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CLINICAL COMMENTARY

Evaluation of the Hot Swollen Joint: Is It Septic?

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The major concern for patients presenting with a monoarticular arthritis is the possibility of septic arthritis. A septic joint is a true emergency condition with a very low prevalence 2 to 10 per 100,000 person-years but carries very high morbidity and mortality approximating 7-15%.¹ Given these potential consequences, clinicians should always consider the possibility of a septic joint when evaluating monoarticular arthritis.

Unfortunately, there are few clear guidelines to help clinicians when they suspect a septic joint on clinical grounds. Interpretation of synovial fluid after aspiration can be misleading as normal, inflammatory, and infectious processes may have similar findings. In addition, the presence of crystals does not rule out a septic joint as it will only definitively rule in the presence of a (concomitant) crystal arthropathy. The following three illustrative cases demonstrate this diagnostic conundrum.

Case 1

A 64-year-old male with a history of gout, hepatitis C cirrhosis, significant alcohol use, previous IV drug abuse, and opioid dependence on methadone presented to his primary care doctor for severe right lower extremity pain. The patient noted sudden onset of acute leg swelling and pain about 1 day after riding his bicycle. At that time, he had a temperature of 100.7 and a noticeable left knee effusion. He had a negative ultrasound to evaluate for deep vein thrombosis, and he went home, instead of to the Emergency Department as instructed, because he felt better. He returned to the ED the next day for worsening pain with weight-bearing. At that time, his temperature was 99.1. He had prior gout flares of his foot and toes but not in the knee. He had a small scrape on lower leg from bike-riding, distant from the knee, without apparent overlying infection.

On exam, his right knee joint was described as irritable with a small effusion, surrounding soft tissue swelling, without apparent cellulitis. X-ray demonstrated a small effusion. Serum labs showed no leukocytosis and a low uric acid level. A knee aspiration was attempted but was dry. The patient was sent home with colchicine with a presumptive diagnosis of pseudogout based on the serum tests.

Four days later, the patient returned for worsening pain and cellulitis. The orthopedics consultant was able to aspirate the joint, which demonstrated a wbc >61k without crystals. A presumptive diagnosis of septic joint was then made, later confirmed by cultures.

Case 2

A 43-year-old male with end-stage renal disease on hemodialysis, diabetes, and history of bilateral chronic osteomyelitis of his feet, presented with right knee pain for one month. Two weeks prior, the patient had finished a 2-week course of doxycycline for a right diabetic toe ulcer. In the ED, the patient was noted to have a right knee effusion and no foot ulcers. X-ray of the right knee demonstrated a small suprapatellar joint effusion. He was afebrile, and labs did not show a leukocytosis. The patient underwent aspiration, which yielded visibly non-purulent fluid with wbc 16k (94% neutrophils), a negative gram stain, and no visualized crystals. The patient was discharged home with a plan for rheumatology referral.

The rheumatologist upon receiving the referral electronically reviewed the patient's records. He noted a remark from the lab that a few *Staphylococcus aureus* colonies were present despite lack of growth for 24 hours in the culture and an initial negative gram stain report.

Patient was advised to return to the ED immediately but did not return until about 1 week later. The final culture of the fluid had not yielded any reportable growth. He was afebrile and ambulatory, although with severe pain. Right knee exam showed irritability. Serum labs showed no leukocytosis with sedimentation rate of 130 mm/hr (normal: 0-29). Repeat knee aspiration showed straw colored, slightly opaque fluid, which yielded wbc >37k with 90% neutrophils. The gram stain was negative and there was no evidence of crystals in the fluid. A presumptive diagnosis of septic joint was made, and patient was taken to the operating room for wash out. Final cultures grew out *S. aureus*.

Case 3

A 63-year-old male presented to the Emergency Department complaining primarily of recurrent dyspnea and chest pain, as well as acute right wrist pain. He had a complicated past history, including chronic pulmonary infiltrates, mycoplasma avium complex (MAC) pneumonia, and prior intravenous and oral antibiotics at various times over the past few months, last given about 1 month ago. He also had a history of chronic knee and shoulder osteoarthritis without a history of joint effusions. He was currently taking prednisone 40 mg daily for presumed temporal arteritis. However, his most recent ESR level of 103 mm/hr had not improved since starting steroid therapy.

