Typical and atypical haemolytic uraemic syndrome: a brief case comparison report for nurses

Yogarani Jeyakumar & Paul N Bennett

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Abstract

Background: Haemolytic uraemic syndrome (HUS) is one of the main causes of acute kidney injury in children. It is a multifaceted disease, characterised by microangiopathic haemolytic anaemia and thrombocytopaenia. It can often affect multiple organ systems, including the central nervous and renal systems.

Objectives: Two case studies are presented that highlight the differences between typical and atypical HUS. Treatment and prognosis differ, depending on the type of HUS. These complex case studies will demonstrate the strategic medical and nursing management required.

Key messages: Typical HUS starts with severe symptoms but it is the atypical form that has long-term consequences. It is important to ascertain the correct diagnosis early and initiate appropriate therapy accordingly. Multidisciplinary care, including nurses, is involved in the management of care for these children and can support and educate their families to assist them through this debilitating disease. New treatments such as Eculizimab hold new promise in the treatment of atypical HUS.

Keywords

Haemolytic uraemic syndrome, plasma exchange, peritoneal dialysis, nursing.

Introduction

Haemolytic uraemic syndrome (HUS) is a clinical syndrome defined by the simultaneous occurrence of microangiopathic haemolytic anaemia, thrombocytopenia and acute kidney injury (Ariceta *et al.*, 2009). HUS is the most common cause of acute kidney injury (AKI) in children resulting from an abnormal, premature destruction of red blood cells (Andreoli, 2002). The care of children with HUS is complex, requiring a multidisciplinary approach. The purpose of this paper is to use two case studies to demonstrate the strategic medical and nursing management required.

In HUS, damaged red blood cells infiltrate the kidney's filtering system, resulting in life-threatening renal failure (Besbas *et al.*, 2006). The initiating factor is often due to an injury to the glomerular endothelium or an imbalance of platelet aggregation factors, resulting in fibrin deposits and clumping of platelets within the capillaries. As this process continues, the capillaries occlude, causing a reduction of glomerular filtration rate leading to AKI. Red blood cells travelling through the plugged capillaries are damaged, causing haemolytic anaemia. Platelets are consumed in this clumping process and are damaged in the blood vessels, causing a reduction in platelets. (Mayer, Leibowitz, & Kurosawa, 2012).

HUS is classified into two main categories: those occurring after a diarrhoeal illness (typical) and the other in the absence of a diarrhoeal illness (atypical) (Boyer & Niaudet, 2011). Typical HUS is more common and accounts for approximately 75% of presentations (Besbas *et al.*, 2006). The most common causative strain is *Escherichia coli* (*E. Coli*) that produces a Shiga toxin with bloody diarrhoea (Paton & Paton, 1998). Sources of contamination include under-cooked meat, unpasteurised milk, juice or contaminated water (Proulx, Seidman, & Karpman, 2001). Other bacterial diarrhoeal agents that can cause HUS include Shigella and Salmonella (DuPont, 2009). Typical HUS is also referred to as diarrhoea-associated HUS, typical HUS or Shiga toxin-associated HUS and has a more favourable prognosis (Geerdink *et al.*, 2012).

Atypical HUS is a rare disorder distinguished by the absence of diarrhoea, with an estimated prevalence of 7 per one million children in Europe (Boyer & Niaudet, 2011). Atypical HUS is also known as non-diarrhoeal associated HUS, D–ve HUS, sporadic or familial HUS and can occur without an initial gastrointestinal symptom (Rahman *et al.*, 2012). Outcomes are poorer in atypical HUS as 50% of presentations can progress to chronic kidney disease (CKD) stage 5 (Loirat, Noris, & Fremeaux-Bacchi, 2008). This familial form is associated with

Author details: Ms Yogarani Jeyakumar RN, MN. Nurse Unit Manager, Paediatric Renal Unit, Monash Children's, Monash Health, VIC, Australia. Professor Paul Bennett RN, Renal Cert. MHSM, PhD. Professor, Deakin University – Western Health Partnership, Melbourne, VIC, Australia

