SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Nephrology

Hypokalemic Nephropathy: Case Report

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DOI: 10.36347/sasjm.2023.v09i12.003 | **Received:** 28.10.2023 | **Accepted:** 04.12.2023 | **Published:** 09.12.2023

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Abstract **Case Report**

Hypokalemic nephropathy is a rare tubulointerstitial disorder due to chronic hypokalemia that can lead to serious morphological or functional renal alterations. We report a case of a 31-year-old patient from North Africa, admitted to the Department of Nephrology for exploration of proteinuria at 1.2g/24h associated with renal failure at 21mg/l of plasma creatinine in a context of chronic hypokalemia around 2.5mEq/l. The nephropathy check up didn't show anything particular. The renal biopsy performed revealed renal tubes with vacuolation of the epithelium, with the presence of a few hyaline casts. The interstitial tissue showed minimal fibrosis and a moderate inflammatory infiltrate composed of lymphocytes and histiocytes, all easing the diagnosis of hypokalemic nephropathy. The patient was treated with potassium supplementation in combination with an angiotensin converting enzyme inhibitor (ACE inhibitor). The evolution was marked by a progressive improvement of renal function going from an glomerular filtration rate (GFR) of 28 ml/min (at admission) to 55 ml/min after 6 months, with negativation of proteinuria. Although the hypokalemic nephropathy seems to have disappeared, it must be considered in the face of any alteration of renal function in a context of chronic hypokalemia. Histology is essential to confirm the diagnosis.

Keywords: Hypokalemia, hypokalemic nephropathy, histology, vacuolation.

INTRODUCTION

Hypokalemia is defined as a potassium concentration below 3.5mmol/L, the most common hydroelectrolyte disorder in clinical practice (20% of hospitalized patients and 10-40% of patients on thiazide diuretics) [1]. It can occur either by a cellular shift, an increase in losses, or more rarely by insufficient nutrients [2]. Chronic hypokalemia can lead to serious morphological or functional renal alterations,said hypokalemic nephropathy. Histological lesions may be marked by renal hypertrophy, hyperplasia or atrophy of tubular cells, fibrosis or interstitial infiltration by macrophages and vacuolization of the renal tubular epithelium [3, 4]. Hypokalemic nephropathy is rare and has seemingly disappeared [5].

However, we recently received a case that we are reporting. Our aim is to understand the physiopathogenic mechanism involved in our patient and to remind clinicians to always think of this pathology in any context of chronic hypokalemia.

PRESENTATION OF THE CASE

A 31-year-old woman from North African was referred to the department of Nephrology by her physician for proteinuria at 1.2g/24h associated with renal failure at 21mg/l of plasma creatinine in a context of chronic hypokalemia varying between 2.5 and 3mEq/l. Her history was marked by primary infertility (7 years of marriage) for which she was given the hormonal treatment (duphaston) by her gynecologist and hypothyroidism followed for 7 years and controlled with Levothyrox 75 mg.

The anamnesis noted an almost daily intake of a "mixture of traditional plants" (licorice and other unidentified plants) for years "for infertility" and self-imposed intermittent fasting "to lose weight" (obese patient). The patient did not report diarrhea, vomiting or other specific symptoms. No use of diuretics or corticosteroids found.

The clinical examination noted a blood pressure of 120/70 mmHg, a heart rate of 84 beats/min and a respiratory rate of 20 cycles/min. The patient was afebrile. The weight was 116 kg with a body mass index

of 41 kg/m2. She had no lower limb edema and nothing particular was shown by the rest of the examination.

On biological check up, serum creatinine was 21 mg/l, that is, an estimated GFR of 28 ml/min. The serum sodium level was 136 mg/l; serum potassium 2.6mEq/l; the serum magnesium level 20 mg/l; the standing aldosterone level 1183pg/ml (3.5 times the normal value); the standing active renin level 38.9pg/ml (normal), that is a standing aldosterone/renin ratio of 46.83 (normal); alkaline reserves 24mmol/l; the tri-iodothyronine (T3L) and free thyroxine (T4L) normal. Blood cortisol levels at 8 a.m. and 4 p.m. were normal. We performed a 24-hour urine ionogram. The natriuresis was 30mEq/24h; kaliuresis 10mEq/24h (adapted to hypokalemia); the calciuria was 69mg/24h; phosphaturia 538mg/24h; urinary creatinine 552 mg/24h and urinary urea 14.9g/24h. The 24-hour proteinuria was 1.2 g/24 hours. The glycosuria on the sample was less than 0.1g/l. We did not find any biological arguments in favor of tubular acidosis. The urinary sediment was inactive on urine cytobacteriological examination. The blood count noted normochromic normocytic anemia at 8g/dl while the levels of white blood cells and platelets were correct. The seroimmunological assessment (hepatitis, syphilis, HIV, ANA, native DNA, complement, anti-g, anti-TPO) didn't show anything particular.

