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Letter to the Editor

A case of "summer hypokalemia" revealing adult-diagnosed cystic fibrosis

Un caso de 'hipocalemia veraniega' que revela una fibrosis quística diagnosticada en la edad adulta

Dear Editor,

Cystic fibrosis (CF) is an autosomal recessive disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, typically diagnosed in childhood. However, atypical or mild phenotypes may delay diagnosis until adulthood. Electrolyte disturbances are uncommon initial manifestations, particularly in adults.[1–3] We report a rare case of adult-diagnosed CF presenting solely with recurrent summer-associated hypokalemia and metabolic alkalosis.

A 28-year-old Turkish male presented in July 2024 with generalized weakness and excessive sweating during the summer months. Physical examination, chest X-ray, and electrocardiography were unremarkable, and blood pressure was 118/74 mmHg. Laboratory tests revealed moderate hypokalemia (2.9 mEq/L) with metabolic alkalosis; other parameters were normal. Intravenous potassium replacement (60 mmol KCl in 1 L saline) normalized potassium levels, which remained stable during follow-up in November 2024, January 2025, and April 2025 (Table 1).

In June 2025, he was re-admitted with recurrent weakness. Serum potassium was 2.6 mEq/L and increased to 3.4 mEq/L after intravenous replacement. Additional tests revealed sodium 137 mEq/L, magnesium 1.1 mEq/L, bicarbonate 34 mmol/L, urinary potassium 50.8 mmol/L, and elevated renin and aldosterone levels. Vomiting, diarrhea, and diuretic use were excluded.

His medical history included idiopathic pancreatitis in 2017. He denied smoking or alcohol use, and his BMI was 24 kg/m^2. The coexistence of summer-associated hypokalemia, normotension, prior pancreatitis, and excessive sweating prompted evaluation for CF. Sweat chloride was 76.3 mmol/L (normal <60 mmol/L). Genetic analysis of the *CFTR* gene revealed two heterozygous variants: c.2843C > T (p.Ser945Leu) and c.922T > C (p.Ser308Pro). The patient was informed about the diagnosis and expressed relief at having a clear explanation for his recurrent symptoms. Written informed consent was obtained for publication.

CF is a multisystem disease caused by CFTR mutations leading to defective or absent CFTR protein, clinically characterized by recurrent respiratory infections, pancreatic insufficiency, and malabsorption-related complications, and other systemic manifestations.[1] In the present case, the diagnosis was delayed due to several atypical features: the occurrence of hypokalemia only during the summer months, adult age at diagnosis, absence of a history of recurrent pulmonary infections, and lack of other organ involvement apart from an episode of pancreatitis.

In CFTR mutation carriers, excessive sweat sodium and chloride loss during hot months can cause extracellular fluid (ECF) depletion and secondary hyperaldosteronism.[4] ECF volume contraction, activation of the renin–angiotensin–aldosterone system, hypokalemia, and the development and maintenance of metabolic alkalosis have all been proposed as interconnected mechanisms in this context.[5] Consistent with this pathophysiological framework, both renin and aldosterone levels were found to be elevated above the reference range in our patient.

Hypokalemia with sodium and chloride loss can worsen metabolic alkalosis, as chloride depletion alone may sustain alkalosis regardless of volume or potassium status.[6] In the setting of CF, luminal chloride deficiency leads to impaired bicarbonate excretion by the renal collecting ducts despite increased pendrin activity during chloride-depletion alkalosis.[7] This failure to eliminate bicarbonate contributes to the persistence of systemic metabolic alkalosis.

Table 1
Patient's laboratory parameters.

Date	July 2024	November 2024	January 2025	April 2025	June 2025
Na (mEq/L)	138	137	136	139	138
K (mEq/L)	2.9	3.7	3.8	3.6	2.6
Cl (mEq/L)	100	98	99	100	101
HCO_3 (mEq/L)	30	24	23	25	34
BUN (mg/dl)	15	17	14	18	18
Cr (mg/dl)	0.9	0.84	0.85	0.91	0.94
Urine K (mEq/L)	30.4	–	–	–	50.8
Ku/Cru (mmol/mmol)	–	–	–	–	0.96
Urine Cl (mmol/L)	–	–	–	–	<15
Urine Ph	6	6.5	6.5	6	6
Plasma renin (pg/ml)*	–	–	–	–	31.9
Plasma aldosterone (ng/dl)**	–	–	–	–	49.5

* Plasma renin activity reference: 1.3–13.8.
** Serum aldosterone reference: 3.5–30, Ku/Cru: urinary potassium-to-creatinine ratio.

