Sir,

Extreme hypernatraemia is rare in adults. Due to the fact that rapid correction of hypernatraemia may result in neurological complications, a gradual reduction of sodium concentration is generally advised. However, it is difficult in patients with extreme hypernatraemia, severe metabolic acidosis and renal failure. We describe a patient with extreme hypernatraemia (serum Na\(^+\) 202 mEq/l), severe metabolic acidosis (HCO\(_3\)\(^-\) 7.6 mEq/l) and renal failure who was successfully treated with continuous venovenous haemofiltration (CVVH) with a portion of commercial CVVH replacement fluid and additional sodium bicarbonate. We believe this is the first case report of such a novel treatment and may apply to other patients who suffer from extreme hypernatraemia, severe metabolic acidosis and renal failure.

A 69-year-old woman presented at our emergency room with progressive deterioration of consciousness for 4 days. Her past history included hypertension, chronic renal failure with serum creatinine of 3.7 mg/dl 1 month before admission, ischaemic stroke with left hemiplegia, and status post-craniotherapy after stroke. Her consciousness was clear after ischaemic stroke with left hemiplegia, and status post-craniotomy after stroke. Her consciousness was clear after the cerebral vascular accident but she depended on others for daily activity. She ate less and became more and more lethargic over the 4 days before admission.

On arrival at the emergency department, her conscious status was E2M4V2. Vital signs revealed a blood pressure of 137/71 mmHg, heart rate of 62 b.p.m. and respiratory rate of 18 breaths/min. The initial laboratory data showed blood urea nitrogen (BUN) 114.7 mg/dl; creatinine 8.69 mg/dl; serum sodium 202.4 mEq/l; glucose 91 mg/dl; potassium 4.6 mEq/l; and blood osmolality 455 mosml/kg. Under the impression of acute exacerbation of chronic renal failure, extreme hypernatraemia, 5% dextrose water was given at a rate of 120 ml/h. The serum sodium level dropped unexpectedly from 190.5 to 174.8 mEq/l in 6 h after starting CVVH. As her sodium reduction rate was above the target of 1–2 mEq/l/h, the sodium concentration of the replacement fluid was then adjusted by adding 7% NaHCO\(_3\). We added 1.45 ml of 7% NaHCO\(_3\) to 1 liter of commercial replacement fluid mixture for each 1 mEq/l elevation of sodium concentration. By this method, the replacement fluid was adjusted every 6 h with a 3 mEq/l targeted reduction of sodium concentration. As the serum sodium concentration was 174.8 mEq/l, the replacement fluid sodium concentration was set at 172 mEq/l. The serum sodium concentration then decreased gradually to 151.8 mEq/l by 54 h after commencement of CVVH. CVVH was changed to intermittent haemodialysis afterwards.

The patient’s consciousness improved to E4M5-6Vt on the 6th day after admission. She was extubated on the 8th hospitalization day and was transferred to a general ward for further care.

Hypernatraemia is a common problem associated with high mortality and morbidity [1]. Managing extreme hypernatraemia is challenging. Though well-controlled studies to ascertain the optimal treatment of chronic hypernatraemia do not exist, gradual correction of hypernatraemia with a rate of no more than 1–2 mEq/l/h was suggested [1,2]. Free water hydration is the most commonly used method for hypernatraemia. However, fluid overload might develop in patients with heart failure and renal failure, as occurred in our patient. Since conventional haemodialysis and peritoneal dialysis cannot fulfill the requirement for gradual reduction of serum sodium concentration, we chose continuous renal replacement therapy. Moos et al. reported the first case of hypernatraemia (serum Na\(^+\) 189 mEq/l) corrected by continuous arteriovenous haemofiltration in 1990 [3]. The patient died of diffuse alveolar damage and cardiogenic shock. Jen-Jar Lin et al. used continuous venovenous haemodialysis to correct hypernatraemia (serum Na\(^+\) 180 mEq/l), hyperglycaemia and other electrolyte imbalance in a 12-year-old female patient [4]. They used custom-made dialysate with adjustment of dialysate electrolyte every 6 h and controlled the serum sodium level in 4 days. The patient survived without neurological sequelae after the critical episode. Custom-made dialysate and replacement fluid were not available in our hospital. So we chose CVVH, which needs only replacement fluid but no dialysate. The adjustment of sodium concentration was by adding 3% NaCl to the replacement fluid. The concentration of other electrolytes did not change much with 7% NaHCO\(_3\). For example, the elevated [Na\(^+\)] from 142.3 to 190 mEq/l requires 69.2 ml of 7% NaHCO\(_3\) in 1 liter of fluid. The reduction of [K\(^+\)], [Ca\(^+\)], [Mg\(^{2+}\)] and [Cl\(^-\)] is only 6.4%, which is insignificant clinically.

