

# Dialysis disequilibrium syndrome: A preventable fatal acute complication

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## SUMMARY

Dialysis disequilibrium syndrome (DDS) is a neurological disorder with varying severity that is postulated to be associated with cerebral oedema. We described a case of DDS resulting in irreversible brain injury and death following acute haemodialysis. A 13-year-old male with no past medical history and weighing 30kg, presented to hospital with severe urosepsis complicated by acute kidney injury (Creatinine 1422mmol/L; Urea 74.2mmol/L, Potassium 6.3mmol/L, Sodium 137mmol/L) and severe metabolic acidosis (pH 6.99, HCO<sub>3</sub> 1.7mmol/L). Chest radiograph was normal. Elective intubation was done for respiratory distress. Acute haemodialysis performed due to refractory metabolic acidosis. Following haemodialysis, he became hypotensive which required inotropes. His Riker's score was low with absence of brainstem reflexes after withholding sedation. CT Brain showed generalised cerebral oedema consistent with global hypoxic changes involving the brainstem. The symptoms of DDS are caused by water movement into the brain causing cerebral oedema. Two theories have been proposed: reverse osmotic shift induced by urea removal and a fall in cerebral intracellular pH. Prevention is the key to the management of DDS. It is important to identify high risk patients and haemodialysis with reduced dialysis efficacy and gradual urea reduction is recommended. Patients who are vulnerable to DDS should be monitored closely. Low efficiency haemodialysis is recommended. Acute peritoneal dialysis might be an alternative option, but further studies are needed.

## KEY WORDS:

*acute kidney injury; haemodialysis; dialysis disequilibrium syndrome; cerebral oedema*

## INTRODUCTION

Dialysis disequilibrium syndrome (DDS) is defined as a clinical syndrome of neurologic deterioration that seen in patients who undergo haemodialysis (HD). It is more likely to occur in patients during or immediately after their first treatment. We report a case of DDS induced cerebral oedema that resulted in irreversible brain injury and death following HD. Further, we reviewed the relevant literature of the association of DDS and HD.

## CASE REPORT

A 13-year-old male with no past medical illness, presented with progressive dyspnoea and vomiting which preceded by

fever and urinary tract infection symptoms for three weeks. On examination, he was alert but severely dehydrated and tachypnea. His temperature was 35.5°C, blood pressure 121/83mmHg; pulse rate 118bpm, with SpO<sub>2</sub> 100%. Systemic examinations were unremarkable.

Blood investigations showed acidemia and hypocapnia with pH 6.994, pCO<sub>2</sub> 10mmHg, HCO<sub>3</sub> 1.5mmol/L. Renal profile showed Creatinine 1422mmol/L, Urea 74.2mmol/L, Potassium 6.3mmol/L and Sodium 137mmol/L with increased anion gap of 28.8mmol/L and serum Osmolarity was 356.1mOsm/L. He had a raised white cell count of 22.7(x10<sup>3</sup>/ μL). Urine microscopic examination showed pyuria. Hence, patient was treated as severe urosepsis. Unfortunately, he was not responding to aggressive resuscitation. His arterial blood gas showed refractory severe metabolic acidosis with pH of 6.897, pCO<sub>2</sub> 36.2mmHg, HCO<sub>3</sub> 7.0mmol/L. Chest radiograph was unremarkable. Patient was electively intubated and admitted to Intensive Care Unit. Haemodialysis was performed with Qb of 200ml/min, Qd 500ml/min without ultrafiltration for two hours via femoral catheter in ICU. Low Flux Dialyser (Fresenius F8HPS polysuphone, surface area of 1.8 m<sup>2</sup>, Kuf as 18ml/hr x mmHg) and RenaHD-3A dialysate were used. Prior to dialysis, patient was normotensive and good Riker's score of -1. However, patient became hypotensive which required inotropic supports and dropped in Riker's score to -3 drastically immediately after dialysis. Neurological assessment showed bilateral non-reactive and dilated pupils. His brainstem reflexes were absent. Repeated investigations revealed the pH 7.354, pCO<sub>2</sub> 22.4mmHg and HCO<sub>3</sub> 12.4mmol/L; Creatinine 451mmol/L, Urea 23.2mmol/L, Potassium 2.4mmol/L, Sodium 143mmol/L with high urea reduction rate of 54.95% and serum Osmolarity of 313.9mOsm/L. CT brain showed generalised cerebral oedema with obliterated basal cisterns, loss of grey-white differentiation and global hypoxic changes included brainstem (Figure 1). Diagnosis of brain death was declared and family members were informed. His condition deteriorated further and succumbed. No autopsy was done due to family members' refusal.

