Bone and joint infections

Catherine J Mathews

Abstract

The joint is a common site of musculoskeletal infection in adults. Septic arthritis is the most serious, although not the most frequent, cause of a hot, swollen joint or joints. The diagnosis rests principally on clinical suspicion. Investigation of suspected joint sepsis is urgent in order to avoid significant morbidity and mortality. This review covers the aetiology, pathogenesis, clinical features, investigation and management of native joint sepsis in adults, highlights the gaps in the evidence base regarding its pharmacological management and suggests some areas for future research. It also briefly covers osteomyelitis, which is much more common in young children than adults.

Keywords Antibiotics; arthritis; infection; MRCP; osteomyelitis; sepsis

Key points

- A septic joint is associated with considerable morbidity and mortality. If the diagnosis is suspected, investigation and management are urgent
- Septic arthritis does not always present with fever, raised white cell count, raised inflammatory markers or even positive microbiological cultures. It is diagnosed on a clinical basis
- Always aspirate a joint in which sepsis is suspected unless that joint is prosthetic, in which case seek orthopaedic advice
- Always commence antibiotic therapy if septic arthritis is suspected, but obtain microbiological specimens first
- Always ask for local microbiological guidance when choosing appropriate antibiotic therapy

Septic arthritis

The presentation of a patient with one or more hot, swollen joints has a broad differential diagnosis (Table 1). Making the diagnosis of joint infection can be challenging even for practitioners experienced in the management of musculoskeletal disease. These patients should be considered a medical emergency because septic arthritis, although not the most common cause, is a serious condition that carries a significant morbidity and mortality. If treatment is delayed or suboptimal, the outcome can be irreversible joint destruction. Moreover, the mortality is up to 11%, increasing to as high as 50% in polyarticular sepsis.

Epidemiology

Estimates of the incidence of septic arthritis are limited by several difficulties relating to research methodology.[1] Most data are generated from retrospective cohorts. Prospective studies are difficult to conduct because of the infrequent nature of the condition. It is also difficult to categorize the disease consistently as, even in patients in whom septic arthritis is strongly suspected, the subsequent diagnosis might not be firmly established microbiologically. Newman's 1976 modified criteria are those most commonly used to define the diagnosis and require one of four conditions to be met:

- isolation of a pathogenic organism from an affected joint
- isolation of a pathogenic organism from another source in the context of a hot, red, swollen joint where sepsis is suspected
- clinical features of joint sepsis and turbid synovial fluid in the presence of previous antibiotic therapy
- pathological features suspicious of septic arthritis at postmortem.

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The incidence of definite and probable septic arthritis in Western Europe is 4–10 per 100,000 people per year.[2] The incidence of septic arthritis is rising globally, and this has been linked with an ageing population, increased use of immunosuppressive agents, musculoskeletal prostheses and surgical procedures.

Septic arthritis can affect all age groups but is more common in elderly and very young individuals. Further risk factors for the development of septic arthritis are summarized in Table 2. It is much more likely to develop in a joint that is already abnormal. Previous joint damage inflicted by rheumatoid arthritis, osteoarthritis or crystal arthritis predisposes individuals to sepsis in the affected joint(s). Prosthetic joints are also at higher risk of superimposed infection. Other documented risk factors include intravenous drug abuse, alcoholism, diabetes mellitus and skin infection or ulceration.

Instrumentation of a joint, either using a needle or by surgical arthroscopy, has been implicated as a cause of septic arthritis, but studies suggest this is relatively rare. The incidence has been quoted at about four cases per 10,000 injections, and a prevalence of 14 per 10,000 arthroscopic procedures. In the context of immunosuppression for inflammatory arthritis, disease-modifying pharmacological treatment can predispose some patients with rheumatoid arthritis to joint sepsis. The introduction of biologic agents has seen an increased risk of septic arthritis in this cohort. The absolute risk is still small, but in the case of anti-tumour necrosis factor (TNF)-α therapy, there is an approximate doubling of the incidence that is attributable to the drug itself.

The most frequent causative agent identified microbiologically in septic arthritis is *Staphylococcus aureus*, in all age and risk groups.[2] The second most common organisms are other Gram-positive bacteria, predominantly streptococci. In certain risk groups, other organisms rise in prevalence, although *S. aureus* and streptococci remain the most common. Intravenous drug abusers have an increased susceptibility to atypical bacteria and fungal infections.

