

Diagnosis and Management of Gout in Total Knee Arthroplasty

Michelle Buck ▼ Marjorie Delaney

Gout is a common arthritic condition that continues to increase in prevalence. Symptoms of gout include a rapid onset of pain, erythema, swelling, and warmth in the affected joint. These symptoms may mimic cellulitis, thrombophlebitis, and septic arthritis (J. S. Berger & M. M. Weinik, 2009); however, a definitive diagnosis can be obtained through joint aspiration and subsequent fluid analysis to assess for the presence of monosodium urate crystals. Gout can also be present after total joint replacement. Because of the similarity of symptoms to septic arthritis, the diagnosis may be missed. Gout may be present in a prosthetic knee or may coexist with septic arthritis. Therefore, analysis of knee aspirations should include cell count, gram stain, cultures, and an examination of the synovial fluid for crystals. The following case study discusses the complex issues involved in treating coexistent gout and infection in a prosthetic knee.

Introduction

Gout is an arthritic inflammatory disease resulting from the deposition of uric acid crystals (monosodium urate [MSU]) into joints and other soft tissues in the body. These crystals are formed when there is an elevated level of uric acid in the body (hyperuricemia) caused by either an overproduction or inefficient elimination of uric acid. The subsequent crystal deposits cause severe pain, erythema, and swelling in the affected joint and surrounding tissue. The incidence of gout is on the rise; according to a recent survey, gout has increased dramatically in the past 20 years affecting 8.3 million Americans (Zhu, Pandya, & Choi, 2011). Risk factors for increased urate accumulation include purine rich diets, alcohol consumption, advanced age, and male gender. Comorbidities such as metabolic syndrome, hypertension, cardiovascular disease, renal impairment, hyperlipidemia, and obesity are often present in patients with gout (Stamp & Chapman, 2013). Seventy percent of acute gouty attacks are in the great toe; however, the joints in the ankle, knee, finger, wrist, and elbow may also be affected (Suresh, 2005). In addition, gout has been known to occur after total joint replacement surgery including total hip and total knee arthroplasty (TKA). While this is an uncommon event, it is important

to recognize and differentiate the inflammatory response of gout from that of infection in joint replacement.

A recent literature review reveals 13 reported cases of gout after total knee arthroplasty (see Table 1).

Diagnosis of Gout

Acute gouty arthritis can be difficult to differentiate from septic arthritis (Archibeck, Rosenberg, Sheinkop, Berger, & Jacobs, 2001). Patients with either condition may present with joint pain, erythema, and swelling and can experience constitutional symptoms of malaise and fever. Attacks of gout frequently start in the early morning, waking the patient from sleep. Patients report the rapid development of severe pain (“worst ever”) and tenderness that reach their maximum within 6–24 hours of onset. Symptoms resolve spontaneously. This presentation is almost pathognomonic for crystal synovitis (Doherty, 2009). Because of the similarities in the presentation of gout to that of infection, a detailed patient history is essential.

Patients often report a history of gout in another joint or kidney stones. Direct joint trauma, dehydration, rapid weight loss, intercurrent illness, or surgery can all trigger acute gouty monoarthritis. The physical examination is generally the same for both gouty and septic arthritis with pain, erythema, swelling, and decreased range of motion. In gout, the clinical symptoms are caused by the formation of MSU crystals in the joints and soft tissues, elimination of the crystals “cures” the disease, thus making gout a true crystal deposition disease (Doherty, 2009). The presence of the gouty tophi around the joint and in the synovial membranes can become symptomatic and limit motion (Archibeck et al., 2001).

The only definitive means of differentiating between a diagnosis of infection and gout is by analysis of joint

Michelle Buck, APN, CNS, Cadence Physician Group/Orthopaedics, Warrenville, IL.

Marjorie Delaney, APN, FNP-BC, Cadence Physician Group/Orthopaedics, Warrenville, IL.

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TABLE 1. REPORTED CASES OF GOUT FOLLOWING TOTAL KNEE ARTHROPLASTY

Author (Year)	Age/ Gender	# of Years Postop From Original Surgery/Revision	Associated Infection	Previous History of Gout
Archibeck et al. (2001) (bilateral knees)	66/male	10 y	No	No
		12 y	No	
Archibeck et al. (2001)	88/female	9 y from revision	No	Yes
Berger and Weinik (2009)	39/male	2 y	No	Yes
Blyth and Pai (1998) (2 cases) ^a	58/male	4 mo	Yes	Yes
	52/male	4 d	No	Yes
Crawford, Kumar, and Shepard (2007)	58/female	3 mo	No	No
Fotker & Repse-Fotker (2010)	68/male	11 mo	No	Unknown
Freehill et al. (2010) ^a	77/female	10 y	Yes	Yes
Salin et al. (2008) (same patient)	50s/female	4 y from revision (left)	No	No
		4 y (right)	No	Yes (contralateral knee)
Salin et al. (2008) ^a	80s/female	11 y	Yes	Yes

aspirate. The fluid obtained from aspiration of the affected joint should be sent for evaluation of cell count, Gram stain, cultures, and crystal analysis (Archibeck et al., 2001; Fotker & Repse-Fotker, 2010). Serum uric acid levels may be obtained and used to confirm the diagnosis. Complete blood count, erythrocyte sedimentation rate, and C-reactive protein may be elevated with both infection and gout.

