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Recurrent Hypokalemia, Hypomagnesemia and Metabolic Alkalosis Following Preemptive Renal Transplantation: Bartter Syndrome

Preemptif Böbrek Nakli Sonrasında Tekrarlayan Hipokalemi, Hipomagnezemi ve Metabolik Alkaloz: Bartter Sendromu

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ABSTRACT

Native kidney function can still contribute to the total renal function after preemptive renal transplantation, and the primary problems of native kidneys such as tubular disorders may persist or reappear in the post-transplantation period. Bartter syndrome is a rare hereditary tubulopathy characterized by renal salt wasting, hypokalemia, metabolic alkalosis, and normotensive hyperreninemic hyperaldosteronism. In this case report, we described a patient who presented with episodes of recurrent hypokalemia, hypomagnesemia, and metabolic alkalosis in the post-transplantation period, probably due to the tubular disorder of the native kidneys. The primary kidney disease had not been adequately investigated in the pre-transplant period, and Bartter syndrome was the most likely diagnosis. Identifying primary kidney disease in the pre-transplantation period is important for patient follow-up.

KEY WORDS: Bartter syndrome, Preemptive renal transplantation, Recurrent hypokalemia

ÖZ

Preemptif böbrek nakli sonrasında nativ böbrek fonksiyonu toplam böbrek fonksiyonuna hala katkı sağlayabilir ve tübüler bozukluk gibi nativ böbreklerdeki sorunlar nakil sonrası dönemde devam edebilir veya tekrarlayabilir. Bartter sendromu renal tuz kaybı, hipokalemi, metabolik alkaloz ve normotansif hiperreninemik hiperaldosteronozm ile karakterize nadir görülen kalıtsal bir tübülopatidir. Bu olgu raporunda, muhtemelen nativ böbrekteki tübüler bozukluğa bağlı nakil sonrasında tekrarlayan hipokalemi, hipomagnezemi ve metabolik alkaloz nedeni ile izlenen bir hastayı sunduk. Hasta böbrek nakli öncesi primer böbrek hastalığı açısından yeterince değerlendirilmemişti ve Bartter sendromu burada en muhtemel tanıydı. Böbrek nakli öncesinde primer böbrek hastalığının tanımlanması hastaların takibi için önemlidir.

ANAHTAR SÖZCÜKLER: Bartter sendromu, Preemptif böbrek nakli, Tekrarlayan hipokalemi

INTRODUCTION

Preemptive kidney transplantation from living donors without previous initiation of dialysis has become more popular nowadays. Preemptive kidney transplantation is suggested for most patients with end-stage renal disease (ESRD) as it is associated with better graft and patient survival when compared with transplantation after a period of dialysis therapy (1). Since native kidneys can still contribute to the total renal function after preemptive renal transplantation, the primary problems of native kidneys such as tubular disorders may persist or reappear.

Here, we described a patient who presented with episodes of recurrent hypokalemia, hypomagnesaemia, and metabolic alkalosis in the post-transplant period, probably due to the tubular disorder of the native kidneys. Primary kidney disease had not been adequately investigated in the pre-transplant period and Bartter syndrome was the most likely diagnosis.

CASE

A 32-year-old male had undergone preemptive renal transplantation from his sister one year ago at another center. His primary renal disease was unknown.

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He presented to our hospital with complaints of nausea, weakness and fatigue. He did not have diarrhea and he denied use of non-steroid anti-inflammatory drugs (NSAI), diuretics or herbal medicine. He reported having complaints such as nausea, weakness and muscle cramp before transplantation. His arterial blood pressure was about 90/60 mmHg in pre-transplant period. No further investigation had been conducted during that period. Although his mother had chronic kidney disease of unknown etiology, his sister did not have any defined kidney disease. He was treated by prednisolone 10 mg/d, mycophenolate sodium 3x360 mg/d, and tacrolimus 1.5 mg/d as maintenance treatment after transplantation.

Physical Examination: Arterial blood pressure was 115/65 mmHg, and pulse 90/min. Cardiovascular, respiratory and abdominal examinations were all normal. He was normovolemic.

