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GOUT SUCCESSFULLY TREATED WITH DIET AND BENZBROMARONE IN A LIVING KIDNEY DONOR

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ABSTRACT – *Objective:* To describe a patient with gout initiated after living kidney donation successfully treated with benzbromarone.

Case presentation: A 53 years old male with no previous history of prior illness who donated his left kidney to his father. Nine years after the surgical procedure, he had a podagra, and the arthritis progressed to other joints on evolution. He received allopurinol 300 mg/day plus colchicine 1 mg/day. He returned to our clinic 6 years later, referring too high alcohol ingestion, especially beer on the weekend and using colchicine. His physical examination showed a podagra, but no tophi were noted. Laboratory tests revealed uric acid of 9.2 mg/dL (nr: < 7 mg/dL), 24 hours urinary uric acid (UUA) of 220 mg (nr: 25-750 mg/day), and C-reactive protein (CRP) was 8.3 mg/dL (nr: < 3 mg/dL). Benzbromarone and colchicine were prescribed, and the patient was also oriented to increase his oral hydration to 3 liters/day, to adhere to a hypocaloric diet, and to stop alcohol drinking. After three months, he denied arthritis; his uric acid was reduced to 5.1 mg/dL, and UUA increased to 590 mg in 24 hours. After one year of treatment, he is asymptomatic, without alcoholic drinks, has normal inflammatory markers, hIs uric acid is 4.8 mg/dL, and uses only benzbromarone 100 mg/day. No side effect related to benzbromarone was observed in our patient.

Conclusions: To the best of our knowledge, this is the first case illustrating a patient with gout after a living kidney transplant successfully treated with diet and benzbromarone.

KEYWORDS: Gout, Arthritis, Renal diseases, Kidney transplant, Transplantation, Benzbromarone.

INTRODUCTION

Gout is a metabolic disorder characterized by increased serum urate levels that leads to monosodium urate (MSU) crystal deposition in joints, subcutaneous tissue (tophi), and kidneys. Hyperuricemia is caused by reduced renal excretion in 90% of the cases, and in 10%, it is due to the overproduction of uric

acid [1]. Causes of reduced renal excretion of uric acid involve genetic factors, diuretic use, and, uncommonly due to, kidney removal for transplant donors. This condition has been described in some series. In fact, in a large cohort of 1,988 donors compared to 19,880 matched non-donors, the authors verified an increased risk of gout in 3.4% of the donors, with a hazard ratio (HR) of 1.6 (95% CI: 1.2-2.1, p<0.001)[2]. Allopurinol is the primary drug to reduce uric acid in gout[1]. Although, to the best of our knowledge, no report on the use of benzbromarone, a uricosuric agent, was found in patients with gout after a living kidney donor transplant. This article aims to report a patient with gout after living kidney donation successfully treated with benzbromarone. Informed consent was obtained from the patient.

CASE REPORT

A 53 years old male with no previous history of illness was diagnosed and donated his left kidney to his father. His ancestor had chronic renal failure due to hypertensive renal disease and gout. The surgery did not have any intercurrence. The patient had an excellent recovery and no need for any drugs. Nine years after the surgical procedure, he appeared with a podagra, and arthritis progressed to other joints during evolution. He had a history of typical recurrent arthritis, mainly in the first metatarsophalangeal and ankles, and uric acid of 10.5 mg/dL fulfilling the 2015 gout classification criteria[3]. Furthermore, he received allopurinol 300 mg/day plus regular colchicine 1 mg/day for two years. As the treatment improved his clinical condition, he only took these drugs during gout attacks. Although, uric acid was not reduced below 8 mg/dL. He came to our private clinic six years later, saying he used to drink a lot of beer (86.4 g of alcohol per week) on weekends. He was under colchicine 1 mg/day therapy only and had a gout attack at least once a month. His physical examination showed a podagra, but no tophi were noted. The weight was 92 kg, height of 1.78 m, and body mass index (BMI) was 29.0 kg/m^2. Laboratory tests revealed normal blood cell count, creatinine 1.2 mg/dL [normal range (nr): 0.7-1.1 mg/dL], uric acid 9.2 mg/dL (nr: < 7 mg/dL), 24 hours urinary uric acid (UUA) of 220 mg (nr: 25-750 mg/day), total cholesterol 215 mg/dL, HDL-c 32 mg/dL (nr: >50 mg/dL), LDL-c 142 mg/dL (nr: < 130mg/dL) and triglycerides 229 mg/dL (nr: <150mg/dL), C-reactive protein (CRP) was 8.3 mg/dL (nr: < 3 mg/dL), glucose 92 mg/dL, insulin 26 mU/L (nr: 2-19 mU/L), AST 33 U/L and ALT 37 U/L. Rheumatoid factor, anti-CCP, and antinuclear antibodies were absent. A renal ultrasound did not find any abnormality in his right kidney. Benzbromarone 100 mg/day and associated with colchicine 1 mg/day were prescribed since he had a low UUA, and uric acid slightly reduced with allopurinol. He was suggested to increase oral hydration to 3 liters per day, have a hypocaloric diet, and stop drinking alcohol. After three months, he denied arthritis, uric acid reduced to 5.1 mg/dL, triglycerides to 145 mg/dL, glucose to 83 mg/dL, CRP to 2 mg/dL, creatinine to 1.0 mg/dL and AST 38 U/L and ALT 32 U/L. UUA increased to 590 mg in 24-hour excretion. Currently, after one year of treatment, he is asymptomatic, without alcohol drinks, his weight was reduced to 83 kg, and BMI is 26.2 kg/m^2, inflammatory markers are normal, uric acid is 4.8 mg/dL, creatinine 1.0 mg/dL, glucose 81 mg/dL, and lipids are expected, using only benzbromarone 100 mg/day.