Further fluid and electrolyte management. The serum sodium concentration increased to 190.5 mEq/l after infusion of 7% NaHCO\(_3\) for metabolic acidosis.

For the purpose of gradual correction of the sodium concentration, CVVH was the chosen mode of dialysis for this patient. We used an AK 10 blood pump (Gambro, Lund, Sweden) and a Hemofilter 6S membrane (Gambro, Hechingen, Germany) through an 12,12-Fr dual lumen catheter (Arrow, Erding, Germany), which was placed in a femoral vein. The blood flow rate was 200 ml/min during the dialysis procedure. Commercial CVVH replacement fluid solution A and CVVH replacement fluid solution B (Taiwan Biotech Co., Ltd., Taoyung, Taiwan) were mixed with a flow rate of 800 ml/h. The sodium concentration of the mixture is 142.3 mEq/l. The net ultrafiltration rate was adjusted according to her volume status. The serum sodium level dropped unexpectedly from 190.5 to 174.8 mEq/l in 6 h after starting CVVH. As her sodium reduction rate was above the target of 1–2 mEq/l/h, the sodium concentration of the replacement fluid was then adjusted by adding 7% NaHCO\(_3\). We added 1.45 ml of 7% NaHCO\(_3\) to 1 liter of commercial replacement fluid mixture for each 1 mEq/l elevation of sodium concentration. By this method, the replacement fluid was adjusted every 6 h with a 3 mEq/l targeted reduction of sodium concentration. As the serum sodium concentration was 174.8 mEq/l, the replacement fluid sodium concentration was set at 172 mEq/l. The serum sodium concentration then decreased gradually to 151.8 mEq/l by 54 h after commencement of CVVH. CVVH was changed to intermittent haemodialysis afterwards. The patient’s consciousness improved to E4M5-6Vt on the 6th day after admission. She was extubated on the 8th hospitalization day and was transferred to a general ward for further care.

Hypernatraemia is a common problem associated with high mortality and morbidity [1]. Managing extreme hypernatraemia is challenging. Though well-controlled studies to ascertain the optimal treatment of chronic hypernatraemia do not exist, gradual correction of hypernatraemia with a rate of no more than 1–2 mEq/l/h was suggested [1,2]. Free water hydration is the most commonly used method for hypernatraemia. However, fluid overload might develop in patients with heart failure and renal failure, as occurred in our patient. Since conventional haemodialysis and peritoneal dialysis cannot fulfill the requirement for gradual reduction of serum sodium concentration, we chose continuous renal replacement therapy. Moos et al. reported the first case of hypernatraemia (serum Na\(^+\) 189 mEq/l) corrected by continuous arteriovenous haemofiltration in 1990 [3]. The patient died of diffuse alveolar damage and cardiogenic shock. Jen-Jar Lin et al. used continuous venovenous haemodialysis to correct hypernatraemia (serum Na\(^+\) 180 mEq/l), hyperglycaemia and other electrolyte imbalance in a 12-year-old female patient [4]. They used custom-made dialysate with adjustment of dialysate electrolyte every 6 h and controlled the serum sodium level in 4 days. The patient survived without neurological sequelae after the critical episode. Custom-made dialysate and replacement fluid were not available in our hospital. So we chose CVVH, which needs only replacement fluid but no dialysate. The adjustment of sodium concentration was by adding 3% NaCl to the replacement fluid. The concentration of other electrolytes did not change much with 7% NaHCO\(_3\). For example, the elevated [Na\(^+\)] from 142.3 to 190 mEq/l requires 69.2 ml of 7% NaHCO\(_3\) in 1 liter of fluid. The reduction of [K\(^+\)], [Ca\(^+\)], [Mg\(^{2+}\)] and [Cl\(^-\)] is only 6.4%, which is insignificant clinically.
We present an unusual case with extreme hypernatraemia, severe metabolic acidosis and renal failure treated with CVVH and a special formula consisted of addition of 7% NaHCO₃ to commercial solution. The patient’s conscious status returned to her baseline status, suggesting a successful outcome of our treatment.

Conflict of interest statement. None declared.

