26 Periprosthetic Joint Infection: Diagnosis and Principles of Management

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26.1 Introduction

Total joint arthroplasty is the commonly performed lifestyle surgery with excellent outcomes in terms of quality of life and knee function postoperatively. With the advent of newer implant and improved surgical techniques, the excellent postoperative pain management, joint arthroplasty has become a preferred choice for patients to deal with crippling arthritis [1].

In medicine, every newer technique has its own drawbacks and complications. With innovations in clinical management, we try to overcome the complications and drawbacks by newer and newer nuances. Peri-prosthetic joint infection (PJI) is one such complication after total joint arthroplasty which causes significant morbidity and at times mortality of the patient as well. Infection is the most undesired and catastrophic complication following total joint arthroplasty which every surgeon fears of; hence, it is very important to understand the proper diagnosis and the principles of management [2, 3]. Total knee arthroplasty has been more frequently associated with PJI. The improvised surgical techniques and advances in biomedical engineering along with medical microbiology have caused a significant reduction in the incidence of PJI [3]. The diagnosis at times can be very simple and at times really tough as there is no confirmatory test to identify the same. Newer immunological techniques and isotope radiological assessment have led to its differentiation between aseptic and septic loosening of a prosthetic joint [4, 5]. The challenge still remains to follow an evidence-based approach for establishing diagnosis of PJI and then following parameter-based principles of management of PJI. The spectrum of treatment varies right from antibiotic suppression to thorough debridement, to staged revision, to excision arthroplasty, and sometimes to arthrodesis [1, 6, 7]. PJI is getting significant importance due to the morbidity and mortality associated with it, but there is a huge cost involved in the diagnosis and treatment of it. In this chapter, we shall go through the various diagnostic tools and principles of management.

26.2 Classification

Infection following total hip arthroplasty has been classified by Fitzgerald [8], and this can be extended for knee arthroplasty for practical purposes. The classification is based on when symptoms begin and the clinical cause of infection.

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26.2.1 Stage 1 (Acute Postoperative Infections)

The patient is seen during the first postoperative month. The wound may be purulent or discharging. Systemic signs such as fever, chills, and sweating may be present. Type 1 infections are caused by infected hematomas or superficial wound infections spreading contiguously to the periprosthetic space. The major difficulty in Stage 1 infections is differentiating a superficial from a deep infection in a patient with persistent postoperative serous drainage. There are no diagnostic tests that are useful in this stage (Fig. 26.1).

26.2.2 Stage 2 (Delayed Deep Infections)

The patient is seen between 6 months to 2 years from surgery with a well-healed wound and a painful joint replacement. The pain may be caused by aseptic mechanical loosening or low-grade, indolent infection. Type 2 infections are believed to originate at the time of operation, but because of a small inoculum or the low virulence of the organism, the onset of symptoms is delayed. Systemic symptoms are not present. The characteristic feature is a gradual deterioration in the function of the joint and increasing pain, which is often present from the time of surgery and occurs at rest. Type 2 infections pose the greatest diagnostic difficulty.

26.2.3 Type 3 Infection (Late Hematogenous Infections)

Diagnosis poses no difficulty as the patient presents with an acutely painful joint, many years after surgery, with signs of acute infection such as swelling and fever. The patient will frequently have had a recent surgical treatment such as dental manipulation or remote infection. ESR and C-reactive protein will be elevated, and frequently pus can be aspirated from the joint.

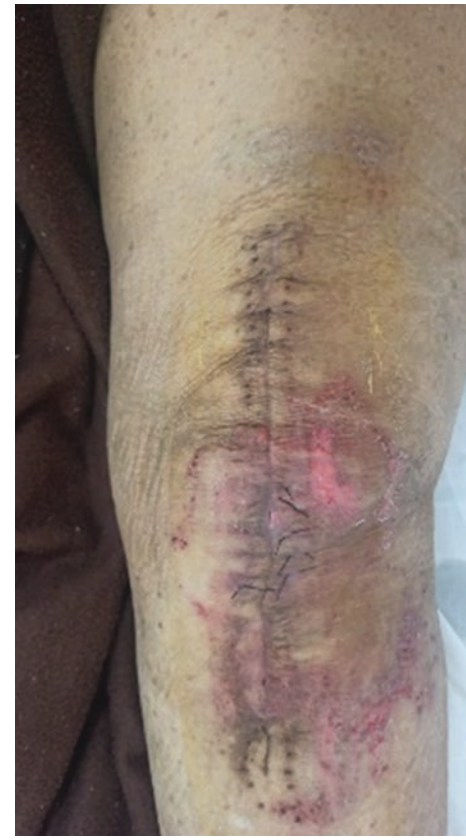

Fig. 26.1 Skin excoriation due to underlying infected TKR with discharge

26.3 Diagnosis of PJI

Establishing diagnosis of PJI is at times quite straightforward (Fig. 26.2) and at times very difficult. A thorough clinical history and examination helps in the majority of the cases; we have to probe into the primary surgery as it leads to the diagnosis most of the times [4–6]. Diagnosis of infection can be challenging as no test is 100% sensitive or 100% specific. However, new immunologic techniques may allow differentiation of aseptic from septic loosening of total joint prostheses. Once the diagnosis of infection is established, treatment options range from antibiotic suppression to exchange revision arthroplasty or removal of the prosthesis permanently. Surgeons need to be aware of the potential sources of infection and prophylactic measures that effectively

