Dermal Tophus: A Complication of Gout in a Kidney Transplant Recipient

Ebru Hatice Ayvazoglu Soy,1 Emre Karakaya,1 Arzu Karatas Togral,2 Aydincan Akdur,1 Gokhan Moray,1 Mehmet Haberal1

Abstract

Gout is a chronic metabolic disease caused by disturbance of purine metabolism that leads to hyperuricemia. Hyperuricemia prevalence after renal transplant is reported as 19% to 84% in different studies. Tophaceous gout in renal transplant recipients is a consequence of increased hyperuricemia. Although tophus formation in skin and soft tissues is an indicator of chronic gout (also referred to as tophaceous gout), tophi may be the first sign of gout. In this study, we report a case of a 62-year-old male renal transplant recipient who had tophi as the first clinical sign of gout. After confirming gout diagnosis, cyclosporine was changed to sirolimus, and allopurinol was added to therapy to decrease uric acid levels. In conclusion, hyperuricemia is a common complication in renal transplant recipients. Presentation might be atypical, and diagnosis can be challenging.

Key words: End-stage renal disease, Hyperuricemia, Tophaceous gout

Introduction

Gout is a chronic metabolic disease caused by disturbance of purine metabolism that results in hyperuricemia. Increased serum uric acid levels cause monosodium urate crystal deposition in joints, kidneys, and soft tissues and an inflammatory response.1,2 If gout is not recognized and treated, it progresses through 4 clinical stages: asymptomatic hyperuricemia, acute gout, interval gout, and chronic tophaceous gout. Chronic gout is associated with heavy alcohol intake, diuretic use, obesity, hypertension, and renal impairment.3

Hyperuricemia prevalence after renal transplant is reported as 19% to 84% in different studies.4 In renal transplant recipients, the prevalence of gout is more than in the general population and reported between 3.5% and 28%.5 Gout in renal transplant patients is described as more aggressive with early onset, fast tophaceous progression, and involvement of unusual joints such as the hip, shoulder, and sacroiliac joints. Tophaceous gout in renal transplant recipients is a consequence of increased hyperuricemia. Previous studies focused mostly on renal transplant with increased hyperuricemia due to cyclosporine use, impaired renal function, and diuretic therapy.6,8 The association between hyperuricemia and azathioprine or mycophenolate mofetil (MMF) use has not been described.

Although tophus formation in skin and soft tissues is an indicator of chronic gout, also referred to as tophaceous gout, tophi may be the first sign of gout. In this study, we report a case of a renal transplant recipient who had tophi as the first clinical sign of gout.

Case Report

A 62-year-old man was admitted to our clinic with gradually increasing multiple, painful subcutaneous nodular lesions. He received renal transplant from his cousin 2 years ago. The etiology of renal failure
was diabetes mellitus. Past medical history included hypertension and coronary artery disease. He received cyclosporine (2.5 mg/kg/d; body weight, 60 kg), MMF (30 mg/kg/d), and prednisolone (10 mg/d) since transplant. Laboratory studies showed that the level of creatinine was 1.4 mg/dL, urea was 32 mg/dL, and uric acid was 10 mg/dL (normal range, 3 to 7.2 mg/dL).

On physical examination, he had white, firm, painful subcutaneous lesions on the palmar aspect of the tips of the fingers, right ear helix, and right elbow (Figure 1). These white subcutaneous lesions were suspected to be gout tophi or dystrophic calcifications. For diagnosis, we performed punch biopsy of the lesions. Pathologic examination confirmed the presence of nodular conglomerates of amorphous material, surrounded by histiocytes. Polarized light microscopy showed needle-shaped monosodium urate crystals, consistent with tophaceous gout (Figure 2). Bacterial smears and cultures were negative. Radiographic examination of the hands revealed osteoporosis and vascular calcifications without any erosive defect or sign of osteomyelitis (Figure 3). After confirming the diagnosis of gout, cyclosporine was changed to sirolimus (3 mg/d), and allopurinol (300 mg/d) was added to therapy to decrease uric acid levels.

Discussion

It has been reported in several studies that the prevalence of gout, one of the oldest forms of arthritis, is increasing worldwide. A previous study showed a prevalence of gout of 1.4% (male:female ratio, 3.6:1).9 Disease prevalence increases with increased age, and is 4% in men aged 75 to 84 years. Although gout is characterized by chronic hyperuricemia, several risk factors (such as purine-rich alimentation, heavy alcohol intake, obesity, hypertension, diuretic therapy, and reduced renal clearance) also play a role in pathogenesis. After renal transplant, the prevalence of gout is more than in the general population, ranging from 3.5% to 28%.10 Immunosuppressive agents, such as

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Figure 1. Tophaceous Gout

(A and B) Multiple firm, white papules and nodules on the digits of both hands. (C) Subcutaneous nodule on the right ear helix.

Figure 2. Tophaceous Gout

(A) Nodular conglomerates consisted of amorphous material surrounded by histiocytes. (B) Polarized light microscopy showed needle-shaped monosodium urate crystals.
cyclosporine and tacrolimus, play a role in inducing hyperuricemia and gout in renal transplant recipients. Cyclosporine induces renal arterial vasoconstriction and causes a decrease in tubular urate secretion. The mean time between transplant and onset of gout ranges from 12 to 72 months, with an earlier onset with cyclosporine use. Our patient had a long history of hypertension that had been treated with different diuretics for several years, and he also used cyclosporine for 12 years.

Untreated gout progresses through 4 clinical stages. Asymptomatic hyperuricemia progresses to acute gout attacks as monoarthritis involving mostly the first metatarsophalangeal joint. Pain, swelling, redness of the joints, onset in early morning, and progression during the following 24 to 48 hours are pathognomonic features of these attacks. Fever and leukocytosis can accompany these findings. Dactyliitis can develop and may take weeks to resolve. With time, attacks become more frequent and involve more joints. The last stage of the disease is tophus formation. Our patient had these tophi for 5 years without any joint involvement. As in our patient, in rare and exceptional cases, gout tophi may be the first symptom of the disease. Tophi can manifest at any location, preferentially at the distal interphalangeal joints, olecranon bursa, dorsal surface of the proximal interphalangeal joints, metacarpophalangeal joints, and dorsum of the toes. Although finger pads are less commonly involved, tophi were observed mostly on the finger pads in our patient. Differential diagnosis of gout depends on the stage of the disease. When evaluating arthralgia, arthritis, or myelopathy in a transplanted patient, the possibility of gout should be considered.

Treatment of gout in transplant recipients is challenging due to the potential for drug interactions and adverse events. Colchicine and/or nonsteroidal anti-inflammatory drugs are standard treatment for acute attacks of gout. Systemic corticosteroids or intraarticular corticosteroid injections are more suitable in renal transplant recipients. Xanthine oxidase inhibitors also are effective, especially for prophylaxis of gout. Azathioprine metabolism is xanthine oxidase-dependent, and coadministration of azathioprine and cyclosporine may increase the risk of bone marrow toxicity; a change from azathioprine to MMF can be considered in this case. Treatment in our patient included allopurinol and a change from cyclosporine to sirolimus because he was using MMF.

In conclusion, hyperuricemia is a common complication among renal transplant recipients. Clinical gout usually occurs several years after renal transplant. The presentation might be atypical, and diagnosis can be challenging. Treatment of renal transplant patients for gout should be adjusted individually due to possible drug interactions and the risks of adverse events.

References


Radiographic examination of the hands revealed osteoporosis and vascular calcifications without any erosive defect or sign of osteomyelitis.

Figure 3. Tophaceous Gout