of renal failure and the presence of a coagulopathy.
2 Attempted correction of acid–base, electrolyte and coagulation disorders prior to surgery. Consultation with appropriate specialty services should be obtained when necessary.
3 Little, if any, premedication is usually required and should be individualized.
4 General anaesthesia should be the technique of choice in all but the most cooperative patients, with "full

stomach" precautions including awake intubation or rapid sequence induction and awake extubation.

5 Anaesthesia should be maintained with an inhalational-relaxant technique. Isoflurane and atracurium are the agents of choice.

6 There should be continual intraoperative monitoring of acid–base and electrolyte status.

7 If repeat anaesthetics are necessary the problems outlined above, as well as the altered physiology associated with ongoing dialysis, should be kept in mind.

The safe anaesthetic management of a patient with the HUS depends upon a thorough knowledge of the disease and its implications.

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Résumé

Le syndrome hémolytique urémique est la cause la plus importante d'insuffisance rénale chez le nourisson et l'enfant. La maladie habituellement est composée d'une triade classique d'insuffisance rénale, anémie hémolytique et thrombocytopénie. Elle est cependant une maladie multisystémique qui peut impliquer aussi le foie ainsi que le système cardiovasculaire pulmonaire et le système nerveux central.

On présente le cas d'un enfant atteint du syndrome se présentant pour la création d'un shunt artérioveineux pour fin d'hémodialyse. La présentation ainsi que la conduite à faire en face de ce syndrome est discutée. La conduite anesthésique du patient atteint de ce syndrome est discutée et des recommandations sont faites.