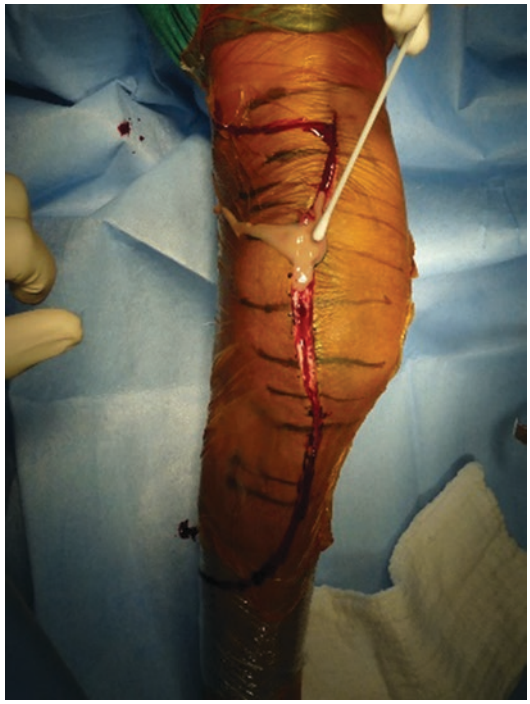

Fig. 26.2 Pus discharge from an infected TKR

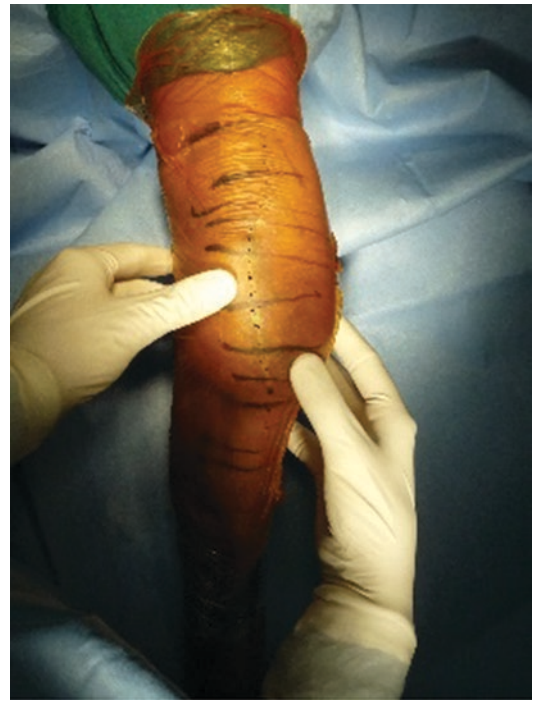

Fig. 26.3 Reactive knee swelling and stiffness in a septic TKR

reduce the incidence of infection postoperatively.

History and physical examination (Fig. 26.3) of the patient with laboratory tests such as ESR and C-reactive protein, serial radiographs, radionuclide scans, and joint aspiration can all help in the diagnosis in prosthesis-related infection. However, definitive diagnosis is only possible by culturing several samples of material obtained from the interface during revision surgery. Intraoperative frozen section of interface tissue is a reliable indicator of infection before cultures are available. Gram stain is of no value [9–11].

Patients with a definitive diagnosis of PJIs, based on identification of the Musculoskeletal Infection Society [12], included the following three conditions:

1. The presence of a sinus tract communicating with the prosthesis
2. A pathogen was isolated by culture from two separate tissues or fluid samples obtained from the infected prosthetic joint
3. Had four of the following six criteria:

- An elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) level
- Elevated synovial fluid white blood cell (WBC) count (WBC > 3000/mm^3)
- Elevated synovial fluid neutrophil [polymorphonuclear neutrophils (PMN)] percentage (PMN > 70%)
- Presence of purulence in the affected joint
- Isolation of a microorganism in one periprosthetic tissue or fluid culture
- Neutrophils in five high-powered fields (400X) observed from frozen histologic section analysis of peri-prosthetic tissue at a magnification more than 5

In *clinical history*, details about the postoperative wound status, persistent discharge from the wound, history of prolonged antibiotic therapy, persistent pain, and swelling postoperatively

extending into early postoperative period at times lead to diagnosis of PJI. History of severe pain and fever associated with knee stiffness also leads to the diagnosis of PJI [13, 14].

In *clinical examination*, a discharging sinus is direct evidence of prosthetic joint infection, unless and until proved otherwise. Knee stiffness, unexplained pain post knee arthroplasty, and raised local warmth are indirect evidence of PJI. Restricted walking ability is also an indicator of PJI. Extensive knee synovitis with effusion is also commonly seen in PJI [14].