Correspondence to: Ms Yogarani Jeyakumar, Paediatric Renal Unit, Monash Children's, Monash Health, 246 Clayton Road, Clayton VIC 3168 Email: Yogarani.Jeyakumar@southernhealth.org.au

genetic abnormalities of the complement regulatory proteins and is frequently dormant and becomes activated with a viral flu episode. Children with typical HUS have a history of diarrhoea with malaena with or without vomiting, followed by sudden onset of symptoms of irritability and pallor. Other symptoms include restlessness, oliguria leading to oedema and macroscopic haematuria. Children presenting with this form of HUS have a good outcome of complete recovery (Lowe & Werner, 2005). For children with atypical HUS, the onset is sudden and prodromal features often include an upper respiratory tract infection (URTI), fever, vomiting, hypertension, haematuria and proteinuria (Mehrazma, Hooman, & Otukesh, 2011). The following two cases illustrate the cases of an atypical and typical presentation.

Case report 1 — Atypical haemolytic uraemic syndrome

J, a five-year-old boy who was previously well, with no family history of renal disease, presented with microangiopathic haemolytic anaemia, thrombocytopenia and AKI (non-dialysis requiring) and was diagnosed with atypical HUS. One week prior to this admission to hospital, J had a viral URTI, with a moist cough and sore throat, for which he was treated with amoxycillin by his general practitioner. Following his episode of URTI, he had a five-day history of vomiting, transient rash and two days of brown urine. At presentation, his initial pathology revealed anaemia, thrombocytopenia, impaired renal function and complement dysregulation. Lactate Dehydrogenase (LDH) and haptoglobin, which are markers of haemolysis, were performed to assess the disease process. Both the LDH and haptoglobin were in the abnormal range, suggesting haemolysis. The low C3 levels indicated systemic complement alternative pathway activation 5 (Loirat, Noris, & Fremeaux-Bacchi, 2008).

J was treated with plasma exchange within 48 hours of presentation, initially daily for five days, followed by five treatments per week for two weeks and then three sessions per week for two weeks, according to the 2009 adult guidelines (Ariceta *et al.*, 2009). After five weeks of the treatment, serum creatinine had reduced, platelet count increased and there was no evidence of haemolysis.

Our unit arranged testing for the whole family through a Paris-based laboratory at the Hospital European Georges-Pompidou (Fremeaux-Bacchi *et al.*, 2013), who have significant expertise in researching atypical HUS and the various genetic manifestations that can cause it. This revealed that J was the only member of his family to have Factor H antibodies, which has been shown to be an association with improved outcomes and mortality

The frequency of plasma exchange was reduced once the Factor H antibodies were identified. Immunosuppression with prednisolone and azathioprine was introduced, with a plan for J to remain on immunosuppressive therapy for a minimum of 12 months. After six months, his parameters had normalised, his HB was 127 g/l with normal platelets, LDH, haptoglobin and no red cell fragmentation. His kidney function, urine and blood pressure all normalised. He remained Cushingoid for 12 months as a result of his prednisolone use.

Case report 2 — Typical haemolytic uraemic syndrome

K, a four-year-old girl, presented to our hospital with a four-day history of bloody diarrhoea, decreased urine output, increasing oedema and hypertension. She had been progressively reviewed at a regional hospital, where her pathology results from day one through to day four had deteriorated. Her creatinine had increased from 37 to 315 mmol/l, haemoglobin (Hb) decreased from 144 to 107 g/l and platelets had decreased from 440 mg/l to 86 mg/l.

On admission, her presentation was clinically and biochemically consistent with typical HUS. Serology from stool was not available. She was dehydrated, hypertensive, anaemic and suffering AKI. Her initial pathology revealed anaemia, thrombocytopaenia and impaired renal function. Her Hb continued to decrease to 64 g/l, for which she received a blood transfusion. Her urea rose to 23.3 mmol/l and creatinine peaked at 572 mmol/l. Her LDH increased to 3016 units/l (normal range is 100–200) and her haptoglobin decreased to 0.19 mg/dL (normal range 0.36–1.95 mg/dL).

