CASE REPORT

Severe hyponatraemia associated with pre-eclampsia

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SUMMARY

Pre-eclampsia is a multisystem disorder with incidence rates ranging from 2% to 5%. Hyponatraemia is a rare complication of pre-eclampsia. A 41-year-old, para 0+1 in vitro fertilisation monochorionic diamniotic triplet pregnancy woman presented at 25 weeks with dyspnoea and general malaise. Her antenatal course was complicated by the diagnosis of intrauterine growth restriction in triplet one at 27 weeks of gestation. At 27+3 weeks gestation, she was diagnosed as having pre-eclampsia. Subsequent biochemical analysis demonstrated hyponatraemia with serum sodium falling steadily to 117 mmol/L over the next 19 days. She was admitted to intensive care unit for stabilisation of fulminant pre-eclampsia and severe hyponatraemia at 30+5 weeks of gestation. Hypertonic saline and intravenous labetalol were administered prior to delivery by caesarean section. She recovered well postdelivery with stabilisation of her blood pressure and normalisation of her sodium level to 135 mmol/L. Awareness and frequent monitoring of hyponatraemia should become an integral part of monitoring women with pre-eclampsia.

BACKGROUND

Pre-eclampsia toxemia (PET) is a multisystem disorder defined as a systolic blood pressure reading of ≥ 140 mm Hg and diastolic blood pressure ≥ 90 mm Hg measured on two separate occasions more than 30 min apart, with proteinuria of ≥ 0.3 g over 24 hours, after 20 weeks gestation. Incidence rates range from 2% to 5% and is characterised by increased endothelial permeability, release of vasoconstrictive agents, microvascular damage and hyperpermeability of capillaries.¹ It may lower the threshold for seizures and may predispose to maternal mortality and fetal damage.^{2–3} Gross ascites is a rare complication of PET and is associated with increased morbidity and mortality.^{4–5} Hyponatraemia is a rare complication of PET and only a few cases have been reported in the literature to date.

CASE PRESENTATION

A 41-year-old, para 0+1 in vitro fertilisation monochorionic diamniotic triplet pregnancy woman presented at 25 weeks with symptoms of dyspnoea and general malaise. Her prior antenatal course had been complicated by a diagnosis of obstetric cholestasis at 24 weeks gestation, treated with ursodeoxycholic acid and vitamin K. This was confirmed with raised fasting bile acids of 21 μ mol/L. She received two doses of betamethasone to accelerate fetal lung maturity. Her medical history was unremarkable, apart from coiling of a

berry aneurysm at the age of 38 years. She had no family history of pre-eclampsia.

INVESTIGATIONS

She was diagnosed with intrauterine growth restriction in triplet one at 27 weeks of gestation, and had serial ultrasound assessment of growth, liquor volume and Doppler studies. There was no evidence of twin–twin transfusion syndrome. At 27+3 weeks of gestation, hypertension and proteinuria was noted. She was diagnosed as having pre-eclampsia and remained as an inpatient. Examination findings revealed pitting oedema extending to the level of umbilicus bilaterally brisk lower limb deep tendon reflexes but no clonus. She had a tense abdomen and bibasal coarse crepitations on auscultation. Her blood pressure was 165–175 mm Hg systolic and 95–100 mm Hg diastolic, a respiratory rate of 20 breaths/min, normal oxygen saturation and heart rate.

Her 24-hour protein collection was 0.58 g/24 hours and her protein–creatinine ratio was 55.8 mg/mmol creatinine. Subsequent biochemical analysis demonstrated hyponatraemia with serum sodium falling steadily to 117 mEq/L over the next 19 days. Her haemoglobin was noted to be 7.5 g/dL and she received 2 units of red blood cell count and two further iron infusions.

Antihypertensive treatment was initiated with labetalol 200 mg three times a day at 29+5 weeks gestation. A repeat protein–creatinine ratio at 29+2 weeks gestation was 141.7 mg/mmol creatinine. She was noted to have developed Bell's palsy which was treated with a tapering dose of steroids over 6 days which was discontinued at 30+3 weeks gestation. She reported abdominal discomfort and increasing dyspnoea in a recumbent position over several days.

At 30+5 weeks of gestation she was admitted to intensive care unit (ICU) for stabilisation of fulminant PET and severe hyponatraemia. On admission to the ICU laboratory results showed the following: sodium level 119 mmol/L, potassium level 4.6 mmol/L, creatinine 67 μ mol/L, urea 7.7 mmol/L, urate 602 μ mol/L, alanine transferase 146 iu/L, haemoglobin 9.3 g/dL, platelet count 156×10^9 /L and coagulation studies were normal. The serum osmolality was 257 mmol/kg. There was a gradual decline in her sodium levels from 135 mmol/L at the time of admission with diagnosis of PET at 27 weeks of gestation to 123 mmol/L at 29+5 weeks of gestation. The trend of her blood tests can be seen in [table 1](#).