DISCUSSION

We report a patient diagnosed with gout nine years after a living kidney donation for transplant successfully treated with diet, lifestyle changes, and benzbromarone.

A recently published review of the complications was presented in living kidney donors in the first decade after the donation[4]. It described two previous studies that showed a higher risk of end-stage renal disease (ESRD) among the donors, but the absolute 15-year incidence of ESRD was less than 1%. Evidence suggests that the 20-year incidence of gout is slightly higher among donors than among healthy non-donors[4].

In another large study totalizing 2,000 living donors, 8 developed ESRD, and this complication appeared from 5 to 27 years after donation. Interestingly, kidney transplantation was necessary for one donor. Moreover, some medical complications included proteinuria, hypertension, diabetes, ischemic heart disease, and gout in 3 donors[5].

Demographic factors linked to gout after living kidney donation were studied in an article with 4,650 donors. The authors verified that the main risk factors were African-American race, older age at donation, and man gender. Nevertheless, donors with gout had more frequent renal problems[6].

Concerning gout mechanisms after living renal donation, a reduction in glomerular filtration rate (GFR) leads to reduced uric acid excretion and consequent hyperuricemia[7]. Importantly, when the GFR is reduced to 25% to 40% of the pre-transplant, the uric acid elevation is more evident[8]. Furthermore, when these donors are followed-up, after six months of the surgery, the uric acid increases by 8.2%, and after seven years, a 20% increase is verified[6].

Regarding the therapeutic employed by the patient evaluated here, benzbromarone is a uricosuric agent used mainly in the last 30 years. It acts through a potent inhibition of the dominant luminal urate exchanger at the proximal tubule URAT1, leading to diminished urate reabsorption, with consequent reduction of uric acid levels[9,10]. This drug was withdrawn from various parts of Europe due to hepatotoxicity, although several countries, including European countries (e.g., Spain, Germany, Netherlands), New Zealand, Brazil, Taiwan, China, Japan, and others, keep this uricosuric use. It was never approved in the US market[9]. A recent review showed that only 11 case reports on hepatotoxicity were published, with nine deaths. These data bring the possibility of reevaluating this agent, especially in Latin America, where no hepatotoxicity has been reported[9].

Concerning alcohol use and gout, reducing its abuse is essential for good disease control. Throughout history, gout has commonly been associated with purine-rich foods and excessive alcohol consumption[11]. Therefore, most guidelines (15 out of 17) of diverse medical societies recommend avoiding or limiting alcohol intake and losing weight as part of optimized gout treatment. Unfortunately, no high-quality evidence seems to have been produced in this field until now[12].

Furthermore, it is essential to emphasize that changes in lifestyle and diet were fundamental in our case. The American guideline for gout management recommends that the patient with gout limits his/her alcohol intake and reduces purine intake and high-fructose corn syrup intake regardless of disease activity. In addition, the guideline states that "using a weight loss program (no specific program endorsed) is conditionally recommended for those patients with gout who are overweight/ obese, regardless of disease activity"[13].

CONCLUSIONS

The present study reports a male patient who developed gout nine years after donating his kidney to his father's transplant. Therefore, following up with living kidney donors is crucial to monitor renal function and uric acid levels.

Informed consent:
Informed consent was obtained from the patient. The authors declare that they followed Helsinki's World Medical Association Declaration in this study.

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All data and materials are available upon request

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