Renal ultrasound showed kidneys of normal size, with echogenic cortex, without obstruction of the urinary tract. On CT scan, the adrenals were of normal size, without nodules or cleavage.

During her hospitalization, a kidney biopsy was performed. The glomeruli were the site of a discreet diffuse thickening of the capillary walls. The interstitial tissue showed minimal fibrosis (10%) associated with a moderate inflammatory infiltrate (20%) composed of lymphocytes and histiocytes. The vascular sections were without abnormalities. The renal tubes were the site of some hyaline casts with vacuolation of their epithelium, in favor of a hypokalemic nephropathy.

Therapeutically, the patient was supplemented with potassium initially intravenously and then orally. She was also treated with ACE inhibitor in addition to other nephroprotection measures. The evolution was marked by the normalization of serum potassium, the negativation of proteinuria (0.2g/24h) with progressive improvement of renal function at 12mg/l (GFR of 55ml/min) of serum creatinine which remained stationary after 6 months of follow-up.

DISCUSSION

Extensive clinical and experimental evidences have shown that prolonged potassium depletion can lead to significant alterations in renal structure and function [6]. In 1919, Jaffe and Sternberg, analyzing autopsies performed on patients with chronic dysentery, found that 25% had a specific histological lesion that they named "vacuolar degeneration", attributed to intestinal losses of non specified "nutritional substances" [4, 7]. Given that serum potassium levels were not measured and kidney biopsy not performed at that time, their study was based on autopsies carried out on victims of chronic diarrhea [5]. It was in 1950 that Perkins *et al.*, attributed the histological abnormalities observed in human kidneys to potassium depletion. The predominant histological abnormality described was vacuolation of the tubular epithelium, found mainly but not exclusively in the proximal convoluted tubule. The vacuoles were generally large and contained neither fat nor glycogen [8, 9].

The renal alterations observed in our patient occurred in a context of chronic hypokalemia. If the exact cause of this hypokalemia has not been elucidated, absence of arguments in favor of renal or extrarenal loss or even intracellular transfer of potassium was then in favor of a lack of nutrients, related to the self-imposed diet by the patient. This is a rare but possible clinical situation. Eliacik *et al.*, had implicated a lack of oral potassium intake as an etiology of hypokalemia in certain patients in their series [10].

Histologically, vacuolation of the tubular epithelium was observed, as it is the case in the literature, but it was localized in certain tubules. Besides, interstitial infiltration by lymphocytes as well as fibrosis were consistent with the findings of Bock and Cremer in 9 patients out of a series of 23 patients [11].

Hypokalemic nephropathy is considered as a progressive form of chronic kidney disease which can ultimately lead to renal failure [12]. Our patient already had a GFR of 28ml/min at admission. It has not been possible to specify the duration of hypokalemia before the deterioration of renal function, but the progressive improvement of this after normalization of serum potassium was in favor of a deterioration associated with hypokalemia.

The mechanisms involved in the pathogenesis of hypokalemic nephropathy are not fully elucidated as it is the case in our patient. Several authors have mentioned vasoconstriction and local ischemia, increased renal ammonium production and intrarenal activation of complement, abnormalities in the production of growth factors and inflammatory cytokines such as insuline-like growth factor-1, insulin growth factor-binding protein-1, vascular endothelial growth factor and angiotensin II [3, 13–15]. Further studies are needed.

CONCLUSION

Although hypokalemic nephropathy is a rare pathology that seemed to have disappeared, our work has shown that the effects of a prolonged hypokalemia on the kidney remain relevant today. This pathology should therefore be taken into consideration in all situations of

chronic hypokalemia which may be due to a cellular shift, either renal or extra-renal losses of potassium or insufficient intakes. The diagnosis is essentially histological and dominated by tubulo-interstitial damage which can regress after correction of serum potassium or become chronic. The pathogenesis is not completely understood and we suggest that further studies be done.

Acknowledgement: We thank all the clinicians and pathologists who somehow contributed to this work.