In *radiological assessment*, radiolucent lines about a prosthesis and cement are frequent findings, and are in themselves helpful in determining septic from aseptic loosening. Endosteal scalloping is more suggestive of infection, but can occur with metallosis. Lacy sub-periosteal new bone formation, particularly around the femoral metaphysis, is pathognomonic of deep infection, but occurs in only 1–2% of cases. Obvious loosening of components needs to be defined as to whether it is due to aseptic or septic loosening (Fig. 26.4) [1, 2, 15].

In *laboratory assessment—ESR/C-reactive protein*: These are the most useful laboratory screening tests for the diagnosis of PJI. ESR > 30 and CRP > 10 is indicative of infection, with a sensitivity and specificity of 0.82 and 0.85 for the ESR, and of 0.96 and 0.92 for the CRP. Sanzen et al. have noted that neither the ESR nor CRP is universally elevated in patients with joint infection [16]. Also, both parameters rise significantly after surgery and remain elevated for some time [17]. The CRP returns to normal more quickly and is more accurate. Furthermore, about 20% of patients with a joint replacement have an associated connective tissue disorder which will keep

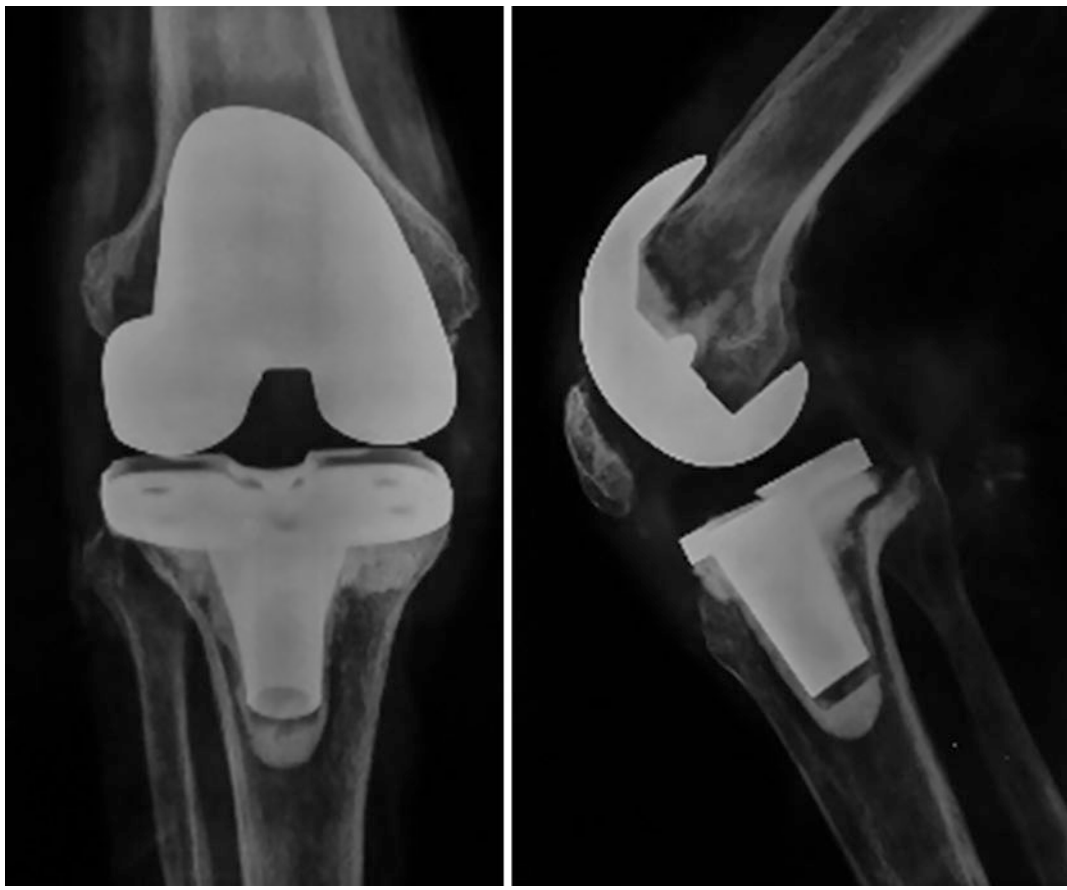

Fig. 26.4 Osteolysis and loosening of components in an infected TKR

the ESR persistently elevated. The increasing or the decreasing trend is very important in the treatment of PJI [17–19].

In knee joint aspirate: This is perhaps the most useful tool in the diagnosis of infection about a joint. Antibiotic therapy is discontinued strictly for a minimum of 2 weeks before aspiration. The joint aspiration is performed at operation room with aseptic technique [20].

Aerobic and anaerobic incubation of the aspirate permits recovery of the causal organism in two-thirds of cases. The results suggest it is a better test for ruling infection in than ruling it out. Inflammatory cells like the total leucocyte count and absolute neutrophil count are important predictors of PJI [20]. The success rate of infection control in culture-negative patients who underwent two-stage revision was comparable with culture-positive cases along with improvement of antibiotic treatment regimens in recent 10 years [21].

In radionuclide imaging, Indium 111-labeled white cell scans have superseded differential imaging with Tc99m and gallium bone scans in the diagnosis of periprosthetic infection. It is not only more specific but more accurate in distinguishing septic from aseptic loosening [22, 23]. Merkel et al. showed an accuracy rate of 88% with indium compared with 62% for Tc99m and gallium ($p < 0.001$) [24].