On exam, he was afebrile with some swelling and erythema over the volar and lateral aspect of his right wrist and irritability. He had a positive Finkelstein's sign. Previous x-rays of his knee and shoulder had shown chondrocalcinosis, although current x-rays of his wrist did not show chondrocalcinosis. Rheumatology felt it was difficult to distinguish between a tenosynovitis and/or a monoarticular arthritis. The patient's wrist was aspirated, which showed wbc 90k with 91% neutrophils, calcium pyrophosphate crystals, and negative gram stain. Given his complicated history and risk for infection, he was continued on intravenous antibiotics until final cultures yielded no growth. His final diagnosis was pseudogout without infection.

Discussion

In patients presenting with monoarticular arthritis, the first critical decision is whether or not to be concerned about a septic joint. Next, one must decide if the joint should be aspirated, which is not always a simple procedure without risks. Even after aspiration, initial synovial fluid results may not definitively exclude a septic joint.

A review entitled "Does this adult patient have septic arthritis?" enumerates several risk factors that increase the likelihood of a septic joint.¹ These include: age >80; history of diabetes, HIV, or rheumatoid arthritis; history of recent joint surgery or prosthesis, skin infection, and synovial aspirate > 25K or >90% PMN. However, the article also notes that though the presence of risk factors is helpful, their absence does not rule out disease.

One study found fever was negatively correlated with likelihood of a septic joint (likelihood ratio [LR] 0.67, 95% confidence interval [CI], 0.43-1.00.). This may be due to the fact that fever is nonspecific and occurs in inflammatory arthropathies, such as gout and rheumatoid arthritis. However, few would argue that the presence of a fever should not raise some concern for infection. The American College of Rheumatology Guidelines Committee recommends arthrocentesis on patients with an established history of arthritis who present with fever and new joint pain or effusion.² The British Society of Rheumatology guideline remarks that "the presence or absence of fever is not a reliable indicator of an infected joint." Their Grade B recommendation is that patients with a short history of a hot, swollen, tender joint – or joints with restriction of movement – should be regarded as having septic arthritis until proven otherwise.³ Their definition of "short" is not clearly specified, although they mention that a patient would typically present in less than 2 weeks.

Serum lab studies like WBC, ESR, and CRP have high sensitivity but poor specificity. For serum WBC count < 10,000, for ESR < 30, and for CRP < 100 mg/L, the -LRs for septic arthritis were 0.28, 0.17, and 0.44, respectively; wide 95% CIs render the tests useless for changing pre-aspiration probability for septic arthritis.² History and physical exam findings such as range of motion and degree of swelling, have not been adequately studied and cannot be well standardized. However, many physicians including specialists often use clinical gestalt in combination with serum testing in their

medical decision-making, which is not supported in the literature.

This overall conundrum on the work up of a swollen joint is highlighted in the following statement:⁴

"Given the wide range of possible presentations of septic joint and the massive implications of mismanagement, appropriate investigation and interpretation of results are crucial. Having established that the history and physical examination cannot reliably exclude the diagnosis, especially in certain populations, providers must rely on diagnostic testing. [Although] commonly drawn (and requested by consultants) ...retrospective and prospective trials have shown that there are no values for serum markers for which one could rule in or rule out septic arthritis," thus concluding that serum lab values are too flawed to be helpful, and aspiration is required in all cases.

That being said, there may be some cases in which one can consider forgoing aspiration. The British Society of Rheumatology guidelines in their algorithm states aspiration is not needed when there is definitive alternative diagnosis, such as inflammatory arthritis based on previous history and exam. Certainly, a history of recurrent swelling in the same joint is highly relevant. Patients with known effusive arthropathies and recurrent attacks in the same joint are often treated with aspiration and/or steroid injections in an outpatient setting. Podagra (i.e., first metatarsophalangeal joint swelling) is a hallmark presentation of gout and is rarely aspirated.³

Statistically, the odds will always favor a non-septic joint diagnosis. For example, the incidence of gout alone in the USA is over 60 cases per 100,000.⁴ Septic arthritis occurs in only 2 to 10 cases per 100,000 person-years.⁴ Unfortunately, this may reinforce a practice of premature diagnostic closure for clinicians who forgo aspiration. That is because the likelihood a clinician is encountering a patient with septic joint is comparatively much lower than an alternative diagnosis, so it provides a somewhat false affirmation of the provider's ability to clinically exclude a septic joint.