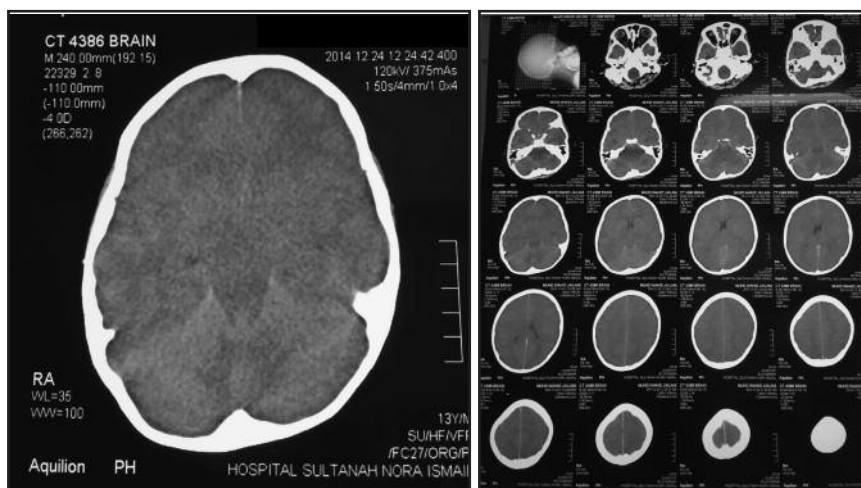
## DISCUSSION

Dialysis Disequilibrium Syndrome (DDS) is more likely to occur in patients during or immediately after their first treatment, however there were also two case reports of DDS happened after few haemodialysis sessions for more than one week.<sup>1</sup> So far, we have not found relevant literature in Malaysia.

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**Fig. 1:** Generalised cerebral oedema with obliterated basal cisterns, loss of grey-white differentiation and global hypoxic changes included brainstem.

The predisposing factors for DDS in this case are small body size (paediatric population), severe uraemia, severe metabolic acidosis, sepsis (widespread immune activation which may alter blood-brain barrier permeability and predispose to cerebral oedema)<sup>2</sup> and first time dialysis user. The presenting symptoms vary from mild form: nausea and headache to severe form: coma and rarely death, as seen in this patient. However, several mechanisms causing cerebral oedema have been debated for years. The first mechanism is ‘Reverse urea effect’, which was suggested by Kennedy *et al.*<sup>3</sup> in 1962. The syndrome was attributed to the delayed exit of urea from the brain post rapid dialysis-induced decline in blood urea level, thus creating an osmotic gradient that favoured the shift of water into the brain from the blood which generates the cerebral oedema as what had happened in this patient. The second mechanism is “Cerebrospinal fluid acidosis” theory.<sup>4</sup> During haemodialysis, existing systemic metabolic acidosis is promptly corrected, but the corresponding CSF pH level remains low. Hence, plasma CO<sub>2</sub> diffuses rapidly to the CSF, increasing its pCO<sub>2</sub> or to the production of an unidentified organic acid by the brain during dialysis. The CSF and brain acidosis somehow brings about oedema of the brain. However, studies lending support to this particular theory are few. In this patient, the pCO<sub>2</sub> was reduced instead of raised, from 36.2 mmHg to 22.4 mmHg. Lastly is the “Idiogenic osmoles” theory. There are organic osmoles produced by the brain to counteract various hyperosmolar states so that brain shrinkage does not occur. However, there is no increase in idiogenic osmoles has been observed during experimental hemodialysis.<sup>5</sup> In the nutshell, the “reverse urea effect” theory appears the most promising.

Prevention is the core management for DDS traditionally and despite the absence of evidence-based guidelines, the conventional aim is a gradual clearance of urea. However, in a district hospital which without nephrologist and limited resources, the low flux conventional haemodialysis is the only option for this patient. In a paediatric patient with

advanced uraemia, an initial urea clearance of 3 ml/min per kg, which is calculated from the specifications of the chosen dialyser and the blood flow attainable is suggested to avoid disequilibrium. The acute peritoneal dialysis might not be a good modality in reverting this life threatening severe metabolic acidosis with high catabolic state.

In hospital with nephrology service, the simplest way to do this is to perform hemofiltration on the patient instead of haemodialysis. This method of treatment relies on the convective removal of solute from the patient in place of diffusive removal. Thus, the osmolalities of the body fluid compartments will not change as rapidly as they do during standard haemodialysis. The other way is to use of a smaller, less efficient dialyser or lower the targeted blood flow rates by use of sustained low-efficiency dialysis (SLED) but prolonged the treatment period, or initiation of continuous renal replacement therapy (CRRT) with more gradual clearance of urea.

In conclusion, patients who are vulnerable to DDS should be monitored closely with low efficiency renal replacement therapy and nephrology consultation. Acute peritoneal dialysis might be an alternative option, but further studies are needed.

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