She received a loading dose of magnesium sulfate followed by a maintenance infusion, which was discontinued 24 hours postnatally. On day 17

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Table 1 Trend of blood investigations

Investigation	Day													
	1 (admission)	4	7	9	11	14	17	20	21	22 (delivery)	23	24	25	27
Na, mmol/L (133–146)	137	131	128	130	127	129	123	121	117	117	118	119	124	135
K, mmol/L (3.5–5.3)	4.2	4.5	4.3	4.6	4.7	4.1	4.5	4.2	4.9	4.8	4.4	4.6	5.1	4.2
Urea, mmol/L (2.5–7.8)	3.2	2.4	2.7	2.2	2.5	2.9	4.5	5.4	6.1	6.5	8.5	7.7	8.2	5.6
Creatinine, μ mol/L (50–80)	60	62	56	57	55	55	67	70	68	68	80	67	69	62
ALT, iu/L (10–35)	10	10	11	8	7	14	16	47	73	72	134	146	137	104
Albumin, g/L (35–50)	22	21	21	21	21	19	19	20	19	22	21	19	16	19
Urate, μ mol (140–360)	419	420	406	389	400	381	387	418	506	530	530	602		
Hb, g/dL (11–14)	10.2	10.3	10.2	10.6	9.4	10.2	10.6	9.8	10.3	9.9	9.9	9.3	7.5	10.0
Platelets, $\times 10^9$ /L (155–400)	124	127	149	178	186	140	117	117	133	152	137	154	115	149

ALT, alanine transferase; Hb, haemoglobin; K, potassium; Na, sodium.

hypertonic saline was administered at 27 mL/hours (0.38 mL/kg) which initially caused an increase in plasma sodium concentration of ~ 4 mmol/L over 8 hours as measured after 10 hours; however, the plasma sodium concentration continued to fall over the next 24 hours. At this stage a decision was taken to perform a caesarean section due to worsening hyponatraemia despite active medical management. Intravenous labetalol to control hypertension was used prior to delivery.

She was delivered by elective caesarean section with general anaesthesia at 30+5 weeks of gestation. She experienced considerable difficulty lying supine, thereby necessitating the use of an Oxford Help pillow. Prior to and during induction, heated and humidified high-flow nasal cannula oxygen therapy (HFNC) was used because a difficult intubation was anticipated. Airway examination at laryngoscopy revealed marked upper airway oedema and a grade 2B Cormack-Lehane view through which was passed a size 7.0 endotracheal tube. There was marked skin and soft tissue oedema, and ~ 2000 mL of ascitic fluid was aspirated from the pelvic cavity. The neonates weighed 990 g, 1.3 kg and 1.4 kg for triplets 1, 2 and 3 respectively. All were noted to have hyponatraemia at the time of delivery ranging from 119 to 124 mmol/L.

OUTCOME AND FOLLOW-UP

On day 1 post section she was started on a prophylactic dose of heparin. She recovered well postdelivery with stabilisation of her blood pressure on oral labetalol. Normalisation of her sodium level to 135 mmol/L occurred at day 2 post caesarean section. She was discharged home day 12 postnatal and the triplets were all discharged by 35 weeks. Her blood pressure and blood biochemistry had normalised by 5 weeks gestation and antihypertensives were discontinued at 16 days postnatally. Proteinuria resolved postnatally.

DISCUSSION

Hyponatraemia is a common finding in older patients and is commonly associated with increased mortality. It is however rare in younger patients even in the face of conditions such as pre-eclampsia. Extracellular and intracellular fluids are in osmotic equilibrium due to the free movement of water across most cell membranes; hence plasma tonicity is equal to the effective intracellular osmolality and to the effective osmolality of the total body water (TBW). A fall in serum osmolality suppresses the release of antidiuretic hormone (ADH), allowing excretion of the excess water in dilute urine.

An inability to suppress ADH release is the most common cause of hyponatremia and can be seen in the following settings;⁶

- ▶ True volume depletion, which can be due to gastrointestinal losses (eg, vomiting or diarrhoea) or renal losses (most often thiazide rather than loop diuretics).
- ▶ Decreased tissue perfusion (also called effective arterial volume depletion) due to reduced cardiac output in heart failure or to systemic vasodilation in cirrhosis.
- ▶ A primary (ie, not hypovolemic) increase in ADH release in the syndrome of inappropriate ADH secretion, including an infrequent variant characterised by resetting of the osmostat.
- ▶ Decreased vasopressinase production and a resultant decrease in the breakdown of ADH.