Laboratory Findings: Serum sodium was 119 mEq/L, potassium 2.46 mEq/L, calcium 9.3 mg/dl, phosphorus 3.3 mg/dl, serum creatinine 1.95 mg/dl, pH 7.51, HCO_3 31 mEq/L, and pCO_2 43 mmHg. Urinalysis revealed pH of 7, density of 1007, and normal microscopy. Urinary potassium excretion was 60 mEq/d, magnesium 72 mg/d, sodium 263 mmol/d, chloride 380 mmol/d, calcium 255 mg/d, protein 671 mg/d, and tacrolimus level 6 ng/ml. Abdominal ultrasonography revealed bilateral nephrocalcinosis of the native kidneys (Figure 1). A scintigraphic functional study (Tc-99mMAG3) was performed to evaluate the functional contribution of both the native kidneys and the allograft. The functional contribution of the native kidneys was 25%. We could not compare urine electrolytes of the native and transplant kidneys, as an invasive procedure would be required to collect 24-hour urine separately. Kidney donor did not declare any symptoms of electrolyte imbalance, and test results did not reveal findings of tubulopathy. Therefore we concluded that source of the problem was not the transplant kidney. He had been hospitalized 4 times in the last 8 months because of vomiting, hypokalemia, metabolic alkalosis and hyponatremia. Oral potassium and magnesium replacement had been started at the previous admission and the same clinical problems reappeared when he discontinued supplementation treatment. Hyponatremia accompanied as he insisted to take a lot of water and salt free diet (5000-6500 cc/d).

We supposed that he had Bartter syndrome with insignificant symptoms before transplantation. He did not have any laboratory tests except the ones that had been done just before transplantation in which severe renal failure was detected. As renal failure progressed, signs and symptoms due to electrolyte imbalance might become less significant. Electrolyte imbalance might become apparent with the contribution of the drugs used in the post-transplant period and the residual native kidney function. Genetic analysis could not be performed.

Oral potassium and magnesium replacement and spironolactone were started and patient is still followed under this treatment without any symptoms.

DISCUSSION

Renal transplant recipients should be evaluated for primary renal disease in pre-transplantation period as it may suggest risk of recurrence of primary renal disease and affect the long-term follow-up schedule after transplantation (2). This is not only true for glomerular diseases but also for tubular disorders. Preemptive renal transplantation makes this even more important because of the continued effect of the native kidneys.

Bartter syndrome was first defined in 1960 by Dr. Frederick Bartter and is a rare hereditary tubulopathy characterized by renal salt wasting, hypokalemic metabolic alkalosis and normotensive hyperreninemic hyperaldosteronism (3). A defect in the thick ascending limb of Henle's loop is usually responsible for the pathogenesis of Bartter syndrome (4). This causes impaired sodium chloride reabsorption and therefore volume depletion and renin-angiotensin-aldosterone system activation. Secondary hyperaldosteronism and increased distal flow and sodium delivery may increase potassium and hydrogen secretion.

