

■ Case Report

Advanced Erosive Gout as a Cause of Fever of Unknown Origin

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A 61-year-old man was referred to our hospital due to a 3-month history of fever of unknown origin, and with right knee and ankle joint pains. At another hospital, extensive investigations had produced negative results, including multiple sterile cultures of blood and joint fluids, and negative autoantibodies. His serum uric acid level was not elevated. However, after admission to our hospital, we performed right knee arthrocentesis, which revealed uric acid crystals. These findings, combined with the results of imaging tests, which showed joint degeneration, led to a diagnosis of advanced erosive gout. After receiving a therapeutic non-steroidal anti-inflammatory drug and a maintenance dose of colchicine for prophylaxis against recurrence, the patient's symptoms subsided and did not return. Advanced erosive gout should be considered a possible cause of fever of unknown origin and diagnostic arthrocentesis should be performed in patients with unexplained arthritis.

Keywords: Advanced Erosive Gout; Fever of Unknown Origin; Inflammatory Arthritis; Uric Acid Crystals

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INTRODUCTION

Advanced erosive gout is a manifestation of gout that can have a similar presentation to rheumatoid arthritis,^{1,2)} and can cause fever of unknown origin. This diagnosis can be made by identifying urate crystals through arthrocentesis from a joint with degenerative changes.³⁾ An important risk factor for gout is hyperuricemia,⁴⁾ but the threshold serum uric acid level that leads to a gouty attack varies between individuals.⁵⁾ In this case study, we have described a unique case of a patient with no known history of hyperuricemia, who presented with fever of unknown origin, but was ultimately diagnosed with chronic gout.

CASE REPORT

A 61-year-old man with a history of hypertension was referred to our hospital due to a 3-month period of right knee and ankle pain and low-grade fever. He was initially admitted to another hospital, where he was unable to walk and could not perform usual daily activities. He complained of knee and ankle pains, fever, fatigue, and appetite loss. His laboratory data showed elevated peripheral white blood cell count and C-reactive protein (CRP). The results of an esophago-gastro-duodenoscopy, abdominal ultrasound, and chest-abdominal computed tomography (CT) scan produced no relevant findings. A culture of knee joint fluid was tested, without examining fluid crystals by microscopy, but no abnormalities were found. The patient

received multiple antibiotics and antipyretics, but his symptoms did not resolve. He had hypertension and dyslipidemia, but neither diabetes mellitus nor hyperuricemia. He had fractured (closed fracture) his right ankle 10 years earlier and had sprained his right knee 3 years ago. He smoked 5 cigarettes per day and drank a moderate amount (about one to two liters of beer) of alcohol, only occasionally. His baseline medications were amlodipine (5 mg a day) and valsartan (160 mg a day).

On physical examination, the patient's details were as follows: a blood pressure of 107/69 mmHg, heart rate of 100 beats/min, temperature of 37.8°C, normal respiratory rate, and pulse oximetry oxygen saturation of 98% while breathing ambient air. There were no remarkable findings in the head, neck, chest, abdomen, extremities, or skin. A neurological examination was also normal, but his right knee joint showed mild swelling.

The laboratory data were as follows: peripheral white blood cell (WBC) 7,600 cells/ μ L, CRP 12.52 mg/dL, erythrocyte sedimentation rate (ESR) 137 mm/h, hemoglobin A1c 6.6%, low density lipoprotein cholesterol 200 mg/dL, uric acid 6.2 mg/dL, ferritin 205 ng/mL, thyroid stimulating hormone 2.27 μ IU/mL, negative hepatitis B surface antigen, negative hepatitis C virus antibody, negative human immunodeficiency virus antibody, prostate specific antigen 3.42 ng/mL, rheumatoid factor 5 IU/mL, antinuclear antibody < 1:40, complement C3 component 159 mg/dL, complement C4 component 35 mg/dL, anti-double stranded DNA antibody < 2.0 IU/mL, anti-cyclic citrullinated peptide antibody 1.6 U/mL, proteinase 3 antineutrophil cy-