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Differential diagnosis of the acute hot joint

Differential diagnosis	Clues to this diagnosis
Septic arthritis	Short history, 1–2 weeks, pain and restriction of movement of the affected joint(s)
Crystal arthritis (gout, pseudogout)	First metatarsophalangeal joint suggests gout. History of diuretic use, particularly in older women, suggests pseudogout
Trauma	History, bloody joint aspirate
Haemarthrosis	History, bloody joint aspirate
Systemic inflammatory arthritis (rheumatoid arthritis, seronegative arthritis)	Systemic symptoms, multiple joint involvement ± axial skeleton; psoriasis; inflammatory bowel disease; gastrointestinal or genitourinary infection; conjunctivitis/uveitis
Extra-articular pathology (tenosynovitis, bursitis)	Full range of movement of the joint, visible inflammation of extra-articular structures

Table 1

Gram-negative organisms are more frequently seen in elderly individuals, which may be a result of co-morbidities including urinary tract infections and skin ulceration.[2] Gonococcal infection, although frequently quoted as a cause of septic arthritis in young adults, has been established as a relatively rare cause of so-called dermatitis–arthritis syndrome in North America and Europe. Studies using polymerase chain reaction methods have revealed that *Neisseria meningitidis* is the most common cause of this syndrome.[1]

Hospital-acquired meticillin-resistant *S. aureus* (MRSA) infection is on the increase as a cause of septic arthritis, particularly in patients who have other risk factors for infection. New strains of community-acquired MRSA have also been identified in both Europe and North America, and these have different antibiotic sensitivities from hospital-acquired organisms.[1]

Pathogenesis

There are two ways by which infection can be introduced into a joint. The most common route is via haematogenous spread.

Risk factors for the development of septic arthritis

- Underlying joint pathology (e.g. rheumatoid arthritis, osteoarthritis)
- Prosthetic joint
- Low socioeconomic status
- Intravenous drug abuse
- Alcoholism
- Diabetes mellitus
- Previous intra-articular injection or instrumentation
- Cutaneous ulceration
- Immunosuppression

Table 2

Less commonly, a joint can be directly inoculated by organisms either as a result of trauma, or iatrogenically via needling or arthroscopy. In patients who are immunosuppressed or who have had invasive procedures, an established bacteraemia is more likely and can result in established joint infection, particularly if the patient has a joint that is already damaged.

Key advances have been made in understanding the pathogenesis of septic arthritis through work in experimental mouse models of both staphylococcal and streptococcal disease. Genetic manipulation of these animal models has revealed that the elimination of host factors including macrophage-derived cytokines (e.g. lymphotoxin-α, TNF-α, interleukin (IL)-1 receptor) and anti-inflammatory cytokines (e.g. IL-10) can increase the severity of septic arthritis as well as causing increased morbidity and mortality. Conversely, the absence of IL-4 appears to confer a protective effect. Bacterial factors including proteinaceous cell wall components and bacterial adhesins appear to modulate bacterial virulence. Data from animal models indicate that considerable variability exists from one pathogen to another.[3]

Clinical features

The diagnosis of septic arthritis principally rests on the clinical features. Typically, individuals with septic arthritis present with a short, 1–2-week history of one or more red, painful, restricted joints. Presentation can be more insidious if fungal or mycobacterial pathogens are causative.

Large joints are more likely to be affected than small ones, with the lower limb being more commonly affected than the upper limb. Although septic arthritis is often thought of as affecting only one joint, most studies report that up to 20% of patients have a polyarticular presentation. In patients with underlying rheumatic disease, the infected joint typically shows signs that are out of proportion to the disease activity detected in other joints.

Symptoms of systemic upset are not a prerequisite for the diagnosis of septic arthritis. Fever and rigors at presentation occur much less commonly than might be expected, and the diagnosis of septic arthritis must not be ruled out on the basis of their absence.

Laboratory investigation

No single investigation has anything approaching 100% sensitivity for the diagnosis of septic arthritis. For this reason, the diagnosis principally rests on clinical suspicion. To maximize the chances of confirming the diagnosis and obtaining a causative organism together with its antibiotic sensitivities, the affected joint(s) must be aspirated.[4]

Synovial fluid, if it is obtained, can be the key to diagnosis and should be sent for Gram stain and culture. Gram staining of synovial fluid identifies the pathogenic organism in 50% of cases, rising to 67% after culture.[2] Joint aspiration should always be performed before starting antibiotic therapy, and the aspirate sent fresh to the laboratory for processing.

Blood should also always be cultured to maximize the microbiological yield.[4] One study has shown that blood cultures were positive in 24% of cases in which synovial fluid had revealed a causative organism. More telling, however, was the 9% of cases in which synovial fluid culture was negative but

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