New Definition for Periprosthetic Joint Infection

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Over the last few years, periprosthetic joint infection (PJI) has moved to the forefront of complications following total joint arthroplasty. The 3 articles published in the supplement, "Managing Surgical Site Infection," that accompanies this issue of *The American Journal of Orthopedics* elegantly highlight some of the challenges we face related to this serious complication. Dr. Froimson has highlighted the evidence behind some of our practices, while Dr. Barnes provides insight into the economic burden of PJI on health care. The challenge of diagnosing PJI is well outlined by Dr. Garino, as is the lack of a "standard" definition for PJI.

Recently, the Musculoskeletal Infection Society convened a workgroup to evaluate the available evidence and propose a definition for PJI. The intention of the workgroup is to propose a definition for PJI that can be adopted universally by physicians, surveillance authorities (including the Centers for Disease Control and Prevention), medical and surgical journals, the medicolegal community, and all involved in the management of PJI. It is hoped that this definition will be used as the "gold standard" against which new diagnostic tests for infection will be measured, although it is recognized that, as new tests become available, this definition too may need to evolve.

Definition of Periprosthetic Joint Infection

A summary of the recommendations were published recently in orthopedic journals and are outlined here (Figure).

Considerations

Microbiologic Testing

It is imperative that tissue for culture be obtained from representative periprosthetic tissue or fluid. In order to limit the risk of contamination, each sample should be taken with separate, sterile instruments. The definition of phenotypically identical organisms should be based upon phenotypic similarities and in vitro antimicrobial susceptibility testing since confirmation of genetic identity is not routinely performed on clinical isolates. It is recommended that at least 3, and no more than 5, periprosthetic specimen culture samples are taken and incubated in an aerobic and anaerobic environment. Fungal and mycobacterial cultures should not be done routinely, but rather reserved for higher risk scenarios. The time of culture incubation has not been standardized yet. Isolation of a single low virulent pathogen (such as coagulase negative *Staphylococcus*, *Propionibacterium acnes*, or *Corynebacteria*) in the absence of other criteria, is not felt to necessarily represent a definite infection. Isolation of a single virulent organism, however, such as *S aureus*, may represent a PJI. Furthermore, recent evidence has identified that certain tests, such as Gram stain of periprosthetic tissue or fluid are not sensitive for diagnosing PJI.[1]

Serum Tests

Based on previous publications, an erythrocyte sedimentation rate (ESR) of greater than 30 mm/hr and a C-reactive protein (CRP) level greater than 10 mg/L would represent elevated levels. [2,3] However, it is important to note that there are variations in measuring these markers between laboratories. Furthermore, the level of these serum markers is affected by age, gender, and medical comorbidities of the patient. It also has been reported that these markers can be elevated for approximately 30 days to 60 days in the immediate postoperative period.[4,5]

Synovial Tests

Multiple studies have provided thresholds for synovial white blood cell (WBC) count and synovial neutrophil percentage (PMN%) in the differential. In the chronically infected knee

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A DEFINITE PROSTHETIC JOINT INFECTION (PJI) EXISTS WHEN:[a]

1. There is a sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from 2 or more separate tissue or fluid samples obtained from the affected prosthetic joint; or
3. When 4 of the following 6 criteria exist:[b]
   a. Elevated serum erythrocyte sedimentation rate and serum C-reactive protein concentration,
   b. Elevated synovial white blood cell count,
   c. Elevated synovial neutrophil percentage (PMN%),
   d. Presence of purulence in the affected joint,
   e. Isolation of a microorganism in 1 culture of periprosthetic tissue or fluid, or
   f. Greater than 5 neutrophils per high power field in 5 high power fields observed from histological analysis of periprosthetic tissue at 400 x magnification.

[a]The panel acknowledges that, in certain low-grade infections (eg, *Propionibacterium acnes*), several of these criteria may not be routinely met despite the presence of PJI.
[b]Please note that a PJI may be present if less than 4 of these criteria are met.

Figure. Definition of periprosthetic joint infection as established by the Musculoskeletal Infection Society Workgroup.

arthroplasty, these values have been reported from 1,100 to 4,000 cells/μL and 64% to 69%, respectively. [6-8] In patients with acute periprosthetic knee infections (less than 3 months from index surgery or from the onset of symptoms), the level of synovial cell count and PMN% are much higher (approximately 20,000 cells/μL and 89%, respectively). The level of synovial fluid cell count and PMN% in the infected hip arthroplasty has not been well delineated. A sole study has provided a threshold of 3,000 cells/μL for leukocytes and 80% for PMN% for the infected hip arthroplasty.[3] None of these studies have included patients with underlying inflammatory arthropathies and related diseases. Research is currently proceeding to provide more definitive thresholds for all patients.

Histology

Examination of periprosthetic tissues for evidence of neutrophils traditionally has been conducted by specially trained musculoskeletal pathologists. Histological examination consequently may be operator dependent. It is, therefore, incumbent on the surgeon to ensure that their pathologist is in agreement with the diagnostic criteria for periprosthetic infection. When examining for the presence of neutrophils, the histopathologist should disregard neutrophils entrapped in superficial fibrin or adherent to endothelium or small veins. Also, caution should be exercised in quantifying neutrophils in patients where elevated neutrophils might be expected, such as a recent periprosthetic fracture or an inflammatory arthropathy.

Future Developments

This proposed definition was based on evidence supporting the role of various tests in diagnosis of PJI that are available in the literature. There are numerous other tests in evaluation, including the measurement of CRP from the synovial fluid,[9] synovial leukocyte esterase,[10] and sonication of explanted prosthesis,[11] as well as molecular techniques, such as polymerase chain reaction,[12] and other molecular markers, including interleukin-6.[13-15]

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