Analysis of joint fluid is the gold standard for diagnosis of gout. The identification of needle-shaped urate crystals under polarized light microscopy provides a definitive gout diagnosis (Chimenti & Hammert, 2012). During an acute attack of gout, the presence of MSU crystals has the highest diagnostic value (Zhang et al., 2006) (see Tables 2 and 3).

The misdiagnosis of septic arthritis following total knee replacement in a patient with gouty arthritis may lead to unnecessary surgical intervention including open debridement or component removal. Because it is so difficult to discern between a septic and gouty joint on initial presentation, the patient often undergoes an open debridement of the prosthetic knee joint. The presence of chalky white or yellow deposits upon examination of the synovium or bone are indicative of gout; however, this diagnosis can be confirmed only with histologic evaluation of these tissues. Prosthetic components can be retained if Gram stain and cultures from joint aspiration are negative and the components are

well seated. Five percent to 15% of patients with gout may present without uric acid crystals in the synovial fluid aspirate (Emmerson, 1983) (see Figure 1).

Review of Literature

Williamson, Roger, Petrera, and Glockner (1994) report on a patient who was admitted to the hospital and presumed to have an infected total knee arthroplasty. The synovial fluid revealed an elevated white blood cell count and was negative for crystals. The patient was taken to the operating room for irrigation and debridement and possible removal of the prosthesis. The prosthesis was found to be intact and there were no signs of infection; however, tophaceous, yellow deposits were found on the bone, the tibial component, and synovial tissue. Subsequent analysis of the tissue revealed needle-shaped crystals, consistent with gout.

There are three reported cases of coexistent infection and gout in patients following TKA (Blyth & Pai, 1998; Freehill, McCarthy, & Khanuja, 2010; Salin, Lombardi, Berend, & Chonko, 2008). All of these patients presented with classic signs of infection: pain, swelling, erythema, and warmth to the operative knee. Knee aspirations were performed and the synovial fluid appeared yellow and cloudy. The gram stains were positive and subsequent microscopic analysis revealed urate crystals. All of the patients were taken to surgery. Salin et al. (2008)

TABLE 2. CLASSIFICATION OF SYNOVIAL FLUID AND ASSOCIATED DISEASES

Effusion	Diseases
Noninflammatory	Osteoarthritis, trauma, osteochondritis, sickle cell disease, neuropathic, pigmented villonodular synovitis
Inflammation	Rheumatoid arthritis, systemic lupus erythematosus, Reiter's syndrome, ankylosing spondylitis, ulcerative colitis, psoriasis
Infection	Bacteria, fungi, mycobacteria
Crystal	Gout, pseudogout
Hemorrhage	Trauma, hemophilia, hemangioma, anticoagulant therapy, tumor, pigmented villonodular synovitis

Note. Synovial fluid effusions are classified into five diagnostic categories. The following tests can be performed on synovial fluid: visual examination, cell count, gram stain, culture, and polarizing microscopic crystal examination.

TABLE 3. TYPICAL LABORATORY FINDINGS FOR EACH CATEGORY OF JOINT DISEASE

Test	Normal	Noninflammatory	Inflammatory	Sepsis	Crystal	Hemorrhage
Clarity	Clear	Slightly turbid	Turbid	Turbid	Turbid	Bloody
Color	Yellow	Yellow	Yellow	Gray-green	Yellow-milky	Red-brown
Viscosity	High	Reduced	Low	Low	Low	Reduced
Mucin clot	Firm	Firm to friable	Friable	Friable	Friable	Friable
Clotted	No	Occasional	Occasional	Often	Occasional	Yes
White blood cell count/ μ L	0–200	0–2000	2000–100,000	50,000–200,000	500–200,000	50–10,000
% Polys	<25	<30	>50	>90	<90	<50
Glucose difference	0–10	0–10	0–40	20–100	0–80	0–20
Crystals	Absent	Absent	Absent	Absent	Present	Absent
Culture	Sterile	Sterile	Sterile	Positive	Sterile	Sterile

Note. Crystal identification aids in the diagnosis of joint disease. Monosodium urate crystals are seen in gouty fluids. Urate crystals are mainly needle-shaped and may be found within leukocytes.

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report that the patient had a polyethylene insert exchange as the components were found to be well fixed. However, prosthesis removal was required in the two other patients (Blyth & Pai, 1998; Freehill et al., 2010). Freehill et al. (2010) report that the arthrotomy revealed thick white fluid in the supra-patellar pouch and gutter; the synovium was hyperemic and boggy, and the femoral and tibial components were loose with bony destruction. In addition, areas of bone under the cement were found to be covered with topaceous white deposits.

