The Infected Total Knee Arthroplasty Part 1: Identification and Diagnosis in the Primary Care Setting

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Deep infection represents one of the most devastating complications of total knee arthroplasty, imposing heavy emotional and financial tolls on the patient, the physicians involved, and society as a whole. Often, the primary care physician is the first physician a patient sees when problems with total knee arthroplasty arise. Knowledge of the clinical presentation of arthroplasty infection and a high level of suspicion on the part of the primary care physician may speed the diagnosis and treatment of infection and ultimately improve the outcome of a patient with an infected total knee arthroplasty.

This is the first in a 2-part series on infected total knee arthroplasty. Part 1 provides an overview of the epidemiology for infection of total knee arthroplasty and discusses evaluation, diagnosis, and classification of infection from a primary care physician's perspective. Part 2 in the series, to be published in the February 2006 issue of *Hospital Physician*, discusses management of infected total knee arthroplasty from a surgical perspective.

TAKE HOME POINTS

- The key to successful management of an infected arthroplasty is an expeditious diagnosis.
- Physicians should have a high level of suspicion for infection in any patient presenting with problems concerning their arthroplasty.
- A clear, concise history and appropriate radiologic and laboratory work-up, including arthrocentesis, are combined to make the diagnosis.
- A positive culture of joint aspirate is the most helpful finding, but it is not required to make the diagnosis.
- Empiric use of antibiotics in a painful total knee arthroplasty is discouraged until the diagnosis has been confirmed.
- Immediate referral to an appropriate orthopedic surgeon is imperative once infection of a total knee arthroplasty is diagnosed or suspected.

EPIDEMIOLOGY

Although most studies report a 1% to 2% incidence of infection of total knee arthroplasty, studies have shown an incidence as high as 12.4% in certain patient populations.[1–8] At the Mayo Clinic, 1.2% of 3000 consecutive primary total knee arthroplasties developed infection.[6,9] Bengtson and colleagues[1–3] reviewed data from the Swedish Knee Arthroplasty Project, which revealed an infection rate of 1.7% after total knee arthroplasty performed for osteoarthritis and a 4.4% infection rate for procedures performed for rheumatoid arthritis (RA) in a series of 12,118 primary total knee arthroplasties.

Risk factors for infection in total joint arthroplasty have been identified (**Table**). In a study by Wilson et al,[8] patients with RA, skin ulceration, and a history of previous surgical procedures showed a statistically significant increase in infection rate. There was also a trend towards infection in obese patients, those with recent urinary tract infections, and patients taking oral corticosteroids.[8] In a large retrospective review, Peersman et al[10] also determined an increased risk in patients with diabetes, poor nutrition, hypokalemia, and those who smoked. Increased operative time also was found to be a risk factor.

Although infection can occur at any time, the risk is highest within the first 3 months after the index operation. Despite the best preventative efforts, infection inevitably will occur following total knee arthroplasty in

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Table. Risk Factors for Infection in Total Knee Arthroplasty

Medical conditions
Diabetes
Obesity
Hypokalemia
Rheumatoid arthritis
Urinary tract infection
Operative technique
Prolonged operative time (ie, > 2.5 h)
Other factors
Immunosuppressive therapy (ie, cortisone use)
Malnourishment
Smoking
Skin ulceration
Previous surgery

a certain number of patients. Although risk factors should heighten suspicion for infection, the lack of such risks should not cause complacency in diagnosis.