There are also disorders in which hyponatremia occur despite appropriate suppression of ADH secretion. These include psychogenic polydipsia, a low dietary solute intake and advanced renal failure.

Pregnancy heralds the release of many hormones which alter TBW and salt leading to a drop in serum sodium of about 5 meq/L which, in turn causes a drop in plasma osmolality.⁷ During pregnancy, human chorionic growth hormone, oxytocin and relaxin act together to reduce the plasma osmolality mainly by increasing TBW more than total body sodium. In the face of pre-eclampsia there is a decrease in the effective circulating volume leading to non-osmotic release of ADH.⁸ The placenta helps to control fluid balance by releasing vasopressinase which is an enzyme that breaks down and deactivates ADH, hence a defective placenta in pre-eclampsia may lead to further excess water retention.⁹

Hyponatremia is defined as a serum sodium concentration below 135 meq/L. Hyponatraemia may be asymptomatic if it is mild (>125 mmol/L) and occurs over a prolonged period of time.¹⁰ Once serum sodium drops below 120 mmol/L cerebral oedema, encephalopathy and death may ensue.¹¹ Where oedema is present, it indicates that there is increased body sodium and water. The increase in TBW is greater than the total body sodium level, and therefore oedema occurs.¹²

In our case, other medical causes of hyponatraemia were excluded including heart failure, nephrotic syndrome, liver cirrhosis and iatrogenic fluid overload. The patient did not report any diarrhoea or vomiting or any medication use that may cause hyponatraemia. The pathogenesis of the severe hyponatraemia in this case is not fully understood as most women with PET do not develop hyponatraemia. It is hypothesised that the non-osmotic stimulation of vasopressin release in the setting of a

hypervolemic state with low-effective circulating plasma volume is the main mechanism of hyponatraemia. Previous case reports have described hyponatraemia with PET with and without nephrotic syndrome.^{2,3}

Ascitic fluid accumulation occurs in both pregnancies complicated by PET and normal pregnancies, however, gross ascites is a rare complication of PET.¹³ There is a sixfold incidence of congestive heart failure and ninefold incidence of adult respiratory distress syndrome in women with hypertension, elevated Liver enzymes, low platelets (HELLP) syndrome and large-volume ascites compared to those without ascites.¹⁴ It is hypothesised that the widespread endothelial cell dysfunction causes a generalised capillary leak resulting in oedema, proteinuria, hypoalbuminaemia and decreased colloid osmotic pressure.¹⁵ Low-serum albumin levels, as was found in our case, is an indicator of severe PET.¹⁶ It is important that this is identified in women presenting with PET and monitored closely. The low colloid osmotic pressure results in effusions causing ascites and pulmonary oedema.

PET has the potential to cause airway compromise as a result of oedema. At baseline, the pulmonary reserve is greatly reduced by a combination of reduced functional residual capacity and airway oedema.¹⁷ This case was further complicated by pulmonary oedema and more pronounced airway oedema. Given the potential difficulty in obtaining a secure airway and the reduced hypoxic time, it was decided to use a heated and humidified HFNC oxygen therapy. This device produces a positive end-expiratory pressure (PEEP), reduces pharyngeal dead space, recruits alveoli and also allows oxygenation during the apnoeic period. During induction this patient's oxygen saturation remained at 100%.

Learning points

- Most women with pre-eclampsia toxemia (PET) do not develop hyponatraemia, and therefore the pathogenesis is not fully understood. It is hypothesised that the non-osmotic stimulation of vasopressin release in the setting of a hypervolemic state with low-effective circulating plasma volume is the main mechanism of hyponatraemia.
- Awareness and frequent monitoring of hyponatraemia should become an integral part of monitoring women with PET.
- Neurological complications associated with hyponatraemia may simulate those of eclampsia and hyponatraemia in combination with PET is a rare indication for urgent delivery.
- PET-related fluid shifts causing gross ascites and pulmonary oedema require intensive monitoring to avoid complications during the ante and postpartum periods as this is associated with increased morbidity and mortality.

To the best of our knowledge we present the first case of PET complicated by hyponatraemia and gross ascites in the literature. Awareness and frequent monitoring of hyponatraemia should become an integral part of monitoring of women with PET. Neurological complications associated with hyponatraemia may simulate those of eclampsia and hyponatraemia in combination with PET is a rare indication for urgent delivery. PET-related fluid shifts causing gross ascites and pulmonary oedema require intensive monitoring to avoid complications during the ante and postpartum periods as this is associated with increased morbidity and mortality.

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