

Case patient. A 52 year old man presents to the ED with two days of a painful left knee, limiting ambulation. He has no past medical history and takes no medications, but admits to frequent excessive alcohol use. He has a low grade fever (100.7° F), and his exam is remarkable only for a warm, swollen and red left knee. He vigorously resists your attempts to move the joint, but can move it a bit, painfully, on his own.

What questions do you have for this patient?

What is your differential diagnosis?

How will you pursue a diagnosis?

Acute Arthritis

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Initial Questions

1. *Is there a history of trauma?* Can result in internal derangement (e.g. meniscal pathology, fracture) or hemarthrosis. In osteoporosis or other bone disease, joint pathology can be caused by lesser trauma. Traumatic pain is appreciated immediately, as compared with other forms of arthritis, where onset is subacute.
2. *Does the patient have underlying joint disease?* A diseased joint is at higher risk for septic arthritis. Other risk factors include increased age (>80), DM and immunocompromise (i.e. HIV).
3. *Is the arthritis mono- or polyarticular?* Bacterial septic arthritis is generally monoarticular. Only 10-20% is polyarticular, usually seen in the setting of RA, connective tissue disease or sepsis. This contrasts with gonococcal arthritis, in which 40-70% of patients will have two to three joints involved.

Differential Diagnosis

1. **Infection:** Usually occurs when bacteremia seeds the joint space. Also occurs in the setting of joint surgery or other iatrogenic instrumentation.

Non-gonococcal bacterial arthritis (NGBA): Associated with greatest potential for joint destruction. One very painful, red, warm, swollen joint (hip or knee) that developed over a short period of time. Most patients have a fever, but chills and spiking temperatures are not common in adults. Most common organisms:

S. aureus, group A β -hemolytic streptococci. *S. pneumoniae*: adults

Group B, C and G streptococci: immunocompromised patients, secondary to GI/GU infections.

Gram negatives: IVDU, older adults, immunocompromise

Anaerobes: prosthetic joints, DM, extremity wounds, GI cancer

Gonococcal arthritis (GA): Most common bacterial arthritis in sexually-active young adults in the US. Untreated gonococcal dissemination is a prerequisite for arthritis. Usually, more than one joint is involved and symptoms may migrate. Patient may also have rash (vesicular/pustular lesions on arms, legs and trunk) and symptoms of tendon involvement. <50% of gonococcal joints have an effusion. Females > males.

Mycobacterial: A monoarthritis of gradual onset. Most common in weight-bearing joints (e.g. spine). Significant joint effusions may be present, but other signs of inflammation may be absent. Pulmonary TB is present in only 1/2 of patients with bone and joint involvement. PPD usually positive. Usually seen in HIV.

Fungal: In normal hosts, manifests as a rapid-onset, self-limited polyarthritis. Skin lesions (e.g. erythema nodosum) can be key to diagnosis. Usually seen in HIV.

Lyme disease: Suggested by endemic exposure, erythema migrans, polyarthralgias/viral symptoms, Bell's palsy). The knee is frequently involved, with swelling > pain.

Viral: includes parvovirus, hepatitis B and C and rubella

HIV: Arthritis can be seen with acute HIV infection alone, but is also a risk factor for all types of infectious arthritis.

2. Crystal arthropathies: Includes gout and calcium pyrophosphate disease. Recurrent monoarthritis, typical symptoms or location, or evidence of chondrocalcinosis on plain films are most suggestive of crystal-related arthritis. Fever can be present and high (in one series, 10% had T >39°).
3. Osteoarthritis: Affects the elderly, is chronic, and worsens with activity. Joint swelling can develop with worsening of pain.
4. Osteonecrosis: Also referred to as *avascular necrosis*. Common in the femoral head. Consider in sickle cell disease or other hemoglobinopathies, steroid use, EtOH, elderly diabetics.
5. Hemarthrosis: Most common in patients with bleeding diatheses (e.g. hemophilia) or on anticoagulation.
6. Systemic disease: e.g. RA, reactive arthritis, endocarditis

Diagnosis

Physical examination. A patient with intact, non-painful ROM is unlikely to have septic arthritis. Deep joints are the hardest to assess.

Joint aspiration and synovial fluid interpretation. Should be performed in every patient with monoarthritis. Ultrasound can be useful if no clear effusion present. Send fluid for cell count and differential, Gram stain and culture and crystal examination. Only 1-2 mL necessary.

Cell count and differential. >50K WBCs suggestive of inflammation or infection. If WBC >90% PMNs, consider infection or crystal disease.

Gram stain. May be negative in the setting of recent antibiotic therapy.

Synovial fluid cultures: Yield improved with direct inoculation into bottles at bedside. No organism identified in 50% of clinical cases of septic arthritis.

Blood cultures. Cultures positive in 50-70% of NGBA, but rarely in gonococcal arthritis (GU cultures 70-90% positive in this setting).

The utility of laboratory tests.

