



An uninvestigated case of hypokalaemia with profound weakness and tiredness in New Zealand: Gitelman's Syndrome

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Gitelman's syndrome is a primary renal tubular disorder resulting from a defective absorption of sodium chloride in the distal convoluted tubule. It has variable clinical expressions, from asymptomatic to multiple organ dysfunction; however, fatigue and weakness are the most common symptoms.

Case report

A 64-year-old man, noted to have been taking eight potassium chloride tablets daily for over 20 years for an uninvestigated hypokalaemia, presented for treatment.

We stopped his potassium tablets and he developed weakness, tiredness and mobility problems.

There was no history of renal disease, nausea, vomiting, diarrhoea, nor usage of kaliuretic agents.

He was diagnosed hypokalaemic in the 1970s (serum potassium -2.6 mmol/l) and had suffered supraventricular tachycardia in the 1980s requiring betablockers and potassium supplements. He had also had non-Hodgkin's lymphoma involving para-aortic lymph nodes cured by conventional chemotherapy in 1985. There were no signs of subsequent relapse nor was renal involvement noted at any stage.

He had no significant family history.

Examination findings were normal. A renal tubular disorder was suspected and investigations (Table 1) confirmed the diagnosis of Gitelman's Syndrome.

He was treated with slow K and aldactone, on which he remains asymptomatic.

Table 1. Investigations confirming diagnosis of Gitelman's syndrome

Blood (reference ranges)		Urine (reference ranges)	
Complete blood screen	Normal	Microscopy	Unremarkable
ESR	13 mm/hr (0–15)	Urine Na ⁺	237 mmol/l
CRP	9 mg/l (<10)	Urine K ⁺ *	123 (high)
Serum Na	140 mmol/l (135–145)	Urine Mg ⁺⁺	2.4 mmol/l (3.0–5.0)
Serum K*	3.3 mmol/l (low) (3.5–5.0)	Urine Ca ⁺ *	0.4 mmol/d (2.5–7.5)
Serum Cl ⁻	100 mmol/l (98–105)	Urine Cl ⁻ *	251 (high)
Serum Mg ⁺⁺ *	0.58 mmol/l (low) (0.7–1.00)	Urine Cr	11.8 mmol/d (7.0–25.0)
Serum Ca ⁺⁺	2.15 mmol/l (2.10–2.55)	Radiology	
Ionized Ca ⁺⁺	Normal	Chest X-ray	Unremarkable
Serum PO ₄ ⁼	1.4 mmol/l (0.81–1.45)	CT abdomen	Liver/spleen unremarkable No evidence of adrenal mass No paraortic lymphadenopathy Normal kidneys and adjacent retroperitoneal structures
Serum Urea	5.4 mmol/l (3.2–7.1)		
Serum creatinine	76 umol/l (71–133)		
Albumin	39 g/l (35–50)		
Serum HCO ₃ ^{-*}	29 mmol/l (22–28)		
Supine aldosterone*	<50 pmol/l (50–450)		
Ambulatory aldosterone	112 pmol/l (100–850)		
Ambulatory renin*	95 mU/L (5–75)		
Aldosterone: renin = 1.2	<20=> hyperaldosteronism unlikely		
Parathyroid hormone*	5.9 pmol/l (1.0–5.0)		
Thyroid function test	Normal		

Discussion

Gitelman's syndrome, first elucidated by Dr Hillel Gitelman in 1966,¹ has an unknown incidence and prevalence. It occurs in both sexes with no racial predisposition and presents later than Bartter's Syndrome² (86% after six years of age), usually as a coincidental finding.

There is a genetic heterogeneity with autosomal recessive and autosomal dominant (with increased phenotypic variability) mode of transference resulting in non-conservative mutation in the thiazide-sensitive Na-Cl co-transporter (NCCT) SLC 12A3 on chromosome 16 (resulting in the defective absorption of sodium chloride in the distal convoluted tubule).^{3,4}

Clinical presentation varies from asymptomatic to that which includes tetanic episodes, polyuria, polydipsia, and effects of hypokalaemia and hypomagnesaemia on skeletal muscles and cardiac, gastrointestinal and renal tissues. Fatigue and weakness are the most common symptoms. Patients are normotensive unlike those with Bartter's Syndrome (low BP with a postural drop).

Our patient's symptoms were mainly malaise, fatigue, muscle weakness and effects on cardiac function.

The laboratory features of Gitelman's Syndrome are hyponatraemia, hypokalaemia, hypomagnesaemia, hypochloridaemia, and raised bicarbonate levels with alkalosis.⁵ The serum calcium, phosphate and prostaglandin E2 levels tend to be normal contrary to those seen in Bartter's syndrome.⁶

Plasma renin activity is increased (because of extracellular fluid contraction) and, with low potassium levels, tends to decrease aldosterone levels.⁷

Urine examination shows inappropriately increased potassium, chloride and magnesium levels. Urinary calcium levels are decreased in contrast to Bartter's Syndrome.⁸ The molar urinary calcium/urinary creatinine ratio is less than 20 unlike Bartter's where it is greater than 20. Urinary osmolality increases with desmopressin (as countercurrent mechanism is still intact unlike in Bartter's Syndrome).⁹

Our patient had low serum potassium and magnesium, and high serum renin and bicarbonate levels, whilst his urine calcium and magnesium levels were low with inappropriately high urine potassium and chloride levels. These features are congruent with Gitelman's Syndrome and the low urine calcium/creatinine ratio differentiated it from Bartter's Syndrome.⁹

Little is known regarding radiological images and renal histology in Gitelman's Syndrome. Chondrocalcinosis (secondary to hypomagnesaemia) may be seen.

Treatment of Gitelman's Syndrome includes dietary adjustments along with potassium and magnesium supplements. ACE inhibitors and spironolactone can be used. Prognosis is good. However, the treatment may only partially correct the electrolyte defects. The effects of Gitelman's Syndrome on pregnancy are unknown and whether the diagnosis could be made prepartum, by testing aldosterone levels in the amniotic fluid, is also unknown.

In conclusion, it is important to delineate the underlying cause for hypokalaemia. Doing so may save the patient from taking medications (and experiencing their side effects). However, in our patient the treatment remains supportive with supplementation of electrolytes for life.

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