Case Study

The patient is a 65-year-old woman with a complex medical history including gout, polyarticular septicemia of the right knee, left and right shoulders due to methicillin-susceptible *Staphylococcus aureus* (MSSA), chronic *Clostridium difficile* infection, and recent acute renal failure secondary to diuretics and *C. difficile*. Her

antibiotic suppression was being held for 2 weeks because of difficulty eradicating the *C. difficile*. During this time she was awakened from sleep because of severe right knee pain. Following 2 days of symptoms, she presented to physical therapy by which time the pain had decreased markedly. Two days later the patient was seen in therapy again and found to have redness to the anterior portion of her right knee. On inspection the knee showed a subcutaneous fluctuant area anteriorly, a surrounding 7-cm area of erythema and +1 effusion. The fluctuant area was aspirated and approximately 2 cc of pus was obtained. The knee joint was aspirated and approximately 20 cc of purulent-appearing fluid was obtained and sent for Gram stain, aerobic and anaerobic cultures, fungal and TB cultures, and cell count with differential and crystal analysis.

The patient was admitted for right knee arthritis with a differential diagnosis of sepsis and/or uric acid-induced arthritis. The aspiration was positive for uric acid crystals and few gram-positive cocci. The cultures were positive for MSSA. The patient's allopurinol dose was increased from 100 to 200 mg as her uric acid levels were elevated. The *C. difficile* was treated with vancomycin. She was taken to the operating room for irrigation and debridement and poly exchange of the right knee. The surgeon anecdotally reports that the intraoperative appearance of the tissue was that of infection. No obvious chalky deposits were appreciated. The patient was evaluated by the infectious disease service and was treated with 6 weeks of intravenous cefazolin (Ancef) via a peripherally inserted central catheter and had physical therapy/occupational therapy in the home. Patient seen in the office postoperatively reports reduction of pain and examination showed decreased erythema and increased motion.

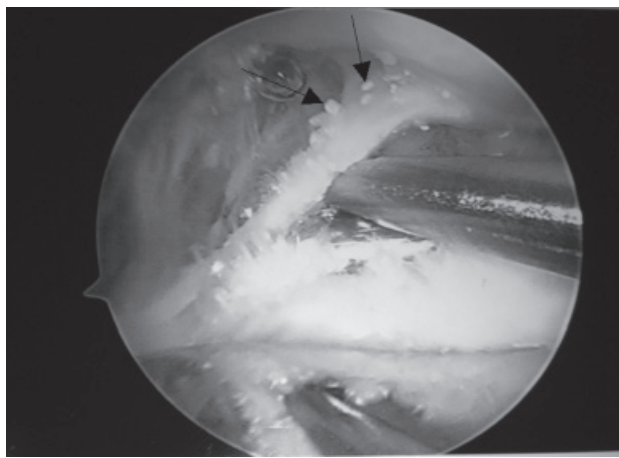


FIGURE 1. Arthroscopic image reveals crystals in the synovial tissue of a knee following total knee arthroplasty. In this case, a knee aspiration was performed preoperatively. Crystal analysis was not ordered because of the patient's history and physical examination.

Nonsurgical Management of Acute Gout

The primary goal of acute treatment of gout is to reduce pain and inflammation. In an orthopaedic setting, treatment with nonsteroidal anti-inflammatory drugs

(NSAIDs) should be initiated upon presentation. NSAIDs are the most commonly used first line treatment. Head-to-head studies show few differences between drugs (Cronstein & Terkeltaub, 2006). Prior to initiation of treatment with an NSAID, the patient's medical history should be reviewed to assess for any history of allergy or sensitivity to NSAIDs. Patient education should include information about proper administration and potential adverse effects of the medication prescribed.

Colchicine (now marketed as Colcrys) is commonly prescribed for treatment of acute gout in the primary care setting. The usual dose of colchicine is 0.6 mg, twice daily. The most common adverse effects of this medication include nausea, vomiting, diarrhea, anorexia, and abdominal cramps. The severity of these gastrointestinal disturbances is in relation to the amount of medication consumed. Patients who take higher doses of colchicine tend to have more adverse side effects; therefore, lowering the dose to once daily can help increase the tolerance of the medication.

Following resolution of the acute attack, primary care providers generally begin treatment for chronic gout management with allopurinol. Initially treatment begins with a low dose, titrating up as needed for long-term reduction of gouty flares. Continuation of colchicine and/or anti-inflammatory agents is recommended during adjustment of the allopurinol dose until the serum uric acid concentration has been normalized and no acute gouty attacks have occurred for several months.

Conclusion

Although relatively rare, gout should be considered in the differential diagnosis when patients present with a sudden onset of pain in their prosthetic knee joint. While the analysis of joint aspirate for crystals is the gold standard for diagnosis, it is essential for the orthopaedic nurse to obtain a thorough history and physical examination to determine the correct course of treatment.

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