New scintigraphic modalities: Two new agents are currently undergoing FDA evaluation in the USA. *Indium111-labeled IgG* is a new agent that can be used for the diagnosis of low-grade sepsis. European experience suggests that it will enhance the diagnosis rate if there is no inflammatory reaction from particulate debris [24]. *Tc-99 m monoclonal antibody* is also being evaluated, and early results suggest that it may be more accurate than indium-111 IgG. Both tests are prohibitively expensive at present [22].

Intraoperative frozen section of interface membrane: Several studies have shown this to be a reliable indicator of periprosthetic infection prior to definitive cultures of infected material being available (Fig. 26.5) [5, 15, 25, 26]. It allows the surgeon to make accurate intraoperative decisions in terms of single or staged revision surgery. Three specimens should be sent for frozen section: pseudocapsule of the joint and membrane between each of the components of the joint being removed. The frozen section looks at polymorphs per high-powered field over five representative high-powered fields. 0–5 polymorphs eliminate infection, 5–10 is equivocal, and >10 is highly suggestive of infection [1, 25, 27].

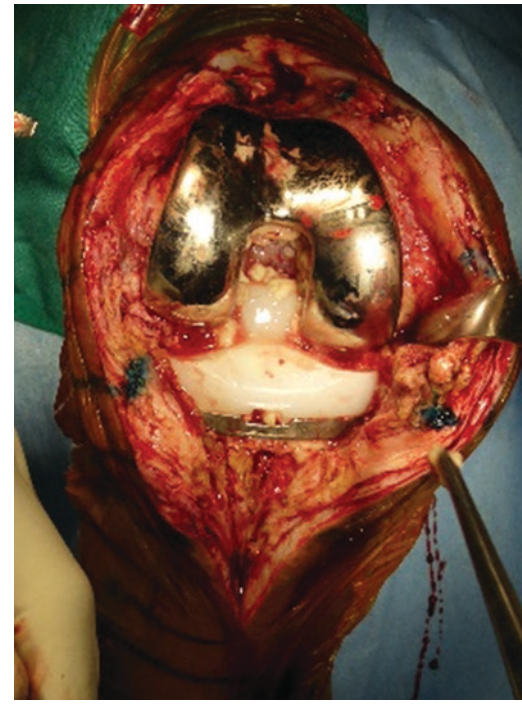

Fig. 26.5 Dirty granulation tissue with synovitis all around the joint

26.4 Principles of Management of PJI

Once periprosthetic infection is suspected and/or diagnosed, a number of options exist. Options include medical therapy alone or surgical treatments in combination with antibiotics [2, 12, 15]. Surgical treatments involve debridement with preservation of the implant, debridement with a single-staged revision, or debridement with a two-stage revision, with or without the use of an antibiotic-loaded cement spacer [28]. Of these options, one- and two-staged revisions are the two main and controversial approaches for treatment. Although a two-stage revision was preferred by most surgeons and widely accepted as

the gold standard protocol, controversies still exist with regard to the ideal interval between implant removal and reimplantation, the usefulness of antibiotic-loaded cement spacers, and the duration of systemic antibiotic treatment [15, 25, 26].

After going through the current literature and guidelines for the treatment of PJI, there is no evidence that a two- or more-staged procedure has a higher success rate than a one-staged approach. The current literature on one-stage exchange procedure is promising, with comparable results to two-stage revisions for infected hips and knees in selected patient. Zeller et al. recently performed a large prospective cohort study on one-stage exchange arthroplasty for chronic peri-prosthetic hip infection which included 157 patients. After a median follow-up of 41.6 months, only two relapses and six new infections occurred [29].

26.4.1 Medical Therapy (Antibiotic Suppression)

Medical or antimicrobial therapy alone is rarely indicated. Such situations occur when the patient is so medically high risk that a surgical procedure is likely to induce mortality. It may be that the consequences of removal result in significantly worse function than currently exists [13, 14]. The thrust of management here is to control rather than cure the infection. It involves the use of lifelong suppressive antibiotics. In general, recurrence is expected if the patient lives long enough. Results of antibiotic suppression therapies alone have been reported. Widmer et al., in 1992, reported a 60% success rate with 6 months of rifampicin and a fluoroquinolone. This study, however, did not follow the patients for the past 2 years [30].

26.4.2 Debridement with Implant Retention

This strategy may be suitable in the early postoperative or very early hematogenous infection. It involves dislocation of the implant, thorough debridement of hematoma, and scrubbing of all exposed surfaces with an exchange of poly (Fig. 26.6). Concurrent antibiotic therapy based on cultures is given. Aggressive debridement is the mainstay of this modality of treatment; the patients underwent general or epidural anesthesia through an incision along the previous operative scar [7, 15, 31, 32] (Fig. 26.7).

