CASE REPORT

Renal tubular acidosis type 4 in pregnancy

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SUMMARY

We describe the clinical course of renal tubular acidosis (RTA) type 4 in pregnancy, which has not been previously published. Renal tubular acidosis type 4 is a condition associated with increased urinary ammonia secondary to hypoaldosteronism or pseudohypoaldosteronism. Pregnancy may worsen the hyperkalaemia and acidosis of renal tubular acidosis type 4, possibly through an antialdosterone effect. We advise regular monitoring of potassium and pH throughout pregnancy to ensure safe levels are maintained.

BACKGROUND

Renal tubular acidosis (RTA) type 4 is a condition associated with increased urinary ammonia secondary to hypoaldosteronism or pseudohypoaldosteronism. The underlying causes are usually associated with aldosterone deficiency (adrenal insufficiency) or resistance, including drugs that decrease its secretion such as ACE inhibitors, non-steroidal anti-inflammatory drugs and ciclosporin.¹ This leads to hyperkalaemia and a hyperchloraemic metabolic acidosis with a normal anion gap. Treatment is usually with sodium bicarbonate and mineralocorticoid replacement.

Pregnancy causes a number of physiological changes within the renal and endocrine systems. The glomerular filtration rate increases and there is upregulation of the renin-angiotensin system.² There is no published literature describing the clinical course and management of renal tubular acidosis type 4 in pregnancy.

CASE PRESENTATION

A 30-year-old south Asian woman was admitted to hospital with right iliac fossa abdominal pain, initially thought to be appendicitis. An abdominal CT scan was performed, which demonstrated a normal appendix, adrenals and kidneys, with a right corpus luteum and a small amount of free fluid in the pouch of Douglas. The pain settled with ibuprofen, however, the patient was found to have a serum potassium level of 7.2 mmol/L with no ECG changes, and serum creatinine was 56 µmol/L. Venous blood gas demonstrated a pH of 7.250, bicarbonate 18.0 mmol/L and base excess -8.0 mmol/L with a normal anion gap. The hyperkalaemia was managed medically with insulin. The patient was referred to the endocrine team and advised on a low potassium diet.

On review in clinic, her potassium was 6.0 mmol/L. Her father, together with both, her paternal aunt and grandfather, also had a chronic potassium problem and were currently receiving calcium resonium. She had no other significant

medical history and no allergies, and was currently not taking any regular medications. It was noted she had had high serum potassium results (5.8–6.2 mmol/L) a year previously, however, this was thought to be due to haemolysis of the blood samples. Examination was unremarkable with no oedema, and blood pressure was 105/68 mm Hg. Further investigations were within normal range including a short Synacthen test, aldosterone (274 mmol/L), renin, thyroid function (thyroid-stimulating hormone 0.92, T₄ 12.3), protein electrophoresis and immunoglobulins. Urinary sodium was 94 mmol/L (normal range >20 mmol/L) and urinary potassium was 26.8 mmol/L (normal range >25 mmol/L). The patient's 17-α hydroxyprogesterone was not significantly raised. The diagnosis of renal tubular acidosis type 4 was made and treatment with sodium bicarbonate 500 mg orally three times a day was started.

She was also found to have a positive urinary β human chorionic gonadotropin test with her last menstrual period being 5 weeks earlier. Prior to pregnancy, she had had a regular 28-day menstrual cycle. She had had one previous pregnancy, resulting in a miscarriage at 4 weeks' gestation. Her antenatal infection screen was negative including hepatitis B and C, HIV and syphilis. Her body mass index was 23 kg/m².

At 11 weeks gestation, a routine blood test revealed potassium of 5.9 mmol/L. Venous blood gas demonstrated a pH 7.287, bicarbonate 21.6 mmol/L and base excess -5.0 mmol/L. The patient was subsequently started on fludrocortisone 100 µg once a day.

At 12 weeks' gestation, the patient was admitted due to persistent vomiting, 3–4 times a day. She was unable to tolerate oral fluids and had +1 ketones in her urine. The diagnosis of hyperemesis gravidarum was made and she was treated with intravenous fluid and antiemetics. Her serum potassium was 6.0 mmol/L, pH 7.315, bicarbonate 19.3 mmol/L and base excess -6.3 mmol/L. Medical treatment including insulin and intravenous bicarbonate was initiated. On discharge, her oral sodium bicarbonate was increased to 1 g three times a day, with once daily fludrocortisone 100 µg.