1Division of Nephrology Ya-Fei Yang
Department of Internal Medicine Vin-cent Wu
China Medical University Hospital Chiu-Ching Huang
2Division of Nephrology
Department of Internal Medicine
National Taiwan University Hospital
Taiwan
Email: cch@www.cmuh.org.tw


doi:10.1093/ndt/gfh958

Advance Access publication 5 July 2005

Development of Graves’ disease during cyclosporin treatment for severe Henoch–Schönlein nephritis

Sir,

A 10-year-old girl presented with palpable purpura and abdominal pain. Routine laboratory tests were normal, but urinalysis revealed microscopic haematuria [5–10 red blood cells/highpower field (RBCs/HPF)]. A skin biopsy demonstrated leukocytoclastic vasculitis. A diagnosis of Henoch–Schönlein purpura (HSP) was made, and oral prednisolone was started, with rapid improvement. One month later, she was admitted to our hospital for macroscopic haematuria and heavy proteinuria (2.3 g/day). She had no significant past medical history but her mother had Graves’ disease. Her blood pressure was 100/60 mmHg and the physical examination was unremarkable. Laboratory findings showed a serum albumin of 4.0 g/dl, and C3 and serum IgA levels were normal. A renal biopsy revealed diffuse mesangial proliferative glomerulonephritis with 12% crescents and deposits of IgA, C3 and IgG. She was commenced on prednisolone (48 mg once qod) and cyclosporin (75 mg twice daily). Cyclosporin was given for 10 months with the desired level of 100–200 ng/ml, and prednisolone was tapered during cyclosporin therapy. Her proteinuria resolved (0.05 g/day) within 2 months of cyclosporin therapy, but microscopic haematuria persisted at 2 year follow-up.

At 6 months after onset of the HSP, she developed a goitre and mild exophthalmos. A clinical diagnosis of Graves’ disease was given and she was immediately started on propranolol at a dose of 20 mg twice daily (1 mg/kg/day). Subsequently her thyroid-stimulating hormone level was found to be 0.04 μU/ml (normal 0.34–3.5 μU/ml), free thyroxine 2.6 ng/dl (normal 0.73–1.95 ng/dl) and triiodothyronine 270.27 ng/dl (normal 80–220 ng/dl). Thyroglobulin and microsomal antibodies were raised at 427.91 μU/ml (negative: <60 μU/ml) and 1086.31 μU/ml (negative: <60 μU/ml), respectively. She was commenced on propylthiouracil at a dose of 100 mg twice daily (5 mg/kg/day) and thyroid function became normal over 7 months.

There have been some reports that HSP is associated with autoimmune thyroiditis or transient hyperthyroidism [1]. However, the association between HSP and Graves’ disease has not been reported previously in children. Graves’ disease is a multifactorial disease which is caused by genetic susceptibility and environmental triggers. It has been suggested that HLA-DR3 and cytotoxic T-lymphocyte antigen 4 increase the risk for Graves’ disease in both the sporadic and familial forms [2]. However, additional genes which contribute to the aggregation of Graves’ disease within families have not been identified yet.

Renal involvement in thyroid diseases is rare, but immune complex glomerulonephritis such as membranous nephropathy has been reported in association with Graves’ disease [3]. Activation of the complement cascade can take place in ~40% of patients with Graves’ disease, and IgG, IgA and C3 immune complex depositions in the extrathyroidal tissues are possible as the manifestations of Graves’ disease [4]. In the present case, immunofluorescence demonstrated mesangial depositions of IgG, IgA and C3 consistent with an immune complex glomerulonephritis, suggesting common immunological mechanisms may be implicated between HSP nephritis and Graves’ disease.

Both prednisolone and cyclosporin are used as the treatment of Graves’ ophthalmopathy by inhibiting T-cell function. In contrast, these drugs can cause the development of Graves’ disease in a transplant recipient by abnormal modulation of the immune system [5]. Although there have been no reports describing the development of Graves’ disease during immunosuppressive treatment in patients with other autoimmune diseases, a familial tendency to Graves’ disease in our patient may affect the subsequent expression of Graves’ disease.

In conclusion, the sequential occurrence of HSP and Graves’ disease in our patient suggests a possible immunological link between two diseases, and a familial predisposition and immunosuppression by cyclosporin may have been triggering factors in the development of Graves’ disease. Clinicians should pay more attention to the use of immunosuppressants in susceptible patients with Graves’ disease.

Conflict of interest statement. None declared.

1Department of Paediatrics Jae Il Shin
2Department of Pathology Jee Min Park
The Institute of Kidney Disease Jae Seung Lee
Yonsei University College of Medicine Duk Hee Kim
Seoul Hyeon Joo Jeong
Korea
Email: jsyonse@yumc.yonsei.ac.kr