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Original Contributions

DOES THE PRESENCE OF CRYSTAL ARTHRITIS RULE OUT SEPTIC ARTHRITIS?

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□ **Abstract—The objective of this study was to determine the incidence of septic arthritis in the presence of joint crystals. A retrospective study was conducted at a university tertiary care referral center. The study population included all patients with synovial fluid crystals in the joint aspirate sent to the laboratory during the 7-year study period. Septic arthritis was defined as a positive synovial culture. Of the 265 joint aspirates containing crystals, 183 (69.0%) contained gout crystals, 81 (30.6%) contained pseudogout crystals, and 1 (0.4%) contained both. Four (1.5%) of the aspirates had positive cultures. The mean synovial WBC of the 4 samples with concomitant crystals and septic arthritis was 113,000 (95% confidence interval [CI] 72,700–153,200), which was significantly higher than the entire population at 23,200 (95% CI 19,400–27,000; $p < 0.01$). Of note, all 4 patients with concomitant disease had significant co-morbidities and synovial WBC counts greater than 50,000. Septic arthritis and acute crystal-induced arthritis can occur simultaneously; there were 4 cases (1.5%) of concomitant disease in our study population. The presence of crystals cannot exclude septic arthritis with certainty.** © 2007 Elsevier Inc.

□ **Keywords—septic arthritis; crystal arthritis; synovial fluid; gout; pseudogout**

INTRODUCTION

It is clinically difficult to distinguish the difference between a swollen joint due to crystal arthritis and a swollen joint due to septic or bacterial arthritis (1). This distinction is critical because septic arthritis is associated with a much higher rate of morbidity (2). Bacterial infection in the joint can cause significant joint destruction (3).

Arthrocentesis and synovial fluid analysis are used to diagnose both conditions (4). The presence of crystals may confound the synovial fluid interpretation and lead the clinician to diagnose isolated crystal arthritis when co-existing septic arthritis may go unrecognized. The joint fluid white blood cell (WBC) count is often used to help distinguish inflammation from infection (5). Crystal arthritis, such as gout and pseudogout, can elevate the synovial WBC count. It is not clear whether the presence of crystals (one definite diagnosis) nullifies the value of the WBC count in excluding the possibility of septic arthritis.

We conducted a retrospective study of all patients with joint fluid containing crystals (specifically, monosodium urate and calcium pyrophosphate crystals) to determine the incidence of concomitant septic arthritis and to determine the value, if any, of the synovial WBC count to diagnose septic arthritis in the presence of crystals.

METHODS

Study Design

This was a retrospective study conducted at an urban, university tertiary care referral center with 50,000 annual

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Table 1. Characteristics of Study Population with Synovial Fluid Crystals

	Total (95% CI) n = 265	Gout (95% CI) n = 183	Pseudogout (95% CI) n = 81
Mean age	65.0 (63.2–66.9)	63.0 (61.0–65.0)	76.0 (73.4–78.6)
Male:female ratio	179:86	143:40	36:45
Mean synovial WBC	23,200	23,000	23,600
Concomitant septic arthritis	4 (1.5%)	1 (0.5%)	3 (3.7%)

CI = confidence interval; WBC = white blood cell count.

adult emergency department (ED) visits. Our local institutional review board approved the study.

Study Setting and Population

The study population included all adult patients (18 years of age and older) with crystals in the joint aspirate sent to the laboratory during the study period of January 1996 to December 2002.

Study Protocol

The hospital medical database was queried for all joint fluid samples containing crystals during the 7-year study period. Using a structured, standardized form, the following data were explicitly extracted from the patients' medical records: age, gender, joint aspirated, synovial fluid culture, Gram's stain, synovial WBC count, type of crystals, and the discharge diagnosis. Septic arthritis was defined a priori as a positive synovial fluid culture. Based on chart review, fluid samples that were found to originate from a bursa were excluded. In addition, all repeat joint aspirates on the same admission were excluded. A more detailed past medical history and hospital course were obtained on patients with concomitant crystal arthritis and septic arthritis.

RESULTS

The database identified 365 fluid samples containing crystals. Eighty patients had a repeat arthrocentesis of the same joint and 20 patients were found to have fluid sent from a bursa rather than a joint; these 100 patients were excluded. Of the remaining 265 synovial fluid samples, 183 (69.0%; 95% confidence interval [CI] 63.5–74.6%) contained monosodium urate crystals (gout), 81 (30.6%; 95% CI 25.0–36.1%) contained calcium pyrophosphate crystals (pseudogout), and 1 (0.4%) contained both.

The average age and male to female ratio (M:F) were significantly different between the group containing gout crystals and the group containing pseudogout crystals (Table 1). The gout group was younger than the pseudogout group (mean age of 63.0 years [95% CI 61.0–65.0] compared to a mean age of 76.0 years [95% CI 73.4–78.6], $p < 0.01$), respectively. The gout group had a male predominance with a M:F ratio of 143:40 and the pseudogout group had a female predominance with a M:F ratio of 36:45. The mean synovial WBC count for the entire population was 23,200 (95% CI 19,400–27,000) and was the same for both crystal arthritis groups at approximately 23,000.

Four (1.5%; 95% CI 0.0–3.0%) of the crystal-containing samples had positive cultures (2 beta-hemolytic streptococcus and 2 staphylococcus aureus). One sample contained monosodium urate crystals and 3 samples contained calcium pyrophosphate crystals. The mean synovial WBC count of the 4 samples with concomitant crystals and septic arthritis was 113,000 (95% CI 72,700–153,200), which was significantly higher than the entire population at 23,200 ($p < 0.01$). Of note, all 4 patients with concomitant disease had significant co-morbidities and synovial WBC counts > 50,000. See Table 2 for details of these 4 patients.