DIAGNOSIS

History and Physical Examination

A high index of suspicion is needed to diagnose infection after total knee arthroplasty. A combination of patient history and physical examination and various laboratory and radiographic studies is required for diagnosis (**Figure**). A patient presenting with an acute, painful, fulminate infection shortly after total knee arthroplasty is rarely observed; more commonly, infection is less obvious. Persistent, moderate pain or stiffness after total knee arthroplasty should always alert the physician to the possibility of postoperative infection. Early diagnosis of deep arthroplasty infection is imperative to maximize the likelihood that the prosthesis will be salvaged with débridement and retention.[7] Superficial cultures of wound drainage are of little diagnostic value and are discouraged. Joint arthrocentesis and evaluation of the aspirate with cell count, Gram stain, and bacterial culture should be performed if infection is suspected. Observation of superficial wound problems and treatment with oral antibiotics often leads to the development of resistant deep infection. These wound problems should be referred to the orthopaedic surgeon, where aggressive management of refractory wound healing is recommended.

Important historical factors to consider when subacute or chronic infection is a concern include persistent pain, postoperative wound complications, significant wound drainage, chronic or multiple courses of oral antibiotic treatment for wound difficulties, a history of potential hematogenous sources of infection (eg, tooth extraction, urologic procedures), and persistent knee stiffness despite appropriate rehabilitation efforts. Although antibiotics are often started empirically, this practice should be avoided in patients with painful or stiff total knee arthroplasties without a definitive diagnosis of infection because such treatment complicates efforts to both diagnose and treat deep infection once proven.

Laboratory and Radiographic Studies

Laboratory studies should routinely include a leukocyte count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Although these values are useful, they are often nonspecific and difficult to interpret, especially in patients with RA.[11] Sanzen and Sundberg[12] evaluated the laboratory findings in 23 non-RA patients with low-grade periprosthetic hip and knee infections, and false-negative rates of 35% and 22% were seen in ESR and CRP, respectively. However, only 1 patient had normal values for both tests, which supports using both of these laboratory studies in combination. Radiographic evaluation of sequential radiographs to look for progressive radiolucencies or the development of focal osteopenia or osteolysis around the prosthesis is advised. Periosteal new bone formation on radiography is highly suggestive of infection.[9]

Radioisotope scans may also be helpful in the diagnosis of infected total joint arthroplasty. Indium-111 leukocyte scanning appears to be more accurate than technetium-99 diphosphonate scanning alone (78% versus 74%).[13] However, combining indium-111 leukocyte scanning with technetium-99 sulfur colloid marrow scintigraphy provided 95% accuracy. RA and significant osteolysis are risk factors for false-positive results.[14] The sensitivity of indium scanning appears to be dependent on the activity of the infection, with indolent and chronic infections having higher false-negative rates.

Arthrocentesis

Despite false negative rates of up to 15% to 20%, arthrocentesis with bacterial culture and Gram stain should be considered an essential part of the investigative process for an infected total joint arthroplasty and may help guide the appropriate choice for antimicrobial therapy. The use of oral or intravenous antibiotics prior to aspiration will markedly decrease the likelihood that an offending microorganism will be isolated. As such, antibiotics should be discontinued for 7 to 10 days prior to aspiration.