Based on these reviews, any new acutely hot swollen joint, exclusive of classic podagra, must be aspirated to exclude a septic joint. In a patient with a history of inflammatory arthropathy where there is confidence that the episode is a recurrent flare in the same joint, one can likely choose to exclude septic arthritis based on clinical grounds.

In Case 1, there was a concern for septic joint based on the patient's history of gout, however, without a prior episode in the affected joint. He did not have risk factors that would heighten his risk by criteria as listed in the JAMA article, although alcoholism and IVdrug use can be considered risk factors. His wound was not mentioned as infected, although that was likely the portal for his infection. The initial presence of a fever may heighten concern, but the fact he defervesced at the next visit without intervention, can be suggestive of a lesser likelihood of infection.

The decision to consider septic arthritis and to aspirate was appropriate. However, after the failed aspiration attempt, the alternative diagnosis of pseudogout based on serum lab values, i.e., no leukocytosis and low uric acid levels, was flawed. For this patient, either another attempt by a specialist or image-guidance and/or empiric treatment would have been the most appropriate next step. Ultimately, once there is any index of suspicion for a septic joint, aspiration and testing of fluid is the only definitive way to exclude an infected joint.

After a joint has been aspirated to evaluate for an infection, interpretation of synovial fluid studies poses yet another conundrum. This is illustrated in Case 2 and Case 3. The gold standard for diagnosis is a positive culture, which takes days to result. Cell count and gram stain are two more readily available studies, which clinicians are obligated to interpret to make a diagnosis. Higher cell counts increase the likelihood of an infected joint, and a count of $>50\text{k}/\text{mm}^3$ is an often cited threshold. However, there is no absolute cut-off that can rule out a septic joint. A synovial WBC (sWBC) $>25\text{k}/\text{mm}^3$ has a positive LR of 3.2 and sWBC $>50\text{k}/\text{mm}^3$ has a positive LR of 4.7. A high percentage of neutrophils $>90\%$ would favor a septic joint, although there is some debate on its reliability.⁵ The sensitivity of a gram stain is only about 30 to 50 percent.²

Both patients in Case 2 and Case 3 have heightened risk factors for infection and a possibility of misleading synovial study results. Case 2 was a diabetic patient with recurrently infected foot ulcers who recently finished a course of antibiotics, without a previous history of inflammatory arthropathy. The patient in case 2 also had an unimpressive initial synovial studies with a negative gram stain and sWBC $< 25\text{k}$, although a neutrophilia of $>90\%$. Because of his risk factors, empiric treatment for a septic joint with intravenous antibiotics should have been considered.

Case 3 was a patient on high-dose steroids and also had a recent course of antibiotics. His fluids studies had sWBC $> 50\text{k}$ with $>90\%$ neutrophils and the presence of calcium pyrophosphate crystals. One could dismiss his other synovial findings by attributing his symptoms to a new diagnosis of pseudogout. However, both the sWBC and PMN% are highly suggestive of a septic joint. The lack of improvement while taking steroids for presumptive temporal arteritis also argues against the diagnosis of pseudogout. Treatment with empiric intravenous antibiotics was appropriately decided, while awaiting culture results that ultimately excluded a septic joint diagnosis.

In the past, synovial glucose and protein levels had been routinely ordered; however, these have been found to lack utility. One possibly promising test is the synovial lactate, using a threshold above 10 mmol/L to rule in the diagnosis with four studies showing positive LR > 2.4 .

Overall, although positive results can amplify suspicion, the definitive way to exclude the diagnosis of septic arthritis remains elusive. Therefore, when there is a high index of suspicion, one must empirically treat as a septic joint until culture results prove otherwise.

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