The clinical presentation of prosthetic joint infection

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Prosthetic joint infection (PJI) complicates ~1% of arthroplasties but accounts for considerable morbidity. Both the timing and features of PJI can vary widely. Patients may present with early (≤3 months post-operatively), delayed (3–24 months) or late disease (>24 months). They may be acutely unwell with systemic signs of sepsis or describe only a chronically painful joint with or without sinus formation. Diagnostic criteria as proposed by the Infectious Diseases Society of America and the Musculoskeletal Infection Society highlight the importance of joint sampling to obtain histological and robust microbiological evidence. Staphylococcus aureus and coagulase-negative staphylococci account for >50% of infections. Early infections are likely to have been acquired intra- or peri-operatively, whereas late infection is usually haematogenous in origin. Acute joint inflammation suggests the presence of intra-articular free-living bacteria, whereas chronic infections are associated with the formation of biofilm at the bone–cement or bone–prosthesis interface. The most significant risk factors predisposing to PJI are previous operation on the index joint, previous arthroplasty at a different site, American Society of Anesthesiologists’ grade 2, 3 or 4, body mass index >25, malignancy and procedure duration <2 or >4 h.

Keywords: implant-related infection, septic arthritis, bone and joint infection

Introduction

The diagnosis of prosthetic joint infection (PJI) can be challenging, in part due to the variability and non-specific nature of the presenting symptoms. Prompt recognition is important, however, given that diagnostic delay can result in worsened functional outcome and the need for more complex surgical intervention to achieve cure.

Presenting features

A classification system for PJI was proposed by Coventry in 1975 and then modified by Fitzgerald et al. in 1977. Infection is defined as ‘early’ when presentation is within 3 months of prosthesis implantation, ‘delayed’ when presenting between 3 and 24 months and ‘late’ if presenting beyond 2 years. More recently, several authors have proposed more complex PJI classification systems to encompass host status, bone defect and anatomo-pathological features. Furthermore, Romano et al. have formulated a seven point classification that can be applied to any bone and joint infection, with the addition of aetiology/pathogenesis, responsible microorganism and also infection, callus and stability data when PJI is considered. Patients’ symptoms form a spectrum from acute, with rapid-onset joint pain, swelling and wound purulence with or without systemic features of infection, to chronic, with grumbling discomfort, decreased range of movement and/or sinus formation and discharge. This spectrum can be simply displayed as a 2×2 table (Figure 1).

Although early infections typically have a more acute presentation, this is not always the case and late PJI can present with sepsis and bacteraemia. In one study of infections diagnosed in the first year after total hip or knee arthroplasty, the most common symptoms were purulent discharge (72%), pain (42%), wound erythema (42%) and fever (38%). Sinus tract formation was only reported in 5% and systolic hypotension (<90 mmHg) in 6%. Blood markers of inflammation [erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP)] may or may not be elevated. Plain radiographs can be normal but may show joint effusion in acute cases. In delayed or late presentations, examination of serial films is helpful. Loosening of prosthetic material is seen in PJI but can occur in the absence of infection (Figure 2). Formation of new periosteal bone and the presence of a transcortical sinus tract are more specific features but are rarely present. Around 15% of prostheses revised for loosening are found to be infected.

Microbial aetiology

Early and delayed PJI likely reflects the introduction of microorganisms at the time of joint arthroplasty, whereas late presentations reflect seeding of the joint following haematogenous spread of bacteria from another body site. Furthermore, the mode of presentation is related to the pathogenesis of the infection, with acute joint inflammation reflecting the presence of numerous intra-articular organisms in planktonic (free-living) phase. In contrast, more indolent symptoms are produced by the chronic presence of a lower number of sessile (adherent) organisms, often in a slow growth phase and protected from host defences by the ability to persist intracellularly and/or the excretion of exopolysaccharides that
coalesce to form biofilm and promote tissue destruction. Quantitative studies and the yield from clinical samples suggest that, in chronic infection, the majority of organisms are found at the interface membrane between bone and prosthesis or cement (unpublished data from our institution). This is supported by histological studies.

A review of 10 published case series comprising data from 2187 specimens confirmed staphylococci to be the most frequently cultured organism in PJI, with coagulase-negative species and Staphylococcus aureus accounting for almost equal proportions (24% and 26%, respectively). In the UK, methicillin-susceptible strains now account for a greater proportion than methicillin-resistant ones. In a retrospective cohort study of PJI conducted across 10 hospitals in Australia between 2006 and 2008, streptococci, enterococci and diphtheroids were isolated in 8%, 3% and 2% of cases, respectively, whereas Gram-negative organisms collectively accounted for 10%. Polymicrobial cultures were reported in 16% and in 6% no organism was grown. A large Swedish study compared the microbiology of early, delayed and late infections complicating total knee arthroplasty. Although the representation of pathogens was similar to the above across all groups, the percentage of polymicrobial infections was highest and the culture-negative rate lowest in early PJI. Unsurprisingly, when acute haematogenous cases were analysed, S. aureus was isolated in 68%.