Potassium was measured every 2 weeks thereafter. At the beginning of the third trimester, her bicarbonate had been increased to 1 g four times a day and fludrocortisone increased to 200 µg once a day due to ongoing hyperkalaemia and acidosis.

TREATMENT

An ultrasound scan at 35 weeks and 5 days gestation identified a small baby with all biometry

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measurements between 3rd and 10th centile. Umbilical artery Doppler was normal with good end diastolic flow. At 37 weeks gestation, the patient was admitted again because of serum potassium of 6.8 mmol/L. This was treated medically, but after 2 days the decision was made to induce labour, given her ongoing hyperkalaemia. Dinoprostone (prostaglandin E₂) was used for cervical ripening followed by artificial rupture of membranes, a Syntocinon infusion and epidural analgesia. The second stage of labour was delayed (greater than 3 h) and the patient was transferred to theatre where a successful forceps delivery was performed.

OUTCOME AND FOLLOW-UP

The patient gave birth to a 2.244 kg baby girl. There were no peripartum or postpartum complications and estimated blood loss was 400 mL. The neonate had normal serum potassium. The mother remained on the same dose of sodium bicarbonate and fludrocortisone 6 months post partum. Her potassium was 5.9 mmol/L and bicarbonate was 18 mmol/L.

DISCUSSION

We describe the first reported case of RTA type 4 in a south Asian woman who subsequently became pregnant. The diagnosis was made on an incidental blood test, and therefore it is unclear when she developed the condition or whether it had been present from birth and remained undetected. Blood tests 1 year preceding pregnancy indicated an abnormal serum potassium level, however, this was attributed to poor sample storage and haemolysis. In addition, she was not taking any regular medication and had never required medical management for hyperkalaemia in the past. Given the normal aldosterone level and family history of hyperkalaemia, a sporadic or autosomal dominant defect in the mineralocorticoid receptor was thought to be a possible cause. The patient has been referred to the UK 100K Genome project for a full genomic screen to identify a genetic cause.

There is currently no published literature regarding the clinical course of this condition in pregnancy. The hyperkalaemia of RTA type 4 appears to worsen during pregnancy. This may be due to the increased progesterone concentrations throughout pregnancy, which have an antialdosterone effect. This occurs due to progesterone having similar affinity for the mineralocorticoid receptor as aldosterone, resulting in competition for the binding site.³ As progesterone does not stimulate the receptor, it acts as a competitive antagonist. Progesterone concentrations rise throughout pregnancy and peak in the third trimester. This may explain why our patient required increasing amounts of sodium bicarbonate and fludrocortisone in the third trimester.

Alternatively, the increased number of blood tests during pregnancy may reveal abnormal serum potassium concentrations that require treatment but would have normally not caused any

problems. However, serum potassium and pH should be monitored regularly throughout pregnancy, due to the risk of cardiac arrhythmias associated with hyperkalaemia.

The hyperkalaemia remained >6 mmol/L and required medical treatment following the development of hyperemesis gravidarum. This may have been exacerbated by dehydration through persistent vomiting. The acidosis, however, was much improved, which is most likely due to the loss of hydrogen and chloride ions through vomiting, causing a metabolic alkalosis. This is evident by the much improved serum pH of 7.31 compared with the pH of 7.287 taken a week before. The addition of fludrocortisone to the patient's regular medications may have also helped improve the pH.

There was a delay in the second stage of labour, resulting in an instrumental delivery. This may have been due to the effects of hyperkalaemia, which is thought to have a depolarising effect on the muscle membrane, contributing to muscle fatigue.⁴ Unfortunately, no literature exists describing the relationship between myometrial contractility and hyperkalaemia, so this is purely speculative.

Learning points

- Consider a diagnosis of renal tubular acidosis type 4 in patients with persistently high serum potassium.
- Pregnancy may worsen the hyperkalaemia and acidosis of renal tubular acidosis type 4, possibly through an antialdosterone effect.
- We advise regular monitoring of potassium and pH throughout pregnancy to ensure safe levels are maintained.

Contributors All the authors saw the patient in clinic and contributed to the writing of the case report. KB obtained patient consent. ADJ, KB and CN-P approved the final draft.

Competing interests None declared.

Patient consent Obtained.

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