Peripheral WBC is often normal, but ESR usually >30 if a joint is septic. In one study, CRP was elevated in 98% of septic joints. There are no guidelines for the use of ESR and CRP. Other serologies should be checked only when the clinical history is compelling and more common diagnoses have been ruled out.

Imaging

Plain films not unreasonable in most cases of acute arthritis. In trauma, they rule out fractures and other bony lesions. In infectious arthritis, they can be useful in assessing for chronic osteomyelitis and establishing a baseline. They may demonstrate effusions or erosions. CT or MRI useful if plain films are negative, as they are more sensitive for bony changes. Bone scan useful in osteomyelitis and positive in 60% of septic arthritis; false-positives seen in OA.

Synovial biopsy and arthroscopy. May be necessary if initial workup unrevealing, but by the time a biopsy arranged, empiric therapies should already have been started. May reveal the diagnosis in the setting of Mycobacterium, Neisseria, Chlamydia, sarcoidosis, amyloidosis, malignancy.

Synovial fluid PCR. May be useful in identifying organisms that did not grow by other means. Expensive, but quicker than culture.

The prosthetic joint. Pain and swelling of the artificial joint is a true orthopedic emergency! Crystal arthritis in this setting is rare. Aseptic joint loosening is the most common cause of pain and requires prosthetic replacement.

Treatment

General principles

- Do not give antibiotics before synovial fluid and blood cultures have been obtained. Following these tests, treat empirically based on risk factors and Gram stain (see below)
- Use vancomycin if patient has risk factors for MRSA (institutionalization, incarceration, recent hospitalization, IVDU)
- Joint lavage (washout) is required in the setting of suspected septic arthritis. In our system, patients with a septic joint are most often admitted to Orthopedic Surgery. Patients will be taken directly to the OR for washout if the synovial fluid WBC is >100K OR if the synovial fluid WBC is >50K in association with clinical indicators (WBC >11, ESR >20, fever, erythema, rapid onset, inability to bear weight). Orthopedic Surgery does not perform serial arthrocentesis in lieu of washout, but historically, rheumatologists may opt to do this in certain cases. Open drainage is also an option in cases of inaccessible joints (e.g. hips) or when synovectomy is required.
- Earlier surgical intervention is optimal when the following are present: long duration between symptom onset and treatment, complicated joint site (including prosthesis), extremes of age, underlying illness, immunosuppressive drugs, presence of osteomyelitis.

When should a patient be admitted? All patients with septic arthritis should be admitted initially because IV therapy will be required. Serial exams are also useful in assessing the need for operative intervention.

Which antibiotic should I use empirically? Guided by Gram stain. See Sanford. Ceftriaxone is a good choice for sexually active patients or polyarticular arthritis and in penicillin allergy, it is likely safe given a lower risk of cross reactivity as a 3rd-generation cephalosporin. A fluoroquinolone is another option.

How long do I treat? Most agree that 3-4 weeks of therapy is likely adequate. IV therapy should be given initially, but if the pathogen can be treated with an agent with good PO bioavailability, a portion of the course (1-2 weeks) may be oral. There is no basis for intraarticular antibiotics. Approximately 40% of patients with non-gonococcal joint infections will have some residual restriction of joint function, but gonococcal arthritis responds very well and very rapidly to treatment.

Case Follow Up

The patient was admitted to the hospital for further evaluation. Blood and urine cultures were obtained. Although he denied sexual activity since the death of his wife four years prior, GC and Chlamydia cultures were sent. Peripheral WBC was 16. Arthrocentesis was performed easily at the bedside. The patient was started empirically on ceftriaxone.

Labs revealed a synovial WBC of 52K, most of which were PMNs. Gram stain was positive for GPCs in clusters. Synovial fluid and blood cultures grew *S. aureus*, sensitive to nafcillin. GC and Chlamydia were negative. Orthopedics performed an arthroscopic washout. TTE was negative for evidence of

vegetations. It was felt that the likely source of his arthritis was a prior trauma to the lower leg. He received 2 weeks of IV nafcillin at home, and 2 additional weeks of oral levofloxacin, resulting in resolution of symptoms and signs of inflammation.

Clinical Pearls

1. A swollen, painful joint is infected until proven otherwise.
2. Always obtain synovial fluid for analysis. Septic joints are not always red, warm and painful.
3. Patients can have more than one joint process simultaneously (e.g. gout and septic arthritis), and as such, it is best to evaluate each joint broadly at first presentation.
4. A detailed history and physical examination, including a thorough skin exam, is essential in diagnosis.
5. If septic arthritis is suspected, the patient should be assessed for sources of infection (e.g. blood cultures, urine cultures).
6. If gonococcal infection is suspected, in addition to blood and urine cultures, obtain cervical, urethral, rectal and pharyngeal cultures.
9. Consult Orthopedic Surgery in all cases of septic arthritis.
10. Test for HIV in settings where the pathogen is atypical (including mycobacterium, fungi)

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Last update: April 14, 2005/JAB

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