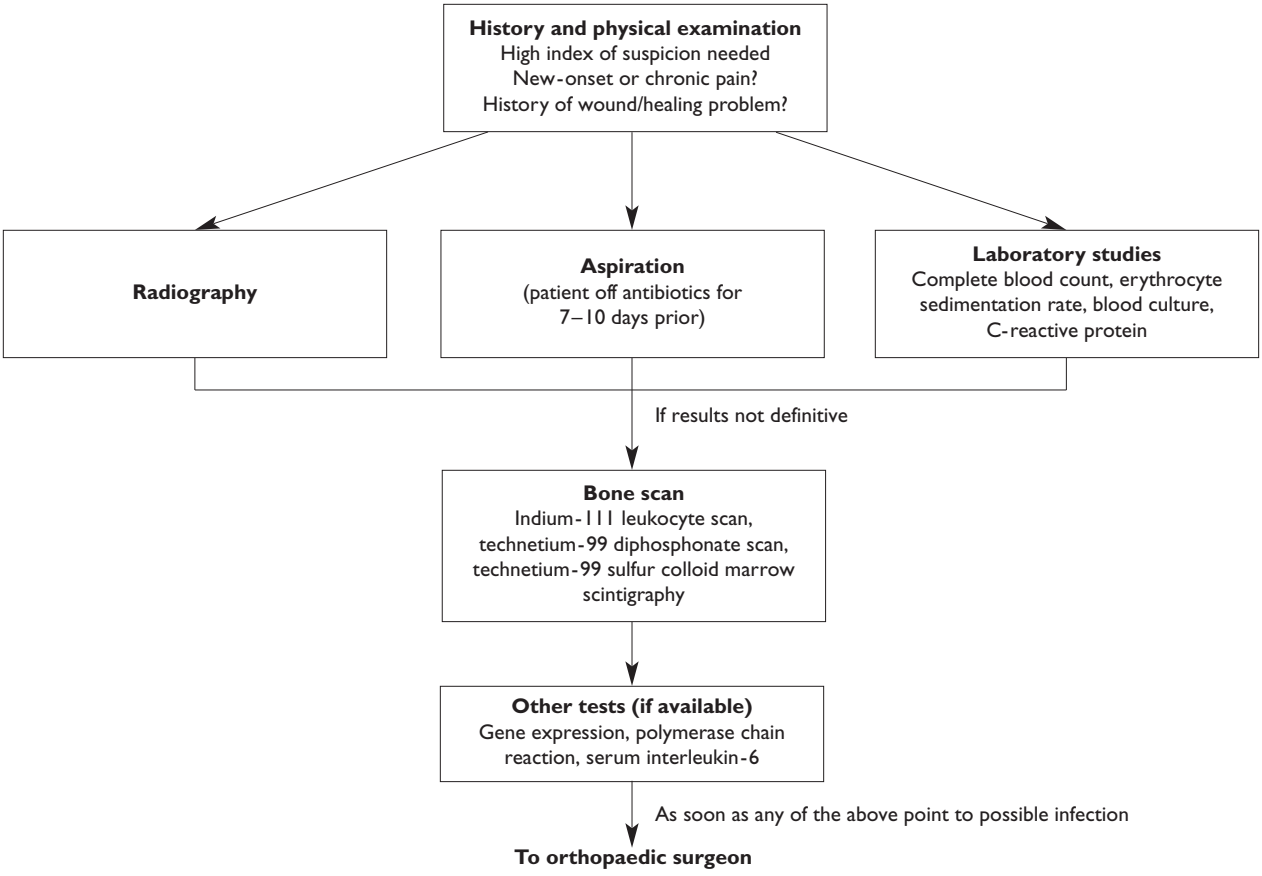

Figure. Algorithm for diagnosis of an infected total knee arthroplasty.

Underdiagnosis of joint sepsis occurs during aspiration when organisms that present in the knee are unable to be grown in culture. Weaknesses in the culture process and in the laboratory diagnosis of infection have recently prompted interest in other forms of diagnoses. The use of polymerase chain reaction to more accurately diagnose periprosthetic infection is currently under review. Very promising results have been reported.[15] Serum interleukin-6 as an infection marker has also been investigated. Di Cesare et al[16] have shown that an elevated serum level is valuable in the diagnosis of periprosthetic infection.

CLASSIFICATION OF INFECTION

Periprosthetic infection is classified based on the onset of infection after the initial index procedure. The use of a classification system is helpful in guiding appropriate management. Initially, Coventry[17] described a 3-stage classification system based on timing of presentation and the presumed mode of infection, and this system has been recently updated and modified by Segawa et al[18] as well as Tsukayama et al.[19] Tsukayama included 4 categories based on clinical presentation.

Type 1 infection is determined by a positive intraoperative culture. In a report by Tsukayama et al,[20] 31 of 97 patients (106 infections) who were initially thought to have aseptic failures were diagnosed with deep infection based on positive intraoperative cultures (a minimum of 2 of 5 cultures were considered positive for infection). Intraoperative culture results must be interpreted in conjunction with preoperative examination as well as laboratory studies and frozen section histology findings. If positive culture results are deemed to be truly positive, appropriate antibiotic therapy should be initiated.