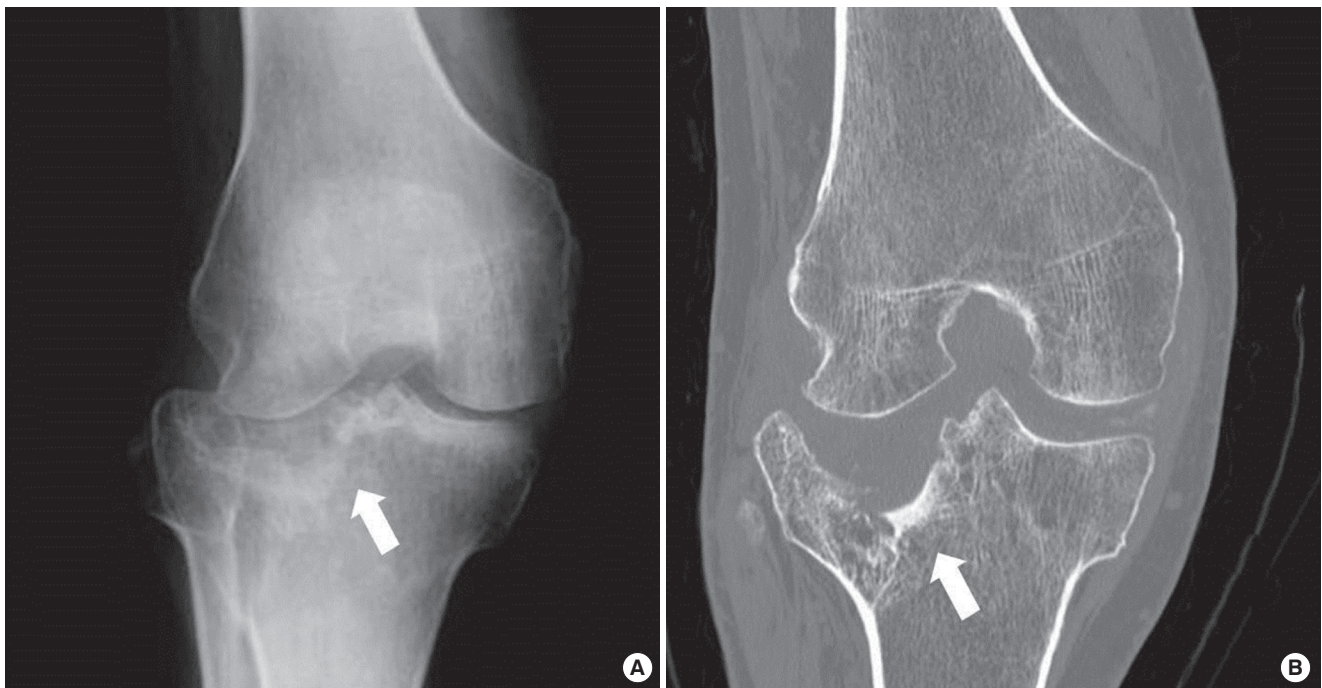


Figure 1. (A) Radiograph of the patient's right knee, showing degeneration of articular surface. White arrow indicates erosive bony lesion. (B) Computed tomography scan of right knee, showing degeneration of tibial joint plateau. White arrow indicates erosive bony lesion.



Figure 2. Radiograph of the patient's right ankle, showing degeneration of calcaneus bone. White arrow indicates erosive bony lesion.

toplasmic antibody 2.5 U/mL, and myeloperoxidase antineutrophil cytoplasmic antibody <1.0 U/mL. Serum and urine protein electrophoresis showed no specific results. The blood culture did not grow any organisms. Repeat electrocardiogram, chest radiographs, heart/abdominal ultrasound, and whole body CT scan showed no remarkable findings. The CT scan showed joint destructions of the right tibial plateau (Figure 1) and right calcaneus (Figure 2). An arthrocentesis of the knee was performed and microscopic examination of the fluid showed uric acid crystals, but no calcium pyrophosphate crystals or organisms.

Based on these results we considered that infection, collagen-vascular disease, or malignancy were all unlikely and a diagnosis of advanced erosive gout was suspected. First, the patient was treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine maintenance therapy (0.5 mg twice a day). Soon after treatment, his symptoms improved significantly with improvement in walking, gain in appetite, and resolution of fever and right knee/ankle pains. The laboratory abnormality of high inflammatory markers, including WBC, ESR, and CRP, showed normalization at follow-ups. The patient had an uneventful recovery and was transferred to the rehabilitation hospital.

DISCUSSION

Our case report suggests that advanced erosive gouty arthritis should be considered as one cause of fever of unknown origin. There are numerous differential diagnoses for a fever of known

origin; sometimes, extensive investigations are required.⁶⁾ As our patient complained of right knee and ankle pains, the possibility of septic arthritis or infective endocarditis was considered, but the joint fluid and blood culture did not grow any organisms.⁷⁾ However, the arthrocentesis revealed uric acid crystals, despite his blood uric acid level not being significantly elevated. Advanced erosive gout was therefore suspected, based on the results of the arthrocentesis and imaging tests. NSAIDs produced an initial resolution of the symptoms and colchicine therapy was added with a good clinical response, confirming a diagnosis of chronic gouty arthritis as a cause of his chronic fever and arthritis. Based on the clinical manifestation, blood test results, and imaging results, it was unlikely to be another condition, such as infectious disease, collagen vascular disease, or malignancy.

Advanced erosive gout is an uncommon manifestation of clinical gout and can have clinical presentations similar to those of rheumatoid arthritis or other inflammatory arthritis.^{1,2)} The gold standard for diagnosis of advanced erosive gout is to identify uric acid crystals in the synovial fluid from the affected joint, even during the asymptomatic inter-critical period or for patients in whom the diagnosis was not previously made.³⁾ Gouty tophi may be observed along the auricles of such patients and the aspirated fluid of the tophi may show urate crystals.

Hyperuricemia is known to be an important risk factor for developing gout,⁴⁾ but there is no consensus of the serum uric acid level that would predict a gouty attack and other factors may be involved in the development of gout, such as mental stress or dehydration.⁵⁾ Our patient also revealed only slightly elevated blood uric acid levels. Mandell⁸⁾ stated that uric acid greater than 6.8 mg/dL is the threshold for manifesting chronic crystal deposition because serum urate levels exceed urate solubility at that concentration.

The first line treatment of acute gout is NSAIDs. A low dose of oral colchicine (e.g., 0.5 mg once or twice per day) may be administered as a prophylactic maintenance therapy for preventing frequent gouty attacks. After resolution of the attacks, further treatment, including uricostatic agents (e.g., allopurinol), uricosuric drugs (e.g., benzbromarone), or uricolytic agents (e.g., rasburicase), in addition to modifications in dietary habits, are need to prevent long term complications.⁹⁾

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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