A Tenckhoff catheter was inserted and peritoneal dialysis (PD) was commenced one day after admission, following lengthy conversations with her parents. PD was commenced using small volumes of 10 ml/kg and gradually increased to 30 ml/kg. The day after she commenced PD she remained hypertensive and anuric. She then suffered a seizure on the ward, a chest x-ray (CXR) revealed left lower lobe pneumonia and she was then transferred from the nephrology ward to the intensive care unit, where she was intubated and received haemofiltration for two days. She required a jugular central venous dialysis catheter (CVDC) which occluded after just one day. The following day, another internal jugular CVDC was surgically inserted and she was ordered three daily treatments of plasma exchange at 35 ml/kg per exchange with fresh frozen plasma (FFP). Due to access problems with the CVDC, she only received two treatments of plasma exchanges.

Fifteen days following admission, her urine output improved and she was extubated and transferred back to the nephrology ward. Her hypertension was initially treated with one stat dose of intravenous (IV) hydralazine and then regular oral propranolol three times a day and a weekly dose of nifedipine. K was treated with phenytoin three times a day for her seizures and this was ceased after two weeks. She had a magnetic resonance image (MRI) of her brain, which was normal. Anaemia was diagnosed on admission for which 200 ml of packed red blood cells was transfused. Nutritional support was managed by the paediatric renal dietician according to the patient's requirements. Pediasure 700 ml/day was given via a nasogastric tube for four weeks. K made a slow but full recovery. Fortunately, her renal function improved and she did not require ongoing renal replacement therapy (RRT).

Discussion

Although typical HUS starts with severe symptoms, it is the atypical form that has long-term consequences. These symptoms are of particular concern as they cause immediate and severe deterioration. Early and correct treatment, as described in the two cases above, is pivotal to the child's outcome, so it is important to identify the differences in presentation and manage typical HUS and atypical HUS appropriately as treatment and prognosis is always dependent on the type of HUS (Besbas *et al.*, 2006).

HUS is a syndrome that has seen several important advances in relation to therapeutic approaches. Case reports have suggested that Eculizimab (SOLIRIS), a humanised monoclonal antibody that blocks complement activity targeted against C5, is effective in the treatment of atypical HUS (Mache *et al.*, 2009; Nürnberger *et al.*, 2009). Data from these case reports have demonstrated the effectiveness of Eculizimab in inhibiting complement activation in atypical HUS. Current clinical trials investigating the role of Eculizimab therapy in the treatment of patients with atypical HUS due to complement dysregulation will provide more insight into the effectiveness of this treatment (Lapeyraque, Frémeaux-Bacchi, & Robitaille, 2011). Results of trials may provide a potential future treatment for atypical HUS in children, which may alleviate the need for ongoing plasma exchange.

Implications for practice

The multidisciplinary team caring for these children typically includes paediatric nephrologists, paediatric nephrology nurses, paediatric surgeons, a paediatric dietician, a paediatric social worker and a general paediatrician. Every member of the multidisciplinary team has a major role in caring for these children. It certainly is a challenging experience for everyone in the team. These complex case studies have demonstrated the strategic medical, nursing, pharmacy, dietetic and psychosocial management of the children and their families.

In particular, nephrology and general nurses are pivotal in the management of care for these children. Nurses provide 24-hour health care and can support and educate families to assist them through this debilitating disease. A greater understanding of the disease trajectory, vascular access requirements, subtle differences between types of HUS and the potential outcomes for each child can assist the family to better understand the challenges faced.

Conclusion

Health professionals are required to quickly ascertain the correct HUS diagnosis early and initiate appropriate therapy accordingly. As there are no internationally agreed paediatric guidelines, further research is required to assist paediatric health care professionals to provide the best evidence-based care for children with HUS.

References

Andreoli, S. P. (2002). Acute renal failure. *Current Opinion in Pediatrics, 14*(2), 183–188.