Exposure is often difficult in a revision procedure, and therefore, a larger incision may be needed. Once the current implant is exposed, aspiration was performed again under direct vision. In addition, several samples (at least five) were acquired from the areas with the most florid inflammatory changes, such as pseudocapsules. Then the samples were sent to a microbiology laboratory for culture, sensitivity tests, and histological evaluation [10, 20, 25, 33] (Fig. 26.8).

After that, aggressive debridement is performed involving the removal of all purulent secretion, fibrous tissue, and a large number of proliferative inflammatory synovitis until healthy musculature was observed. Any potentially con-

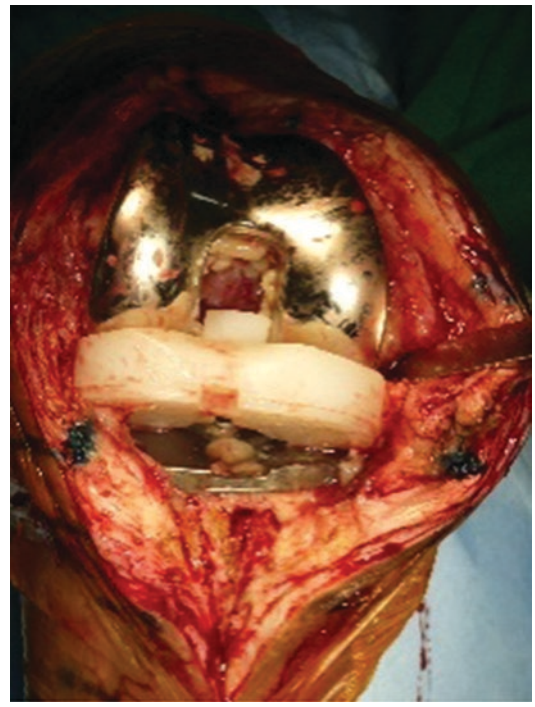

Fig. 26.6 Poly walks off the components with slimy tissue under it

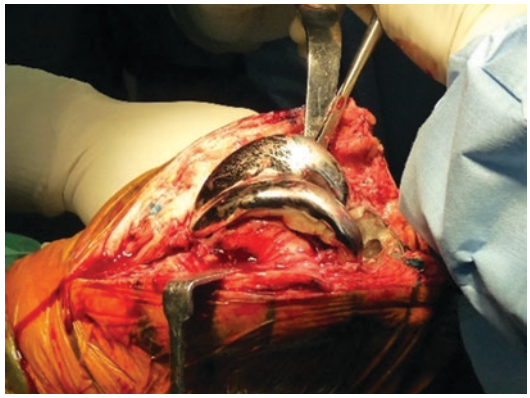

Fig. 26.7 Loose femoral component with osteolysis

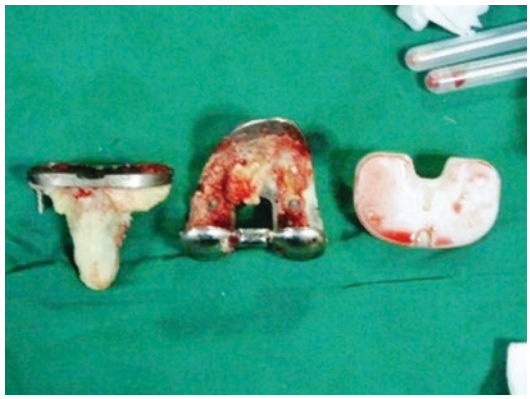

Fig. 26.8 Loose implants excised preserving the bone stock for future revision TKR

taminated or granulating material should be removed, but it is important to recognize key soft tissue structures to prevent unnecessary destabilizing of the joint. Given that, thicker insert should be prepared because we need to keep in mind that thorough debridement is the vital principle in this procedure [34, 35].

The surgical area was then exhaustively irrigated with at least 5 L warm 0.9% saline which combines mechanical debridement to dislodge nonviable tissue, with dilution of the bacterial bioburden [36]. Followed by that, we typically use 100–200 mL 3% hydrogen peroxide across every cancellous region with further mechanical debridement (Fig. 26.9). This is then washed off with more 0.9% sodium chloride solution, and then 400–500 mL 0.1% aqueous betadine solution is poured into the wound and soaked (all soft

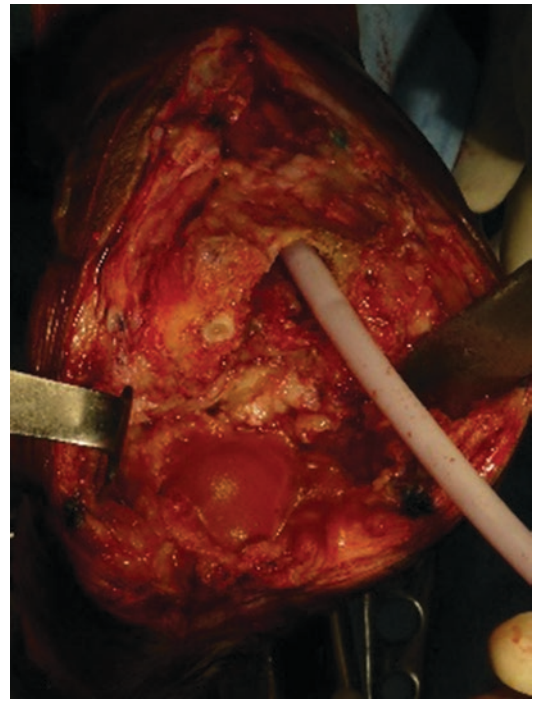

Fig. 26.9 Wound irrigation with hydrogen and betadine solution

tissues steeped) for 15 min (Fig. 26.9). This gives the antimicrobial action of betadine sufficient time to work, rather than washing off the wound immediately after application [34, 35].