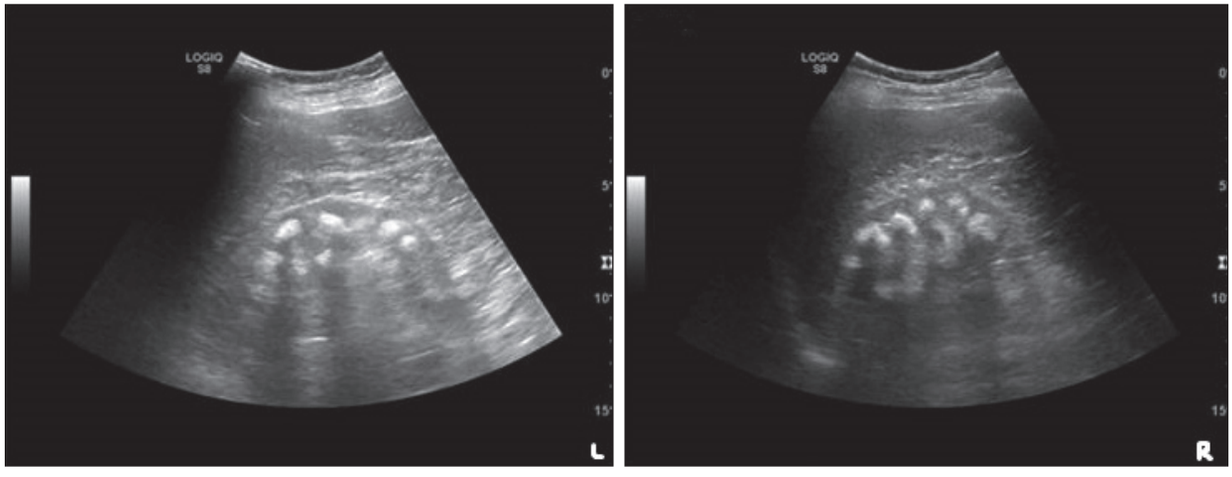

Figure 1: *Ultrasound images of bilateral nephrocalcinosis.*

Hypokalemia and increased angiotensin II lead to an increase in renal release of vasodilator prostaglandins (prostaglandin E2 [PGE2]), which may also contribute to the pathogenesis of Bartter syndrome (2,5).

Although Bartter syndrome is mostly prevalent in children, it can also be diagnosed in adulthood (6). Clinical findings might be mild. Bartter syndrome should be considered when clinical features such as weakness, paralysis, tetany, polyuria, and polydipsia are present with hypokalemic alkalosis and normotension (7,8). Renal stones or nephrocalcinosis may develop due to hypercalciuria (9). Milder forms which were diagnosed incidentally with the presence of nephrocalcinosis have been reported in the literature (10). Proteinuria and hematuria can be seen and chronic kidney disease can rarely develop (6). Focal segmental glomerulosclerosis (FSGS) may occur due to salt-losing nephropathy in some patients with Bartter syndrome and this may progress to ESRD (11). Apart from FSGS, factors like recurrent dehydration episodes, chronic hypokalemia, nephrocalcinosis, long term NSAI drugs, and potassium-sparing agents such as angiotensin converting enzyme inhibitors can affect renal functions (6,11,12).

When a detailed history was taken, we learned that our patient used to have complaints such as nausea, weakness, muscle cramps and low blood pressure in the pre-transplantation period. However, he was not evaluated for these complaints. He only had the tests that were necessary for the transplantation operation when he had severe renal failure. We thought that clinical presentation related to electrolyte imbalance might be milder due to advanced renal failure.

Resolution of symptoms and metabolic findings have been reported in patients with Bartter syndrome and ESRD who underwent renal transplantation (6,11). Patients with severe and refractory Bartter syndrome who are unresponsive to the medical treatment should be considered for native kidney nephrectomy and preemptive kidney transplantation. This approach may improve metabolic abnormalities and improve the quality of life. Although this is a radical solution, it is indeed a cure for the Bartter syndrome which is accepted as an incurable genetic disease (12). In our case, preemptive kidney transplantation was performed without native nephrectomies and in contrast to the reported cases, the metabolic findings became apparent after transplantation instead of resolution.

Functional contribution of native kidneys may still be prominent in preemptive kidney transplant recipients. Besides, native kidney functions may even improve after preeemptive renal transplantation and they may contribute more to the overall glomerular filtration rate (13). In our patient, the diagnosis of Bartter syndrome was unknown in the pre-transplantation period. After preemptive transplantation, the functional contribution of the native kidneys was found to be 25% and electrolyte imbalance became more prominent in the post-transplantation period. After appropriate medical management, electrolyte imbalance was corrected successfully and thus native kidney nephrectomy was not required.

CONCLUSIONS

Identifying primary kidney disease or disorders in pre-transplantation period is important for post-transplantation follow up. Native kidney nephrectomy in the pre-transplantation period can help to improve quality of life in patients with Bartter syndrome who have severe symptoms and are unresponsive to medical treatment.

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