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Brief report

Long-term follow-up of a patient with Gitelman's syndrome

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Abstract. The long-term follow-up (from age 6 to 20 years) of a girl with Gitelman's syndrome, who had four hypomagnesaemic-tetanic episodes associated with normal plasma calcium, hypokalaemia and hypocalciuria, is presented. During and after puberty, hypomagnesaemia was of the order of 0.41–0.49 mmol/l and plasma potassium was at the lower reference limit. The long-term clinical course and growth of this patient appeared good, but, magnesium supplementation reduces the risk of tetanic crises.

Key words: Gitelman's syndrome – Hypokalaemia – Hypomagnesaemia – Hypocalciuria – Growth

Introduction

Gitelman's syndrome [1], also known as familial hypokalaemia-hypomagnesaemia, has recently been re-evaluated as an important renal tubular disease in children and adolescents [2, 3]. There are no long-term studies of this syndrome, probably because many patients have been included in series of Bartter's and Bartter-like syndromes. We present the long-term follow-up of a girl with Gitelman's syndrome from diagnosis at 6 years to adulthood.

Case report

Some data from this patient, relating to first hospital admission and the first 16 months of treatment, have already been reported [4]. Briefly, a 6-year-old girl was admitted to hospital for tetany. Her weight was on the 8th and height on the 20th percentile; blood pressure was 105/70 mmHg. She was hypokalaemic [plasma potassium (K_p) 2.5 mmol/l], with metabolic alkalosis (pH 7.46, base excess +0.5 mEq/l) and normal total plasma calcium (total Ca_p 2.4 mmol/l). Total plasma magnesium (Mg_p), assayed by colorimetry, was reduced (0.57 mmol/l). She also had moderate hyper-reninaemia [plasma reninactivity (PRA) in supine position 2.8 ng/ml per hour, reference values 0.2–2.7] and hyperaldosteronism (plasma aldosterone 281 pg/ml, reference values 90–210). Plasma sodium (Na_p) was 144 mmol/l, plasma chloride (Cl_p) 93 mmol/l and urinary electrolyte excretion was increased. Renal biopsy did not show the juxtaglomerular apparatus hypertrophy typical of Bartter's syndrome. Indomethacin and oral K supplementation were given for 16 months and the response was good. However, 18 and 27 months after the first hospitalization, she had two further episodes of tetany with Chvostek's and Trousseau's signs; the second occurring during tapering of indomethacin. Both were associated with hypomagnesaemia (Mg_p 0.46–0.45 mmol/l), hypokalaemia (K_p 2.4–2.5 mmol/l) and normocalcaemia (total Cap 2.45–2.40 mmol/l). Fractional excretion of (FeK) was 23%, FeNa 1.3% and FeCl 1.0%. Urinary Ca/creatinine, determined after 3-day indomethacin suspension, was 0.014 (mmol/mmol), below the 3rd percentile for age [5], whereas urinary Mg/creatinine was 0.84 (mmol/mmol) (above the 90th percentile) [5]. Urinary osmolality after deamino-D-arginine vasopressin was 760 mosmol/kg; acidification, measured after an ammonium chloride load, was normal; distal fractional Cl reabsorption after an oral water load was 90%. Mg supplementation was prescribed but patient compliance was poor.

After 13.5 years of follow-up, the patient had another tetanic crisis at 19.5 years after discontinuation of weak Mg supplementation. During this episode of tetany, her Mg_p was 0.41 mmol/l, total Ca_p 2.52 mmol/l and K_p 3.1 mmol/l.

The pattern of K_p and Mg_p during the long-term follow-up is presented in Fig. 1. At the last clinical examination, after 14 years of follow-up and at 20 years, the patient's general condition was good; her height was 166 cm (Fig. 2) and weight 54 kg (on the 40th percentile). Major laboratory findings were: Mg_p 0.49 mmol/l, K_p 3.2 mmol/l, Na_p 137 mmol/l, Cl_p 95 mmol/l; bicarbonate 32 mmol/l, total Ca_p 2.47 mmol/l, ionized plasma Ca, 1.31–1.41 mmol/l, creatinine clearance 120 ml/min per 1.73 m^2, PRA 4 ng/ml per hour, aldosterone 419 pg/ml, FeK 27%, FeNa 1.0% and FeCl 1.0%. Urinary Ca/creatinine was 0.019 (mmol/mmol) and urinary Mg/creatinine 0.74 (mmol/mmol).