During the break period, cotton gauze is used to cover the wound and the area around the patient is cleared by removing any other equipment that has already been used during the initial stages, such as the suction catheter, pulse lavage, and any soiled linen. After that, as initiating of any primary joint operation, the surgical team rescrubbed and resterilized the surgical area, put on new gowns, and exchanged the entire set of surgical instruments [28, 36]. After a further pulsatile lavage with 1 L of 0.9% sodium chloride to remove the remaining aqueous betadine solution from the wound, the knee prosthesis is ready for insertion of a new poly of the same or increased thickness depending on the stability of the knee. The surgical field is then washed one last time with 1 L of 0.9% sodium chloride. The wound was closed over a suction drain, which is placed within the joint and retained for 3 days and

removed if the volume of daily drainage was ≤50 mL. The subcutaneous layer is closed using a 2.0 Vicryl suture and 2.0 ethilon to close the skin. The wound is protected by a multilayer gauze, followed by wool and bandage extending from the midtibial region to the middle of the thigh [34].

26.4.3 Single-Stage Revision

Single-stage revision was popularized by Buchholtz and Gartman following their paper in 1972. The technique involves removal of infected components, thorough surgical debridement, and subsequent reconstruction with antibiotic-loaded cemented implants. The paper reported a successful eradication of infection in 77% of 583 patients [37]. Other authors have reported similar success rates with single-stage revision. Works on the similar principles as explained in the debridement technique. The revision knee prosthesis is inserted in the same sitting and the wound is closed [3, 29, 38].

Amstutz, in 1998, reported on 20 patients having single-stage revision for infection [39]. He excluded multi-resistant organisms and immunocompromised patients. They undertook 4.7 months of postoperative antibiotics, and he reported no recurrence of infection. There were, however, two cases of aseptic loosening, which were revised at 12 and 19 years post-revision. In 1999, Callahan reported 24 patients with a 10 year follow-up. It was noted that 12 had deceased and an 8.3% recurrence had occurred [40]. Thus, there is good evidence that single-stage revision can be undertaken. It saves time and money. It requires identity of a susceptible organism and preferably a non-biofilm producer. It is best undertaken in non-immunocompromised. It requires meticulous technique and the recommended use of antibiotic-loaded cement for fixation of the revision implants. It is not clear how long oral antibiotics should be delivered following the index procedure. There are no long-term follow-up reports of uncemented single-stage revision procedures [38].

26.4.4 Two-Stage Revision

The next option in the management of periprosthetic infection is a two-stage revision procedure. Initial descriptions involved the removal of all implants, cement debris, and a meticulous synovial debridement. This was followed by an implant-free interval and subsequent reimplantation. The procedure, however, has evolved to an interval implantation of either antibiotic-loaded beads or an articulating antibiotic-loaded implant. The implant-free period and subsequent medical management in the form of intravenous and oral antibiotics help to eradicate the PJI and make the knee joint more recipient and receptive for a revision knee prosthesis. The patient is serially monitored for a period of 3 months usually with repeated laboratory evaluations of hemogram, ESR, and CRP levels, and the patient's general medical status allows secondary revision. Numerous papers have reported success rates in excess of 90% when using a two-stage technique [9, 38, 41].

The use of antibiotic-loaded cement spacers, however, raises certain questions. The benefit of using a cement spacer or beads is that it delivers a local antibiotic concentration in excess of that possible with systemic antibiotics. There is widespread clinical evidence of the efficacy of such a technique. There are, however, variable factors associated with the use of cement as an interval implant. Such variable factors include antibiotic type, dosage, and configuration [42]. Usually gentamycin, vancomycin, or tobramycin is used, because they are heat stable and broad spectrum (Figs. 26.10 and 26.11).

They do not appear to demonstrate systemic effects such as ototoxicity and nephrotoxicity. It appears that Palacos cement elutes better than Simplex, CMW, and Sulfix cements. This may be due to its higher porosity and its greater ease in being able to mold into an endoprosthesis (Fig. 26.12). The pharmacokinetics of antibiotic elution from cement is incompletely understood. A current recommendation is to include 0.6–1.2 g of tobramycin and 0.5–1 g of vancomycin per 40 g of cement [42, 43]. Masri, in the *Journal of Arthroplasty* in 1998, reported on 3.6 g of