Conflict of Interest: No conflicts declared by the authors.

BIBLIOGRAPHY

1. Katerinis, I., & Fumeaux, Z. (2007). Hypokaliémie : diagnostic et prise en charge. *Rev Médicale Suisse*, *4*.
2. Kardalas, E., Paschou, S. A., Anagnostis, P., Muscogiuri, G., Siasos, G., & Vryonidou, A. (2018). Hypokalemia: a clinical update. *Endocr Connect*, *7*, R135–46. https://doi.org/10.1530/EC-18-0109.
3. Reungjui, S., Roncal, C. A., Sato, W., Glushakova, O. Y., Croker, B. P., Suga, S. I., ... & Mu, W. (2008). Hypokalemic nephropathy is associated with impaired angiogenesis. *Journal of the American Society of Nephrology: JASN*, *19*(1), 125–34. https://doi.org/10.1681/ASN.2007030261.
4. Yalamanchili, H. B., Calp-Inal, S., Zhou, X. J., & Choudhury, D. (2018). Hypokalemic Nephropathy. *Kidney Int Rep*, *3*, 1482–8. https://doi.org/10.1016/j.ekir.2018.07.014.
5. **E**litok, S., Bieringer, M., Schneider, W., & Luft, F. C. (2016). Kaliopenic nephropathy revisited. *Clin Kidney J*, *9*, 543–6. https://doi.org/10.1093/ckj/sfv154.
6. Relman, A. S., & Schwartz, W. B. (1958). The kidney in potassium depletion. *Am J Med*, *24*, 764–73. https://doi.org/10.1016/0002-9343(58)90379-6.
7. Conn, J. W., & Johnson, R. D. (1956). Kaliopenic Nephropathy. *Am J Clin Nutr*, *4*, 523–8. https://doi.org/10.1093/ajcn/4.5.523.
8. MacDonald, M. K., Sabour, M. S., Lambie, A. T., & Robson, J. S. (1962). THE NEPHROPATHY OF EXPERIMENTAL POTASSIUM DEFICIENCY. AN ELECTRON MICROSCOPIC STUDY. *Q J Exp Physiol Cogn Med Sci*, *47*, 262–72. https://doi.org/10.1113/expphysiol.1962.sp001606.
9. Perkins, J. G., Petersen, A. B., & Riley, J. A. (1950). Renal and cardiac lesions in potassium deficiency due to chronic diarrhea. *Am J Med*, *8*, 115–23. https://doi.org/10.1016/0002-9343(50)90348-2.
10. Eliacik, E., Yildirim, T., Sahin, U., Kizilarslanoglu, C., Tapan, U., … & Aybal-Kutlugun, A. (2015). Potassium Abnormalities in Current Clinical Practice: Frequency, Causes, Severity and Management. *Med Princ Pract*, *24*, 271–5. https://doi.org/10.1159/000376580.
11. Bock, K. D., Cremer, W., & Werner, U. (1978). Chronic hypokalemic nephropathy: A clinical study. *Klin Wochenschr*, *56*, 91–6. https://doi.org/10.1007/BF01477459.
12. Wieërs, M. L. A. J., Mulder, J., Rotmans, J. I., & Hoorn, E. J. (2022). Potassium and the kidney: a reciprocal relationship with clinical relevance. *Pediatr Nephrol*, *37*(10), 2245-2254. https://doi.org/10.1007/s00467-022-05494-5.
13. Tsao, T., Fawcett, J., Fervenza, F. C., Hsu, F. W., Huie, P., Sibley, R. K., & Rabkin, R. (2001). Expression of insulin-like growth factor-I and transforming growth factor-β in hypokalemic nephropathy in the rat. *Kidney international*, *59*(1), 96-105. https://doi.org/10.1046/j.1523-1755.2001.00470.x.
14. Tolins, J. P., Hostetter, M. K., & Hostetter, T. H. (1987). Hypokalemic nephropathy in the rat. Role of ammonia in chronic tubular injury. *J Clin Invest*, *79*, 1447–58. https://doi.org/10.1172/JCI112973.
15. Suga, S.-I., Mazzali, M., Ray, P. E., Kang, D.-H., & Johnson, R. J. (2002). Angiotensin II type 1 receptor blockade ameliorates tubulointerstitial injury induced by chronic potassium deficiency. *Kidney Int*, *61*, 951–8. https://doi.org/10.1046/j.1523-1755.2002.00208.x.