中文題目：吉特曼症候群個案報告:以跌倒為臨床表現的老年女性

英文題目：Fall in an older woman: an unusual presentation of Gitelman syndrome

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Background: Gitelman syndrome (GS) is an autosomal recessive disorder caused by mutations in the SLC12A3 gene encoding the thiazide-sensitive Na-Cl cotransporter (NCCT). Clinical symptoms of GS, including episodic muscular weakness, tetany, fatigue and joint pain, are usually reported [1]. Little data regarding older GS patients is available in the literature, especially confirmed by genotyping. Here, we report a case of an older woman who presented with rare manifested frequent fall in whom GS was diagnosed.

Case presentation: A 83-year-old woman was referred to our geriatric clinic due to recurrent falls. Marked weight loss from 45 to 32 kilograms was noted within one year though her appetite was quite well including favorite salty snacks. Chronic hypokalemia and hypomagnesemia were found since 2013 without specific etiology identified. She did not take diuretics, laxatives, beta-2-adrenergic agonists or glucocorticoids. On examination, the body mean index was 15.7 kg/m2, and normotensive. Physical examination showed dry skin turgor. Biochemistry data revealed metabolic alkalosis with severe hypokalemia (2.0 mmol/L), hypomagnesemia (1.1 mg/dL), and hyponatremia (124 mmol/L). Normal thyroid, adrenal function, plasma renin and aldosterone level were noted. Urine analysis revealed high potassium excretion (transtubular potassium gradient 9.3, fractional excretion (FE) of potassium 15.0%), high magnesium (Mg) excretion (FEMg 14.0%), hypocalciuria (calcium-to-creatinine ratio: 0.06 mg/mg) and the urine sodium-to-chloride ratio of 0.92. Autoimmune markers were unremarkable. Radiographic studies displayed chondrocalcinosis in the left shoulder and bilateral knee joints. We performed targeted gene sequencing of SLC12A3 and CLCNKb and found a homozygous mutation c.2881-2AG deletion in the exon 24. Near- normalization of serum potassium and magnesium level was achieved after treatment of oral magnesium and potassium supplement. There was no fall episode during the follow-up.

Discussion: We presented a 83-year-old woman with GS manifesting as recurrent falls and reduced physical performance. Although fall is an unusual presentation of GS, it is a quite common geriatric comorbidity leading to fatal and non-fatal injury in older adults. This case demonstrated how a fall can be caused by an unusual pathology. The homogeneous deletion of 2881-2 AG is identified [2] with an overall estimated prevalence of heterozygous mutation as 0.5-1% among Asian population [3]. Frameshift of NCCT from R959 results in pathogenic protein expression in the cells lining the distal convoluted tubule [4]. Notably, gender differences might account for phenotype variability. Older age, female gender and atypical feature may explain the late diagnosis to late adulthood in our case. Long-term affliction with GS can adversely affect the quality of life (QOL). The degree of reduction in the QOL is similar to that associated with diabetes, coronary disease, or congestive heart failure. GS patients tend to have lower physical activities caused by poor self-assessed health status and depressive mood. To conclude, older adults with refractory hypokalemia and laboratory features supporting NCCT dysfunction should undergo genetic tests as early as possible. Understanding the genetic basis may help the older patients to deal with their disease and strengthen the interaction between patient, family, and their healthcare practitioners.

References

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Table 1. Summary of Blood and Urine Laboratory values

Blood	Value	Normal range	Serum immunological profile	Value	Normal range	Urine	Value	Normal range
Potassium, mmol/L	2.0	3.5-5	ANA	Speckled 1:40(+)		Potassium, mmol/L	20	17-145
Chloride, mmol/L	87	96-106		Cytoplasm 1:40(-)		Chloride. mmol/L	75	20-300
Sodium, mmol/L	124	135-145	ANCA	Negative		Sodium, mmol/L	69	15-267
Magnesium, mg/dL	1.1	1.8-2.4	C3	68.4	58.0-147.0	Magnesium, mg/dL	7.2	1.6-18.7
Calcium, mg/dL	8.7	8.6-10.1	C4	16.4	11.0-35.0	Calcium, mg/dL	1.9	6.8-21.3
Osmolarity, mOsm/kgH_2O	266	278-305	Anti-Ro/SSA	Positive(>240 U/mL)	Negative: < 7 U/mL	Phosphate, mg/dL	7.1	40-136
iPTH, pg/mL	24.3	15.0-65.0	Anti-La/SSB	Negative		Creatinine, mg/dL	32	28-217
pH	7.44	7.35-7.45	ACA	Negative		Osmolarity, mOsm/kgH_2O	285	850-1200
Bicarbonate, mmol/L	31.9	24-28	Anti-ribosomal-P	Negative		TTKG	9.3	
PaCO2, mm-Hg	47	32-48	Anti-Sm	Negative		FEMg, %	14.0	
Renin, pg/mL	27.5	1.8-59.4	Anti-RNP	Negative		FEPO4, %	3.6	
Aldosterone, pg/mL	79.2	48.3-270	Anti-β2GPI	Negative		Daily Ca urine loss, mg	43.2	

Abbreviation: ANA: anti-nuclear antibodies, ANCA: anti-neutrophil cytoplasmic antibodies, ACA: anti-cardiolipin antibodies, Anti-β2GPI: Anti-beta-2 glycoprotein I antibodies, TTKG: transtubular potassium gradient, FEMg: fractional excretion of magnesium, FEPO4: fractional excretion of phosphate

Figure 1. Radiographic image of the shoulder and knee joints. Calcification in the joint space was compatible with chondrocalcinosis (yellow arrow).

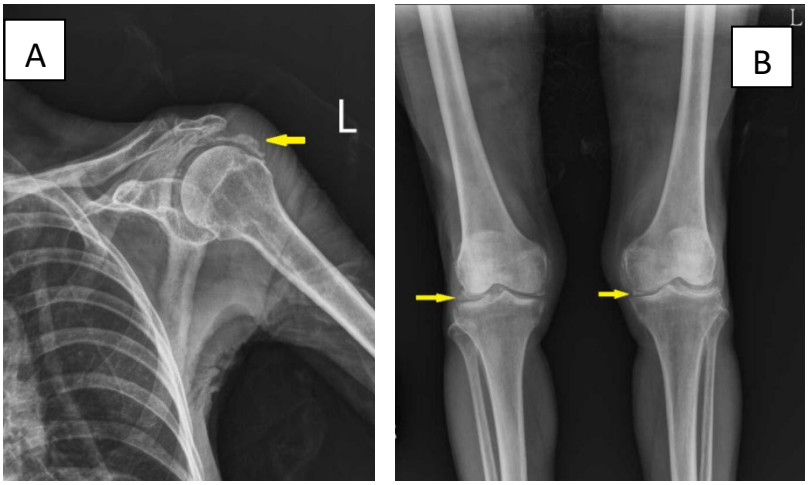

Figure 2. SLC12A3 genetic sequence analysis results of exon 24. Our patient carried a homozygous mutation of del2881-2AG.