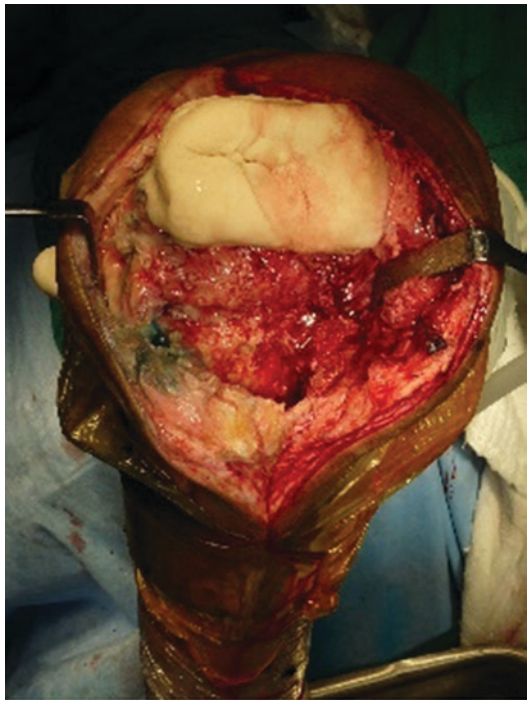

Fig. 26.10 Femoral cement spacer block with antibiotic-loaded cement

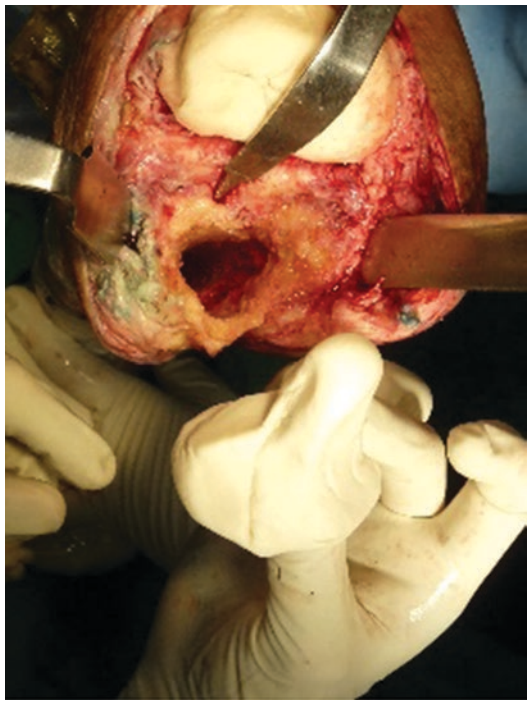

Fig. 26.11 Tibial cement block to fill the tibial metaphysis

tobramycin and 1 g of vancomycin per 40 g of cement with significant success [44].

Residual controversies relating to the use of cement antibiotic local delivery modes includes whether beads or spacers are more effective. It has been shown that an endoprosthesis maintains soft tissue tension and can thus aid in second-stage revision. This appears to shorten revision time and also reduce blood loss and rehab time. Further, the question of whether a spacer acts as a foreign body and thus as a sequestrum or a large antibiotic tablet has not yet been resolved. The pharmacokinetics of the antibiotic within the cement have yet to be completely understood. The time interval between stages remains an issue of controversy [38, 41, 43].

Nevertheless, the gold standard now appears to be a two-stage revision with an interval period of 6 weeks of antibiotic directed against the known organism. Success rates in excess of 90% should be expected. It is noted that infection and its management are costly in terms of time, money, and morbidity (Figs. 26.13, 26.14, and 26.15) [41].

Although the results of two-stage revision were reported with reinfected rate 10.2–17%. Accordingly, a number of studies have been published and emphasized concerning the two-stage revision technique. However, there are an increasing number of researches on one-stage revision along with the more in-depth understanding of the approach [45]. Besides the obvious benefit of eliminating a second major operation, further advantages arise from the reduced duration of postoperative systemic antibiotics in terms of cost and morbidity. Even so, three large systemic reviews recently still indicated that the reinfection rate of one-stage revision was 8.6–16.8%, which is comparable with two-stage revision [46, 47].

26.4.5 Knee Arthrodesis

This surgical technique is preserved as a last resort to treat infected total knee arthroplasty. It is used in select patients where there is persistent infection after repeated staged knee replacement, massive bone or soft tissue loss, and irreparable

