Case report

Nonoperative Treatment of a Periprosthetic Gout Flare in the Setting of a Positive Alpha-Defensin Result

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Gout is a rare cause of pain after total knee arthroplasty, and its presentation can be difficult to distinguish from a prosthetic joint infection. We describe a patient with left knee pain that had a history of gout and left total knee arthroplasty. Synovial fluid demonstrated monosodium urate crystals and positive alpha-defensin assay. Surgery was not pursued given a low clinical suspicion for infection and negative cultures. Her symptoms improved and ultimately resolved. There are limited case reports of periprosthetic aseptic gout flare, and only one case of concomitant positive alpha-defensin assay and monosodium urate crystals in a patient treated surgically. This case raises the possibility that patients with periprosthetic crystal arthropathy and a positive alpha-defensin test can be managed nonoperatively in the appropriate setting.

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Introduction

Pain after total knee arthroplasty (TKA) presents as a diagnostic challenge. Persistence of pain leads to patient dissatisfaction, with about 10% of patients reporting unhappiness with their TKA [1]. There are many causes of a painful TKA, including aseptic loosening, malalignment, instability, or prosthetic joint infection (PJI). Given its devastating complications, infection must be ruled out. While aseptic loosening and malalignment may be diagnosed on imaging, a PJI diagnosis presents more complexity as it is based on physical examination, laboratory markers, and synovial fluid aspiration results.

The International Consensus Meeting (ICM) criteria include serologic, histologic, and intraoperative findings, and have become the gold standard to diagnose PJI [2]. The presence of a sinus tract or 2 positive periprosthetic cultures with the same organism are considered major criteria and diagnostic of PJI. The minor criteria incorporate a point system, with a score of <3 indicating no infection, 3–5 being inconclusive, and ≥6 indicating a PJI. An elevated serum C-reactive protein (CRP, >100 mg/mL in acute phase or >10 mg/mL in chronic phase) or elevated D-dimer (≥860 ng/mL) is given 2 points. An elevated erythrocyte sedimentation rate (ESR, >30 mm/h) is given 1 point. An elevated synovial WBC count (>10,000 cells/μL in acute phase or >3000 cells/μL in chronic phase), positive alpha-defensin (signal-to-cutoff ratio >1), or positive leukocyte esterase (++) is given 3 points. An elevated synovial polymorphonuclear percentage (>90% in acute phase or >70% in chronic phase) is given 2 points, a single positive culture is given 2 points, positive histology is given 3 points, and positive intraoperative purulence is given 3 points [2].

Prosthetic gouty arthropathy has been shown to resemble PJI in previous literature [3–12]. Periprosthetic gout can therefore be difficult to distinguish from infection for a multitude of reasons. In both scenarios, patients may exhibit warmth and erythema at the affected joint, have elevated inflammatory markers, and have elevated synovial cell counts or positive alpha-defensin. An acute gout flare leads to the phagocytosis of monosodium urate crystals by macrophages and neutrophils, leading to further activation of neutrophils [13]. Similarly, an infectious process leads to a cascade that recruits neutrophils to the site of infection. Given that alpha-defensin is a polypeptide secreted by neutrophils, an alpha-defensin assay can therefore become positive in both gout and infection.

There have been several cases of patients diagnosed with prosthetic gout arthropathy treated both operatively and nonoperatively [3–12]. However, alpha-defensin was not tested in these patients. There has been one case published demonstrating a positive synovial fluid alpha-defensin assay in a patient with gout who...
was treated surgically [12]. We believe this is the first case demonstrating a positive synovial fluid alpha-defensin test in a patient with gout treated nonoperatively. This patient provided informed consent for publication of this case report.

Case history

A 61-year-old female with a history of intermittently treated gout presented to the office with a 2-week history of atraumatic left knee pain. She reported pain with ambulation and at rest. She had a history of a left TKA 5 years prior and a right TKA 8 years prior. She used a cane for assistance with ambulation at baseline given her history of fibromyalgia and chronic back pain. She had a remote history of gout in bilateral feet, treated with nonsteroidal anti-inflammatories. Her risk factors for gout included obesity and hypertension treated with lisinopril-hydrochlorothiazide and metoprolol. However, she denied any recent medication adjustments, diet changes, gout attacks, trauma, or surgery. Serum uric acid obtained 3 years prior was within normal limits at 4.0 mg/dL (reference range: 2.3-7.6 mg/dL). She denied any recent illnesses, fevers, or chills.

On examination, the patient’s surgical incision on her left knee was well-healed without erythema or ecchymosis. There was a mild joint effusion with mild warmth and active range of motion from 0 to 95° with pain at the end range of motion. She was tender to palpation over the medial joint line. Otherwise, she was distally neurovascularly intact. Radiographs showed good component alignment without evidence of osteolysis (Fig. 1a and b). The serum inflammatory markers were within normal limits with CRP measured at 6.4 mg/L (reference range: <10 mg/L) and ESR measured at 14 mm/h (reference range: 0-20 mm/h). Serum uric acid was within normal limits at 3.7 mg/dL. Arthrocentesis yielded a cloudy, yellow-appearing aspirate. Synovial analysis revealed 4135 white blood cells/μL, with 69% neutrophils. Microscopy of the synovial fluid demonstrated monosodium urate crystals. The alpha-defensin (Synovasure PJI; Zimmer Biomet, Warsaw, IN) assay was positive. The resultant ICM criteria score was 3, indicating an inconclusive decision on whether this patient had a PJI. However, given the lack of systemic signs of infection, lack of erythema, persistence of baseline ambulatory status, and ability to participate with range of motion testing, there was a low clinical suspicion for infection. Therefore, despite the elevated nucleated cell count and positive alpha-defensin assay, surgical intervention was not pursued, and antibiotics were not administered.

