Paraparesis secondary to hypokalaemia with hyporeninemic hypoaldosteronism during pregnancy: a diagnostic dilemma

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Summary: We report the case of a 22-year-old Ethiopian woman, gravida 1, para 0, who presented at 16 weeks gestation with myalgia and paraparesis.

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CASE REPORT

This Ethiopian woman had immigrated to Australia two months previously and was admitted to hospital with progressive bilateral lower leg weakness and muscle pain. She did not complain of excessive vomiting or diarrhoea and denied pica, ingestion of diuretics, laxatives, baking soda, liquorice or excess caffeine.^{1–3}

She had no recent muscle injury or any history suggestive of myositis. There was no personal or family history suggestive of similar episodes to suspect hypokalaemic periodic paralysis.

On examination, she was normotensive (BP 100/70 mmHg) and euvolaemic. Systems examination was normal apart from bilateral paraparesis with a power of 3/5 in all muscle groups in her lower limbs. Her ECG showed QT prolongation and prominent U waves.

Laboratory assessment revealed serum potassium of 1.9 mmol/L (3.2–4.5), sodium 141 mmol/L (135–145), magnesium 0.7 mmol/L (0.7–1.0), phosphate 0.93 mmol/L (0.7–1.4) and a corrected calcium of 2.45 mmol/L (2.15–2.60). She had a creatine kinase of 2597 U/L (<160). Her renal function was normal and her serum bicarbonate was 28 mmol/L (22–33). Serum urate was 0.18 mmol/L (0.12–0.30).

Her spot urinary potassium was 24 mmol/L, with a potassium/creatinine ratio of 3.8, and 24 hour urine potassium was 42 mmol/day consistent with urinary loss of potassium. Spot urine sodium was 139 mmol/L prior to intravenous fluids. 24 hour urine magnesium excretion was elevated at 7.5 mmol/day (3–5). Urine protein creatinine ratio was 0.01 g/mmol (0–0.03), urine pH was 6.9, and there was no glycosuria (glucose <1.1 mmol/L). There was moderate generalised aminoaciduria with significantly elevated losses of alanine

295 mmol/mmol Cr (5–59), glycine 1458 mmol/mmol Cr (12–199), glutamic acid 141 mmol/mmol Cr (1–3) and lysine 156 mmol/mmol Cr (12–52) suggestive of a renal tubular disorder.

The mother denied any symptoms to suggest Sjögren's syndrome or autoimmune disease. Antinuclear antibody testing revealed a homogenous pattern with titre 320 but negative antibodies to Ro/SSA, La/SSB and double-stranded DNA. Human immunodeficiency virus serology was negative.

Thyroid function was normal. There was hyporeninaemic hypoaldosteronism with serum aldosterone <70 pmol/L and plasma renin activity 3 mU/L. 24 hour urine cortisol was normal excluding ectopic ACTH syndrome. She was Vitamin D deficient with a level of 26 nmol/L (50–80).

The patient's electrolytes took more than a week to normalise despite intravenous and oral potassium supplements. Her paraparesis progressively improved and creatine kinase normalised. She required continuous oral potassium and magnesium supplementation (6 tablets each of 600 mg KCl and 500 mg magnesium aspartate) throughout pregnancy in order to maintain serum electrolytes in the normal range. She delivered a healthy male baby by induction of labour one week post-dates. The baby had no electrolyte abnormalities. She remained normotensive throughout.

Postpartum potassium and magnesium supplements were gradually weaned. Three months post-partum, her potassium was normal at 3.7 mmol/L without supplements. Repeat urine testing revealed complete resolution of aminoaciduria. Hyporeninaemic hypoaldosteronism persisted with plasma aldosterone, <70 pmol/L (100–850) and plasma renin activity 8 mU/L (3–40).

DISCUSSION

Hypokalaemia and myopathy have been reported in pregnancy due to excess caffeine ingestion, pica (geophagia), hyperemesis gravidarum, and renal tubular acidosis. The aetiology of hypokalaemia in our patient is unclear. Hypokalaemic periodic paralysis was considered at her initial presentation; however

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her urine electrolytes were consistent with urinary potassium loss and ongoing significant requirements for potassium and magnesium throughout pregnancy are not compatible with this diagnosis.

Our patient's presentation is not consistent with Gitelman's or Bartter's syndromes, where one would expect elevated levels of aldosterone and plasma renin activity.

A renal tubular disorder was suggested by the presence of mild generalised aminoaciduria; however our patient was not acidotic, and renal tubular acidosis is usually associated with elevated levels of plasma renin activity and aldosterone.⁴ A single case of hypokalaemia with primary hypoaldosteronism has been reported in a patient with Sjögren's syndrome and distal renal tubular acidosis; however this patient had markedly elevated levels of plasma renin activity.

The most striking feature in our patient was the presence of hyporeninaemic hypoaldosteronism, present on repeated measurements during the pregnancy as well as postpartum. Normal pregnancy is associated with early stimulation of the renin-aldosterone system which becomes maximal in the third trimester. Mean plasma renin activity increases sevenfold and plasma aldosterone increases by eightfold compared with non-pregnant values.⁵

Hypokalaemia with hyporeninaemic hypoaldosteronism may occur with Liddle's syndrome or the syndrome of apparent mineralocorticoid excess (AME). Liddle's syndrome is an autosomal dominant condition where there is a primary increase in collecting tubule sodium reabsorption and potassium secretion. It presents with the triad of hypertension, hypokalaemia and metabolic alkalosis, usually at a young age. Our patient's normal blood pressure and acid-base status are not suggestive of this diagnosis. AME may occur as a congenital or acquired condition. Congenital AME results from defective 11 beta-hydroxysteroid dehydrogenase type 2 (11B-HSD2), the enzyme which converts cortisol to its inactive metabolite cortisone. Defective enzyme activity in congenital AME allows the unmetabolized cortisol to act on the mineralocorticoid receptor resulting in hypertension, hypokalaemic alkalosis and hyporeninemic hypoaldosteronism. Affected individuals usually present as children with short stature and severe hypertension, though less severe forms may not present until adulthood. Acquired AME occurs as a result of ingestion of substances such as liquorice and chewing tobacco containing glycyrrhetic acid, and grapefruit juice containing flavonoids that have an inhibitory effect on 11B-HSD2. Our patient repeatedly denied ingestion of substances known to cause AME.

A theoretical cause of our patient's presentation would be a mutation in mineralocorticoid receptors resulting in progesterone causing kaliuresis. It is thought that the hundred-fold elevation of progesterone levels in pregnancy attenuate mineralocorticoid effect both from a point of view of kaliuresis and hypertension.⁶ Thus patients with primary aldosteronism may

have an improvement in blood pressure and hypokalaemia during pregnancy with exacerbation postpartum as progesterone levels fall.⁷⁻⁹ A kindred has been described in which an activating mineralocorticoid receptor mutation results in severe exacerbation of hypertension early in pregnancy accompanied by hyporeninaemic hypoaldosteronism, hypokalaemia and renal potassium wasting.¹⁰ It is thought these effects are due to progesterone activating the mutant receptor. It is possible our patient has a receptor mutation accounting for her presentation though the absence of hypertension is atypical for this.

In conclusion we present a young woman whose pregnancy was complicated by severe hypokalaemia due to renal potassium wasting, myopathy with hyporeninaemic hypoaldosteronism but normal blood pressure.

DECLARATIONS

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