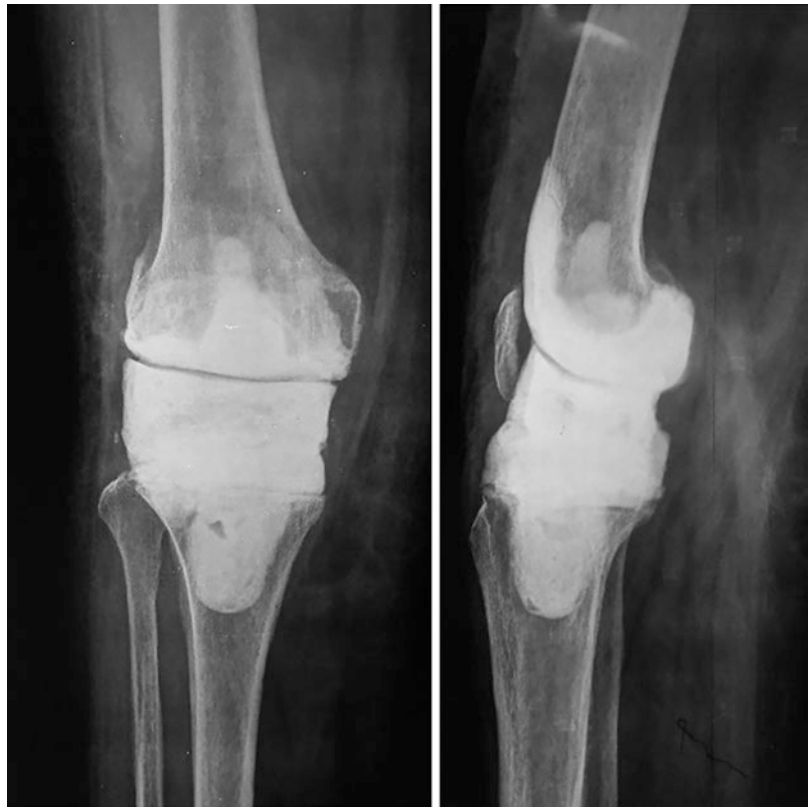

Fig. 26.12 X-ray picture of cement spacer for two-stage revision TKR

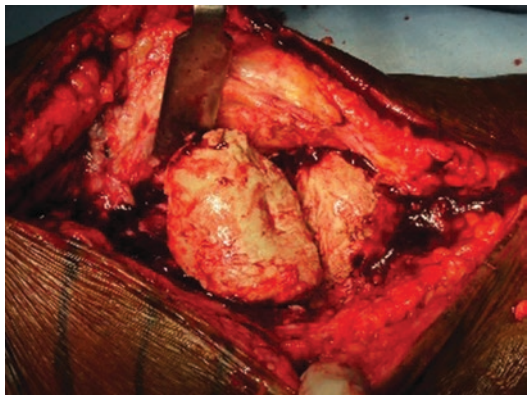

Fig. 26.13 Removal of these cement spacer blocks at the time of revision TKR after 3 months

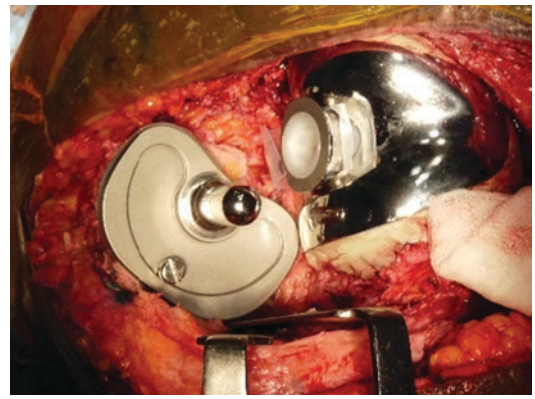

Fig. 26.14 Revision TKR with rotating hinge prosthesis

damage of extensor mechanism. The outcome expected is a fused knee without infection, but it is at the cost of mobility [48].

Various techniques have been described to achieve a solid knee arthrodesis with rates of fusion ranging from 29 to 100%. It has been recognized that rigid fixation and compression reduces failure rates. Intramedullary (IM) nailing has achieved the best fusion rates of 88 to 100% and has the advantage of allowing early weight bearing [49]. The external fixators have several advantages as it corrects malalignment and give a chance to correct shortening with distraction osteogenesis. These fixators provide an excellent

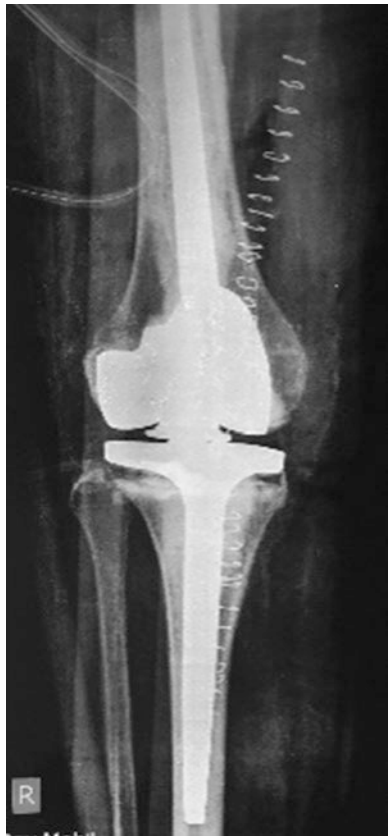

Fig. 26.15 Revision TKR X-ray with rotating hinge prosthesis

stability and early full weight bearing, a continuous compression can stimulate bone healing with a considerably lower risk of infection recurrence. The disadvantage being prolonged use of fixators till the union is achieved [48, 50].

26.5 Summary

We recommend following an evidence-based approach for establishing diagnosis of PJI and then following parameter-based principles of management. The spectrum of treatment varies right from antibiotic suppression to debridement and to single-stage or two-stage revision and may end up sometimes in an arthrodesis.

One- or two-staged techniques should be performed depending on the clinical situation, the local facilities, and the surgical expertise. The key to success of one-stage revision is based on following a detailed protocol, including a meticulous preoperative planning, thorough intraoperative surgical approach, and strict postoperative antibiotic treatment regimens.

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