Subsequently, the patient began colchicine 0.6 mg daily and oral indomethacin 75 mg every 12 hours for 1 week. Her rheumatologist then prescribed her a methylprednisolone 4-mg dose pack and allopurinol 100 mg daily for 3 months. The patient’s knee effusion resolved, and her pain with ambulation improved while awaiting the culture results, which were negative 4 days from the arthrocentesis. She continued to progress well clinically and had painless knee range of motion from 0 to 100° at the 1-year follow-up visit. She ambulated pain-free with a cane and was pleased with her progress.

Discussion

Although the prevalence of gout in native joints is well understood, its prevalence in prosthetic joints is likely underreported. The purpose of this case report was to expand upon the limited literature regarding crystal arthropathy in the prosthetic knee given its clinical importance. If periprosthetic crystal arthropathy is misdiagnosed as a PJI, a patient may undergo unnecessary surgery [3,14].

There have been limited case reports in the literature of patients with simultaneous gout flares and infection, [3-5] but there have only been 10 reported cases of aseptic gout flare after TKA [5-12]. In these previous reports, all without alpha-defensin testing, most patients underwent debridement and implant retention (DAIR) and were treated postoperatively with a combination of nonsteroidal anti-inflammatories or allopurinol [5-8]. Another patient underwent DAIR after an aspiration demonstrated monosodium urate crystals, and the lateral flow assay for alpha-defensin was positive [12]. Cultures remained negative, and the patient had successful resolution of her symptoms after allopurinol treatment and 14 days of antimicrobial therapy. There are only 3 known cases of patients with periprosthetic gout that were treated nonoperatively, and importantly, none of these patients underwent alpha-defensin testing [10,11].

Differentiating crystal arthropathy and PJI remains challenging given their overlapping features. Clinically, patients with either condition may exhibit limited joint range of motion, erythema, swelling, and fever. Traditional biomarkers, such as CRP and ESR, may be elevated in both settings [11,14]. Synovial cell counts from a

![Figure 1. Anteroposterior (a) and lateral (b) radiographs of the left knee in a 61-year-old female who had undergone a cemented left total knee arthroplasty 5 years prior.](image-url)
joint aspirate may also overlap. Synovial cell counts have been reported to range from 1100 to 4000 cells/µL in chronic PJ and >20,000 cells/µL in acute PJ [11]. In native joints, synovial cell counts for gout range from 2500 to greater than 50,000 cells/µL [11]. Given the rarity of reported gout after TKA, cell counts for this condition are not well studied. The Musculoskeletal Infection Society therefore acknowledges that their criteria may be inaccurate in crystalline deposition arthropathy [15].

Newer biomarkers have gained popularity in their utility in diagnosing PJs. Alpha-defensin, an antimicrobial peptide secreted by neutrophils, can be detected by an enzyme-linked immunosorbent assay (ELISA) or a lateral flow assay [16,17]. Studies demonstrate that these tests have a sensitivity of 69%-100% and specificity of 94%-98% for PJ [16,17]. Therefore, the updated ICM definition of PJ now includes alpha-defensin as part of its minor criteria [2].

Unfortunately, there has been a paucity of cases regarding the validity of alpha-defensin testing in the setting of periprosthetic crystal arthropathy. Therefore, there is no clear algorithm in treating a patient whose synovial fluid aspiration is positive for both crystals and alpha-defensin. The only previously reported patient with crystal arthropathy and a positive alpha-defensin assay underwent DAIR [12]. Multiple extended cultures taken before antibiotic administration remained negative, thus strengthening the diagnosis of gout. Therefore, this patient may have improved without operative management. Chen et al. described 2 patients with periprosthetic gout that had symptoms of infection [11]. These patients were not tested for alpha-defensin, but given their overall clinical picture and aspiration results, conservative management with antibiotic medications was started. Given their rapid improvement in symptoms, Chen et al. proposed adding a trial of antigout medication to the algorithm of diagnosing PJ, especially in patients with an aspiration positive for crystals [11].

The limitations of this case report include the absence of several diagnostic tests, the length of culture incubation, and the length of patient follow-up. For a complete diagnostic workup incorporating the ICM criteria, the patient could have been tested for serum D-dimer and would have needed to undergo surgical intervention. However, a serum D-dimer test was not routine practice at this institution at the time of the patient’s encounter, and as nonoperative treatment was pursued, intraoperative purulence and histology were not obtained. Given the possibility of superimposed PJ on gout, the cultures could have been grown for a longer period of time. However, this patient’s aspiration cultures were only grown for 4 days. Finally, the patient only followed up in the office until 1 year after her aspiration, and given that her pain and swelling resolved, she has not followed up since that time.

Summary

We described a case of a gout flare that mimicked PJ. Given the possibility of a superimposed PJ, this patient could have undergone surgical intervention. However, aseptic gout flare needs to always be considered. Although it is possible that our patient had a concomitant infection, the fact that cultures remained negative and the patient improved without antibiotics makes it less likely. The patient’s positive alpha-defensin assay brings into question the specificity of alpha-defensin in making the diagnosis of PJ in the setting of periprosthetic crystalline-induced arthropathy. As opposed to the previously reported patient with gout who underwent surgery and antibiotics after a positive synovial fluid alpha-defensin test, [12] this case demonstrates that a patient with crystal arthropathy and a positive alpha-defensin test can be treated successfully without surgery in the appropriate clinical setting.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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