Discussion

This is probably the first report of a patient with Gitelman's syndrome followed from the appearance of the first symptoms to adulthood. We initially considered the patient to have an atypical form of Bartter's syndrome, but in the

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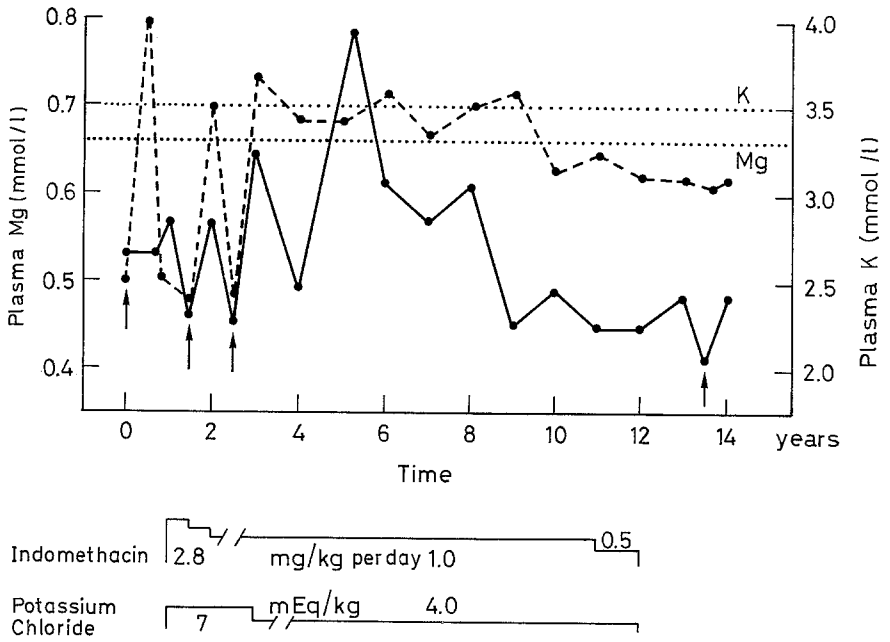

Fig. 1. Plasma potassium (*K*, ●– – –●) and total magnesium (*Mg*, ●——●) levels in our patient at first hospitalization at 6 years (time 0) and during 14 years of follow-up. · · · · ·, Lower reference values; ↑ tetanic episodes

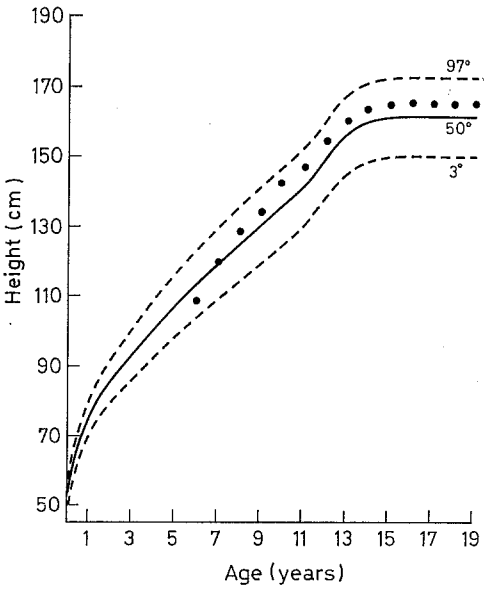

Fig. 2. Statural growth of our patient from 6 to 19 years

light of the review of Rodriguez-Soriano et al. [2], she appeared to have all the most important features of Gitelman's syndrome. The moderate degree of hyper-reninaemia in our patient may explain the absence of hypertrophy of the juxtaglomerular apparatus on renal biopsy, which has been demonstrated only in one patient with Gitelman's syndrome [6]. Distal fractional Cl reabsorption after an oral water load was normal in our patient; this result differed from that obtained by Rodriguez-Soriano et al. [2] after a hypotonic saline diuresis. The different methods used could have influenced these results [7].

Clinical status and growth can be completely normal in Gitelman's syndrome recognized during childhood. Gitelman's syndrome and other Mg-losing renal diseases have been diagnosed in adult patients of normal stature despite the congenital tubular abnormality [8]. The development of a new tetanic episode in our patient, 13 years after the first symptoms and during a period without Mg supplementation, suggests continuous Mg supplementation may be useful, at least in some patients with significant hypomagnesaemia.

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