Ariceta, G., Besbas, N., Johnson, S., Karpman, D., Landau, D., Licht, C., ... Zimmerhackl, L. B. (2009). Guideline for the investigation and initial therapy of diarrhea-negative hemolytic uremic syndrome. *Pediatric Nephrology, 24*(4), 687–696. DOI: 10.1007/s00467-008-0964-1

Besbas, N., Karpman, D., Landau, D., Loirat, C., Proesmans, W., Remuzzi, G., ... Zimmerhackl, L. B. (2006). A classification of hemolytic uremic syndrome and thrombotic thrombocytopenic purpura and related disorders. *Kidney International, 70*(3), 423–431. DOI: 5001581 [pii] 10.1038/sj.ki.5001581

Boyer, O., & Niaudet, P. (2011). Hemolytic uremic syndrome: new developments in pathogenesis and treatment. *International Journal of Nephrology, 2011*, 908407

DuPont, H. L. (2009). Bacterial Diarrhea. *New England Journal of Medicine, 361*(16), 1560–1569. DOI:10.1056/NEJMcp0904162

Fremeaux-Bacchi, V., Fakhouri, F., Garnier, A., Bienaimé, F., Dragon-Durey, M.-A., Ngo, S., ... Loirat, C. (2013). Genetics and Outcome of Atypical Hemolytic Uremic Syndrome: A Nationwide French Series Comparing Children and Adults. *Clinical Journal of the American Society of Nephrology, 8*(4), 554-56

Geerdink, L. M., Westra, D., van Wijk, J. A., Dorresteijn, E. M., Lilien, M. R., Davin, J. C., ... van de Kar, N. C. (2012). Atypical hemolytic uremic syndrome in children: complement mutations and clinical characteristics. *Pediatric Nephrology, 27*(8), 1283–1291. DOI: 10.1007/s00467-012-2131-y

Lapeyraque, A.-L., Frémeaux-Bacchi, V., & Robitaille, P. (2011). Efficacy of eculizumab in a patient with factor-H-associated atypical hemolytic uremic syndrome. *Pediatric Nephrology, 26*(4), 621–624. DOI: 10.1007/s00467-010-1719-3

Loirat, C., Noris, M., & Fremeaux-Bacchi, V. (2008). Complement and the atypical hemolytic uremic syndrome in children. *Pediatric Nephrology, 23*(11), 1957–1972. DOI: 10.1007/s00467-008-0872-4

Lowe, E. J., & Werner, E. J. (2005). Thrombotic thrombocytopenic purpura and hemolytic uremic syndrome in children and adolescents. *Seminars in Thrombosis & Hemostasis 31*(6), 717–730. DOI: 10.1055/s-2005-925478

Mache, C. J., Acham-Roschitz, B., Frémeaux-Bacchi, V., Kirschfink, M., Zipfel, P. F., Roedl, S., ... Ring, E. (2009). Complement Inhibitor Eculizumab in Atypical Hemolytic Uremic Syndrome. *Clinical Journal of the American Society of Nephrology, 4*(8), 1312–1316. DOI: 10.2215/cjn.01090209

Mayer, C. L., Leibowitz, C. S., Kurosawa, S., & Stearns-Kurosawa, D. J. (2012). Shiga toxins and the pathophysiology of hemolytic uremic syndrome in humans and animals. *Toxins (Basel), 4*(11), 1261–1287

Mehrazma, M., Hooman, N., & Otukesh, H. (2011). Prognostic value of renal pathological findings in children with atypical hemolytic uremic syndrome. *Iranian Journal of Kidney Diseases, 5*(6), 380–385. DOI: 454/339 [pii]

Nürnberger, J., Philipp, T., Witzke, O., Saez, A. O., Vester, U., Baba, H. A., ... Kirschfink, M. (2009). Eculizumab for Atypical Hemolytic–Uremic Syndrome. *New England Journal of Medicine, 360*(5), 542–544. DOI:10.1056/NEJMc0808527

Paton, J. C., & Paton, A. W. (1998). Pathogenesis and Diagnosis of Shiga Toxin-Producing Escherichia coli Infections. *Clinical Microbiology Reviews, 11*(3), 450–479.

Proulx, F., Seidman, E. G., & Karpman, D. (2001). Pathogenesis of Shiga Toxin-Associated Hemolytic Uremic Syndrome. *Pediatric Research, 50*(2), 163–171.

Rahman, R. C., Cobenas, C. J., Drut, R., Amoreo, O. R., Ruscasso, J. D., Spizzirri, A. P., ... Gatti, M. C. (2012). Hemorrhagic colitis in postdiarrheal hemolytic uremic syndrome: retrospective analysis of 54 children. *Pediatric Nephrology, 27*(2), 229–233. DOI: 10.1007/s00467-011-1973-z