An infection that occurs in the immediate postoperative period (ie, within 1 month postsurgery) is considered type 2 infection. Type 2 infection is usually evident on history and physical examination, with patients reporting wound complications and/or superficial cellulitis around the time of the index procedure. The etiology of type 2 infections may be wound colonization at

the time of surgery, infected hematomas, or the spread of superficial infection. Many of these infections may be preventable with appropriate preoperative antibiotics and careful operative technique. Type 2 infections are subcategorized into superficial (A) and deep (B).

Type 3 infections are typically presumed to be caused by hematogenous spread to a previously asymptomatic and aseptic joint replacement. There may be a history of associated febrile illness or acute infection (eg, urinary tract infection, pneumonia), followed by deterioration in joint function. Invasive or semi-invasive procedures, such as colonoscopy, dental procedures, or local treatment of cutaneous infections, may be reported. These infections are more common in patients who are immunocompromised, patients who have recurrent episodes of bacteremia (eg, intravenous drug abusers), or those requiring repeat chronic urinary catheterization. Single episodes of bacteremia, such as with dental manipulations,[21–26] respiratory infection, remote prosthetic infection, open skin lesions, endoscopy, or contaminated operations, are often associated with type 3 prosthetic joint infections.

Type 4 infections are referred to as late chronic and are diagnosed more than 4 weeks after the index operation. Type 4 infections may originate during the index surgical procedure, but due to a small inoculum or a low virulent organism, the onset of symptoms may be delayed. These patients typically present with a gradual deterioration in their knee function and overall function as well as an increase in pain. In addition, clear systemic or local findings consistent with definitive infection may not be present, making them difficult to diagnose. There may be a history of prolonged wound drainage at the time of the index procedure, a delay in discharge from the hospital, or previous prescriptions for ongoing courses of antibiotics that may have temporarily improved the patient's symptoms.

TREATMENT

Once infection has been diagnosed, the patient should be referred to an orthopaedic surgeon for definitive treatment. Although not always possible, the goal of treatment is eradication of infection and a painless, well-functioning total knee arthroplasty. In general, the 6 treatment options for an infected total knee arthroplasty include: (1) antibiotic suppression, (2) open débridement, (3) resection arthroplasty, (4) arthrodesis, (5) amputation, and (6) single-staged or 2-staged resection and reimplantation of another prosthesis. These treatment options will be explained in more detail in Part 2 of this article to appear in the February 2006 issue of *Hospital Physician*.

CONCLUSION

Infection of a total knee arthroplasty remains a devastating complication associated with this procedure. The primary care physician must have a high index of suspicion in evaluating these patients and be able to optimize the timeliness of diagnosis. A thorough history and physical examination as well as the appropriate laboratory (ie, blood culture, ESR, CRP) and radiographic studies are essential to the evaluation of suspected total knee arthroplasty infection. It is imperative to diagnose the infection quickly and initiate treatment immediately. Once infection is suspected, the patient should be referred to an orthopaedic surgeon for treatment. **HP**