DISCUSSION

This retrospective study evaluated synovial fluid samples with crystal arthritis over a course of 7 years at a single institution. During this time, there were 4 cases of concomitant crystal and septic arthritis. Based on these findings, the presence of crystals in the synovial fluid cannot conclusively rule out a septic joint. These data are consistent with case reports throughout the medical and rheumatology literature (6–17); of note, the emergency medicine literature has not specifically addressed the issue of simultaneous septic and crystal arthritis.

Although concomitant disease does occur, we found it to be a rare occurrence; only 1.5% of all synovial fluid samples with crystal disease had concomitant bacterial growth. With such a low incidence, it is not reasonable to pursue the possibility of septic arthritis in all case of crystal arthritis. However, in our study, the incidence increases to 11% if we limit the suspected cases to those

Table 2. Patients with Concomitant Crystal Arthritis and Septic Arthritis

	Age (years)	Sex	Joint	Synovial WBC	Crystal	Organism	Co-morbidities	Treatment
#1	72	M	Ankle	125,000	MSU	GBS	Chronic steroids (COPD), IDDM, gout	OR, gentamicin and vancomycin then penicillin
#2	49	M	Knee	68,750	CPP	GBS	TKR, AIDS	OR, cefazolin
#3	57	M	Hip	164,000	CPP	MSSA	NIDDM, right hip DJD	OR, cefazolin then oxacillin
#4	62	M	Knee	94,000	CPP	MRSA	IDDM, CAD, concurrent fem-pop bypass graft infection	OR, ceftriaxone then vancomycin

MSU = monosodium urate; CPP = calcium pyrophosphate; GBS = group B streptococcus; MSSA = methicillin-sensitive staphylococcus aureus; MRSA = methicillin-resistant staphylococcus aureus; COPD = chronic obstructive pulmonary disease; IDDM = insulin-dependent diabetes mellitus; TKR = total knee replacement; AIDS = autoimmune deficiency syndrome; NIDDM = non-insulin dependent diabetes mellitus; DJD = degenerative joint disease; CAD = coronary artery disease; fem-pop bypass = femoral-popliteal bypass; OR = operating room washout.

with a synovial WBC count $>$ 50,000 and 22% if we limit the suspected cases to those with a synovial WBC count $>$ 100,000. If all 35 patients with crystal arthritis and a synovial WBC count $>$ 50,000 in our sample population were admitted and treated with antibiotics until cultures were negative, none of the 4 patients with septic arthritis would have been missed. Approximately 9 patients would have to be treated to help 1 patient. An elevated synovial WBC count may still be a useful marker for septic arthritis, even in the setting of crystal disease. As a precautionary note, very low synovial fluid counts have also been reported; Yu et al described 10 cases of concomitant septic and gouty arthritis with a synovial WBC count $<$ 50,000 (3 of which were less than 6,000/mm^3) in a total of 30 hospitalized cases over 15 years at one institution (6).

Why septic and crystal disease would occur concomitantly is not entirely clear. One theory is that the inflammation created by joint sepsis may release crystals from the synovial membrane, a process referred to as 'crystal shedding and strip mining' (6,18,19). Alternatively, crystal arthritis (similar to rheumatoid arthritis) may be a predisposition to a joint space infection; Lee et al recently reported an unprecedented high rate of gouty arthritis (43.5%) among a series of patients with septic arthritis of the ankle (20,21).

The fact that the subset of patients with pseudogout was significantly older and the subset of patients with gout had a high male to female ratio is consistent with previous findings and the epidemiology of both diseases (22,23). The disproportionately high incidence of septic arthritis with pseudogout (3 of 4 cases in our study) as opposed to gout has not been previously reported. A review of all cases in the literature of concomitant disease by Baer et al. in 1986 revealed 10 cases of gout and 13 cases of pseudogout in association with a septic joint (15). Given the much lower incidence of pseudogout than gout in the general population, it is possible that pseudogout may be a more significant risk factor than gout for concomitant joint infection.

LIMITATIONS

By far, the greatest limitation of this study is the small number of patients with concomitant septic arthritis and crystal arthritis. Although all 4 cases of concomitant disease had WBC counts above 50,000, given the low prevalence of disease, calculations of negative and positive predictive value using a WBC count cut-off of 50,000 would be misleading. Similarly, although 3 of 4 cases of septic arthritis were in the setting of pseudogout, the low number of patients prevents us from making any conclusions comparing the incidence of septic arthritis between gout with pseudogout.

Our study relied upon synovial fluid cultures to define infection. This strict definition of septic arthritis may have resulted in some missed cases of joint infection, such as those patients with positive blood cultures or those with pus seen on joint aspiration or during washout in the operating room. Patients with septic arthritis but no growth on synovial fluid culture may also be the ones with less impressive synovial WBC elevations and more subtle clinical examinations.

Finally, this was a retrospective study at a single institution. A prospective study with a broader definition of septic arthritis at multiple institutions would yield a more accurate incidence of concomitant septic arthritis and crystal arthritis.

CONCLUSION

The incidence of concomitant septic arthritis and crystal disease was 1.5% in this 7-year retrospective study. The presence of synovial crystals is not sufficient to rule out

septic arthritis. Although rare, septic arthritis and acute crystal-induced arthritis can occur simultaneously.

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