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Hyperaldosteronism can promote potassium loss both through sweat and urine, thereby contributing to hypokalemia.[8] Urinary potassium excretion was disproportionately high for the degree of hypokalemia, indicating renal potassium wasting. Excessive sweat loss during hot months likely worsened total potassium depletion. Chronic salt loss and secondary hyperaldosteronism in CF can enhance renal potassium and magnesium loss, while intestinal malabsorption further reduces magnesium absorption. Resulting hypomagnesemia aggravates potassium wasting by impairing Na^+/K^+-ATPase activity, making hypokalemia more resistant to correction.[3,5] The mild hypomagnesemia detected in our patient likely contributed to the persistence of both hypokalemia and metabolic alkalosis through a synergistic effect with hyperaldosteronism and salt loss. However, the persistence of hypokalemia despite magnesium replacement rules out the possibility of hypokalemia secondary to hypomagnesemia alone in this patient. In fact, under high sweat flow rates, sweat potassium concentrations in individuals with CF can reach up to 17.8 mEq/L, compared to 8.4 mEq/L in healthy controls.[9] This difference may be further accentuated during hot summer months, exacerbating potassium depletion in CF patients. A similar summer-related CF case was previously reported in an African American patient.[3]

The c.2843C > T (p.Ser945Leu) variant is classified as pathogenic in several databases and has been associated with classical CF phenotypes.[10] The c.922T > C (p.Ser308Pro) is considered a variant of uncertain significance, but its presence in trans with a pathogenic variant supports the diagnosis in the appropriate clinical context.

Awareness and adult diagnosis of CF are increasing. We report a rare adult case presenting solely with hypokalemia and metabolic alkalosis, emphasizing the need for clinical suspicion even when typical features are absent. CF should be considered in unexplained summer hypokalemia. The detection of the c.922T > C (p.Ser308Pro) variant highlights the importance of early genetic evaluation.

Ethical approval

All procedures performed in this case report were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent

Written informed consent was obtained from the patient for publication of this case report.

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Declaration of competing interests

The authors declare no conflict of interest.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

References

1. Ratjen F, Bell SC, Rowe SM, Goss CH, Quittner AL, Bush A. Cystic fibrosis. Nat Rev Dis Primers. 2015;1:15010.
2. Davé S, Honney S, Raymond J, Flume PA. An unusual presentation of cystic fibrosis in an adult. Am J Kidney Dis. 2005;45:e41–4.
3. Cao Y, Donaldson R, Lee D. "Summer hypokalemia" as an initial presentation of cystic fibrosis in a morbidly obese African American adult: case report. BMC Nephrol. 2020;21:462.
4. Polgreen PM, Comellas AP. Clinical phenotypes of cystic fibrosis carriers. Annu Rev Med. 2022;73:563–74.
5. Zheng Y, Horita S, Hara C, Kunimi M, Yamada H, Sugaya T, et al. Biphasic regulation of renal proximal bicarbonate absorption by luminal AT(1A) receptor. J Am Soc Nephrol. 2003;14:1116–22.
6. Luke RG, Galla JH. It is chloride depletion alkalosis, not contraction alkalosis. J Am Soc Nephrol. 2012;23:204–7.
7. Soleimani M. The multiple roles of pendrin in the kidney. Nephrol Dial Transplant. 2014;30:1257–66.
8. Bates CM, Baum M, Quigley R. Cystic fibrosis presenting with hypokalemia and metabolic alkalosis in a previously healthy adolescent. J Am Soc Nephrol. 1997;8:352–5.
9. Bijman J. Transport processes in the eccrine sweat gland. Kidney Int Suppl. 1987;21:S109–12.
10. Sosnay PR, Siklosi KR, Van Goor F, Kaniecki K, Yu H, Sharma N, et al. Defining the disease liability of variants in the cystic fibrosis transmembrane conductance regulator gene. Nat Genet. 2013;45:1160–7.

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