### Risk factors

The Mayo Clinic in Minnesota has recently proposed a scoring system for the prediction of PJI. The factors found significant in multivariate analysis were previous operation on the index joint, previous arthroplasty at a different site, American Society of Anesthesiologists’ grade 2, 3 or 4, body mass index >25, malignancy and procedure duration <2 or >4 h. Other suggested risk factors include superficial surgical site infection, revision arthroplasty, advanced age, malnutrition, skin disease, diabetes mellitus and rheumatoid arthritis (RA). Patients with RA tend to be younger and present earlier post-operatively than those with other indications for arthroplasty. There appears to be a further increased risk of PJI in those RA patients undergoing antitumour necrosis factor α treatment, which is not seen in those receiving disease-modifying antirheumatic drugs.

Bacteraemia predisposes to haematogenously derived PJI and the rate of occurrence may be as high as 34% when S. aureus is isolated from blood cultures. Consequently, it is important to minimize the use of intravascular devices in patients with joint prostheses. Of note, invasive dentistry has not been shown to increase the risk of PJI and hence antibiotic prophylaxis is not indicated for such procedures. Moreover, the range of organisms that colonize the oral cavity are different from those responsible for post-arthroplasty infection. Several studies have looked for correlation between particular risk factors and the causative organism in PJI. Patients in whom Gram-negative bacteria are isolated have been found to be older, and to present earlier, when compared with those from whom Gram-positive species are cultured. No differences in presentation or demographics were found when cases with culture-negative PJI were compared with those with culture-positive disease; however, the former were more likely to have received antimicrobials in the 3 months prior to diagnosis. The spectrum of microorganisms isolated from RA patients does not differ significantly from those in matched non-RA cohorts, but there is an increased contribution of opportunistic pathogens such as non-tuberculous mycobacteria in immunosuppressed solid organ transplant recipients.

### Definition of PJI

Both the Infectious Diseases Society of America (IDSA) and the Musculoskeletal Infection Society in the USA have published...
definitions of PJI. The latter states that a definite PJI exists when: (i) a sinus tract that communicates with the prosthesis is present; OR (ii) a pathogen is cultured from two or more separate tissue or fluid samples from the affected joint; OR (iii) four of the following six are true: (a) elevated ESR and CRP; (b) elevated synovial white blood cell count; (c) elevated synovial polymorphonuclear cell percentage; (d) pus is present at operation; (e) a pathogen is cultured from one tissue or fluid sample; and (f) more than five neutrophils per high-power field (HPF) in five HPFs on histological analysis of periprosthetic tissue at 400× magnification. The IDSA document provides additional microbiological diagnostic detail and comments on the quality of evidence and hence strength of recommendation for each criterion.

**Illustrative case studies**

**Case 1 (delayed acute PJI)**

A man in his mid 40s with no other past medical history underwent a right knee arthroplasty in 1997 for post-traumatic arthritis secondary to a football injury. He underwent a single-stage revision arthroplasty in late 2011, because of persistent joint stiffness and patella baja (abnormally low-lying patella). No problems were detected at 2 months follow-up. Thirteen months later he presented to the emergency department with a 1 day history of severe joint pain following a minor fall 2 weeks previously. He was systemically well and had a CRP of 20. Plain radiograph showed an effusion but no evidence of loosening. An aspirate was taken and due to patient preference he was discharged pending the result. Three days later he was admitted acutely unwell with fever, hypotension, vomiting and worsening knee pain. An emergency debridement, antibiotics and implant retention including exchange of the rotating hinge liner was performed. He had a stormy post-operative course requiring intensive care admission, inotropic support and two further washouts. The joint aspirate, blood cultures and operative samples all grew methicillin-susceptible S. aureus. He was treated with intravenous (iv) flucloxacinil and oral rifampicin, the former being changed to iv ceftriaxone once he was fit for discharge. Six weeks of iv therapy was followed by oral ciprofloxacin and rifampicin, both to be continued for a minimum of 6 months. He was well at 3 months follow-up.

**Case 2 (early chronic PJI)**

A lady in her late 70s with a background of osteoarthritis and ischaemic heart disease underwent a right hip arthroplasty in early 2013. On the first post-operative day she experienced a non-ST elevation myocardial infarction requiring antiocoagulation with aspirin, clopidogrel and dalteparin. After 1 week, significant bruising around the arthroplasty wound was documented and 5 days later an offensive discharge was noted. The patient was systemically well and afebrile and had a CRP of 47. Plain radiograph was reported as normal. Surgical debridement revealed intra-articular pus but the prosthesis was stable. The femoral head was removed and exchanged. *Proteus mirabilis* was grown from all operative samples and empirical antibiotic therapy with vancomycin and meropenem was rationalized to iv amoxicillin. She will receive 6 weeks parenteral therapy and then the same antibiotic by mouth to complete a total of ≥6 months.

She was discharged 1 week post-operatively and remained well at 2 months follow-up.

**Summary**

Wide variability in both the mode and timing and presentation of PJI presents a diagnostic challenge for the clinician. Risk factors such as previous arthroplasties, obesity, underlying malignancy, diabetes and RA should be sought on evaluation of suspected cases. Non-invasive investigations play a limited role as neither blood markers of inflammation nor plain radiographs are sufficiently specific; hence the need for joint sampling to obtain histological and robust microbiological evidence. Staphylococcal species are the pathogens cultured in the majority of PJIs, whether arising as a consequence of intraoperative inoculation or blood-borne dissemination from another body site.

**References**


