Case Report On Haemolytic Uraemic Syndrome And Cardiovascular Complication

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A 66 year old Caucasian female presented with haemolytic uraemic syndrome (HUS) following a prodrome of diarrhoea. During the course of her illness, she developed acute heart failure secondary to myocardial ischaemia. Cardiovascular complications associated with HUS involving children have been reported in the literature. The mortality of adult patients with acute heart failure is significantly higher even with the initiation of therapeutic plasma exchange.

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Introduction

Haemolytic Uraemic Syndrome (HUS) is a rare condition characterised by clinical and laboratory evidence of microangiopathic haemolytic anaemia on peripheral blood film with acute renal failure or thrombocytopenia. HUS is the most common cause of acute renal failure in children and increasingly recognised in adults. HUS often follows a prodromal infectious diseases usually bloody diarrhoea in 90% of the cases. The most common enteropathic associated diarrhoea implicated in HUS is a toxin produced by Escherichia coli serotype 0157:H7.[1] HUS may be associated with malignancies, medications, autoimmune disorders, sporadically or in families.[2] This condition is associated with multi system complications and the mortality rate during an acute phase is three to five percents and and undetermined number of adult patients developing long term complications.[3] Treatment for HUS remains conservative although therapeutic plasma exchange has been used without proven clinical evidence in large randomised clinical trials.

Case Report

A 66 year old female estate agent was referred to the Nephrology department with a 6 days history of non-bloody diarrhoea one week after returning from two weeks holidays in Cuba. Physical examination revealed severe pallor with bilateral legs oedema. Cardiovascular, abdominal, respiratory and neurological examinations were normal. Laboratory investigations were as follows: haemoglobin (Hb) 7.4g/dL, pack cell volume <30%, platelet count 60 x 10^9/L, total leucocyte count 19 x 10^9/L. Peripheral blood film showed polychromasia with gross fragmented red blood cells. There was reticulocytosis 319x10^9/L, LDH 1406 iu/L and haptoglobin <0.3. In addition she has acute renal failure with creatinine of 400µmol/l (baseline creatinine 83µmol/l in 2004) and metabolic acidosis (bicarbonate = 12mmol/l). The renal immunology screen was normal for ANCA, ANA, C3, C4, immunoglobulin and monoclonal band for myeloma. Coagulation profile and direct Coomb's test were normal. The faecal cultures were negative for salmonella, shigella, campylobacter species, E-coli 0157 and clostridium difficle toxin.

Her clinical condition and renal function deteriorated despite intravenous fluid replacement.

A diagnosis of Haemolytic Uraemic Syndrome was established. She was commenced on plasma exchange 3.5litre exchange of 50ml/kg with Octaplas treated fresh frozen plasma replacement and three units of blood transfusions. After five days of plasma exchange, there was improvement of her renal function (creatinine =319) with urine output of 850ml/24hours and platelet counts remained stable despite laboratory evidence of active ongoing haemolysis. She received a total of fourteen plasma exchanges with six units of blood transfusion. Her renal function improved (Creatinine 193) with urine output of 120mls per hour. On the 15th days of commencing plasma exchange, she developed pre-cordial crushing chest pain with dyspnoea. Electrocardiogram showed T-waves inversion in the anterior-lateral leads. She remained normotensive but has clinical and radiological evidence of acute pulmonary oedema. Her troponin I was raised at 7.6 µg/l and echocardiogram showed dilated cardiomyopathy with significant biventricular systolic dysfunction (left ventricular ejection fraction ≤ 40%). She received treatment for acute cardiac failure with aspirin, heparin, ACE-inhibitor, intravenous frusemide

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250mg once daily and fluid restriction of 1 litre/24h for her acute pulmonary oedema. She remained stable from cardiac and renal functions (creatinine=100_mol/l) with good urine output of 2 litres/24h.

Her symptoms resolved without further intervention. One week after discharge from the nephrology ward, the repeat echocardiogram revealed normal left ventricular size with mildly dilated right ventricle. Left ventricular systolic function is only mildly impaired with normal right ventricular function.

Discussion

Our patient has all the hallmarks of Haemolytic Uraemic Syndrome (HUS) defined by Coomb's negative microangiopathic haemolytic anaemia with evidence of gross haemolysis on peripheral blood film, LDH >1.5 times the upper limit, thrombocytopenia and acute renal failure without an apparent cause. HUS can however occur following non-O157:H7 VTEC infections and those infections are almost certainly under-detected. There have been reports of HUS after non-O157:H7 VTEC infections where the clinical course has been less severe.[3]

The pathophysiology of haemolytic uraemic syndrome remained unclear but recent medical research has postulated several hypotheses to enable us to understand the underlying pathophysiology and complications of HUS. Haemolytic uraemic syndrome is a pro-thrombotic disorder characterised by microvascular thrombi and swollen endothelial cells secondary to endothelial injury.[4,5,6] In the course of HUS, there are prothrombotic coagulation abnormalities identified in patients who subsequently developed haemolytic uraemic syndrome. These patients had significantly increased level of plasma concentrations of prothrombin fragment, tissue plasminogen activator (t-PA) antigen, t-PA plasminogen-activator inhibitor type 1 (PAI-1) complex and D-dimer before and during the course of the disease.[4,5] The increase in these prothrombin factors promotes intravascular thrombin formation. However, unlike classical disseminated intravascular coagulation with consumptive coagulopathy, coagulation abnormalities in haemolytic uraemic syndrome have normal prothrombin time and activated partial thromboplastin time with normal fibrinogen but markedly raised D-dimers. The increase in D-dimers in HUS patients signifies excess fibrin in the vascular seen also seen in patients with deep vein thrombosis and pulmonary embolism. However, in patients with HUS, the excessive large amount of intravascular fibrin signifies the increased rate of plasminogen activation for thrombin formation thus inducing endothelial injury.[4,5] In HUS, the microvascular thrombi appear to be fibrin predominate with few platelets. This distinct entity for HUS was examined histologically in post mortam patients who had active HUS.[6]

Cardiovascular complications have been reported in children in the literature up to 10% of children with HUS during the 1993 epidemic of E-coli 0157:H7 in the Western USA and congestive cardiac failure is more common in adults with HUS.[7,8] The increase in the concentrations of troponin I during HUS in our case with clinical description of cardiac chest pain and radiological of pulmonary oedema should be attributed to cardiac ischaemia.[7,8] This patient has significantly raised troponin I and echocardiographic evidence of acute cardiac failure based on the Framingham Study Criteria (left ventricular ejection fraction ≤ 40% or an acute reduction ≥15%). It has been postulated that the mechanisms leading to acute heart failure in patients with HUS are partly due to microinfarctions caused by diffuse fibrin thrombi and impaired fibrinolysis in the cardiac microcirculation.[8] Current treatment is aimed at cardiovascular supportive measures, anticoagulation with aspirin and heparin with the use of angiotensin-converting enzyme inhibitor and treating pulmonary oedema with diuretics and haemofiltration while awaiting organ recovery. Clinicians should be aware of this potentially life-threatening cardiac involvement in patients with haemolytic ureamic syndrome as the mortality of patients with acute heart failure was significantly higher than that for patients without heart failure (38% vs 17%) even with initiation of therapeutic plasma exchange.[8]

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