REFERENCES

1. Bengtson S, Blomgren G, Knutson K, et al. Hematogenous infection after knee arthroplasty. Acta Orthop Scand 1987;58:529–34.
2. Bengtson S, Knutson K, Lidgren L. Revision of infected knee arthroplasty. Acta Orthop Scand 1986;57:489–94.
3. Bengston S, Knutson K, Lidgren L. Treatment of infected knee arthroplasty. Clin Orthop Relat Res 1989;245: 173–8.
4. Grogan TJ, Dorey F, Rollins J, Amstutz HC. Deep sepsis following total knee arthroplasty: ten-year experience at the University of California at Los Angeles Medical Center. J Bone Joint Surg Am 1986;68:226–34.
5. Petty W, Bryan RS, Coventry MB, Peterson LF. Infection after total knee arthroplasty. Orthop Clin North Am 1975;6:1005–14.
6. Rand JA, Bryan RS. Reimplantation for the salvage of an infected total knee arthroplasty. J Bone Joint Surg Am 1983;65:1081–6.
7. Schoifet SD, Morrey BF. Treatment of infection after total knee arthroplasty by debridement with retention of the components. J Bone Joint Surg Am 1990;72:1383–90.
8. Wilson MG, Kelley K, Thornhill TS. Infection as a complication of total knee-replacement arthroplasty. Risk factors and treatment in sixty-seven cases. J Bone Joint Surg Am 1990;72:878–83.
9. Rand JA, Bryan RS, Morrey BF, Westholm F. Management of infected total knee arthroplasty. Clin Orthop Relat Res 1986;205:75–85.
10. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. Clin Orthop Relat Res. Clin Orthop Relat Res 2001;Nov:15–23.
11. Hanssen AD, Rand JA, Osmon DR. Treatment of the infected total knee arthroplasty with insertion of another prosthesis. The effect of antibiotic-impregnated bone cement. Clin Orthop Relat Res 1994;309:44–55.
12. Sanzen L, Sundberg M. Periprosthetic low-grade hip infections. Erythrocyte sedimentation rate and C-reactive protein in 23 cases. Acta Orthop Scand 1997;68:461–5.

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13. Palestro CJ, Swyer AJ, Kim CK, Goldsmith SJ. Infected knee prosthesis: diagnosis with In–111 leukocyte, Tc-99m MDP imaging. Radiology 1991;179:645–8.
14. Rand JA, Brown ML. The value of indium 111 leukocyte scanning in the evaluation of painful or infected total knee arthroplasties. Clin Orthop Relat Res 1990;259: 179–82.
15. Mariani BD, Tuan RS. Advances in the diagnosis of infection in prosthetic joint implants. Mol Med Today 1998;4:207–13.
16. Di Cesare PE, Chang E, Preston CF, Liu CJ. Serum interleukin-6 as a marker of periprosthetic infection following total hip and knee arthroplasty. J Bone Joint Surg Am 2005;87:1921–7.
17. Coventry MB. Treatment of infections occurring in total hip surgery. Orthop Clin North Am 1975;6:991–1003.
18. Segawa H, Tsukayama DT, Kyle RF, et al. Infection after total knee arthroplasty: a retrospective study of the treatment of eighty-one infections. J Bone Joint Surg Am 1999;81:1434–45.
19. Tsukayama DT, Goldberg VM, Kyle R. Diagnosis and management of infection after total knee arthroplasty. J Bone Joint Surg Am 2003;85-A Suppl 1:S75–80.
20. Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. J Bone Joint Surg Am 1996; 78:512–23.
21. Deacon JM, Pagliaro AJ, Zelicof SB, et al. Prophylactic use of antibiotics for procedures after total joint replacement. J Bone Joint Surg Am 1996;78:1755–70.
22. Hughes PW, Salvati EA, Wilson PD Jr, Blumenfeld EL. Treatment of subacute sepsis of the hip by antibiotics and joint replacement. Criteria for diagnosis with evaluation of twenty-six cases. Clin Orthop Relat Res 1979;141:143–57.
23. Hunter G, Dandy D. The natural history of the patient with an infected total hip replacement. J Bone Joint Surg Br 1977;59:293–7.
24. Rubin R, Salvati EA, Lewis R. Infected total hip replacement after dental procedures. Oral Surg Oral Med Oral Pathol 1976;41:18–23.
25. Stinchfield FE, Bigliani LU, Neu HC, et al. Late hematogenous infection of total joint replacement. J Bone Joint Surg Am 1980;62:1345–50.
26. Vanderhooft JE, Robinson RP. Late infection of a bipolar prosthesis following endoscopy. A case report. J Bone Joint Surg Am 1994;76:744–6.