Peri-proshthetic Joint Infection

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Abstract

Prosthetic joint infections in one of the most serious complication of Joint Arthroplasty. Over the years the understanding and management of PJI has evolved. The current review presents and overviews of the recent advances in the field

Keywords: Prosthetic joint infection, arthroplasty

Introduction

Periprosthetic joint infection (PJI) is a devastating complication and one of the major cause of failure post total hip and knee arthroplasties. The incidence of PJI is reported as 1-4% cases of primary arthroplasty and even higher cases are reported in the revision cases[1,2]. As the number of primary joint arthroplasty has been steadily increasing especially in patients with associated comorbidities, these values are expected to be rising in near future. PJI poses a significant economic and financial burden to the patient, hospital and the healthcare system as a whole [3]. Hence, it is an urgent need of the hour to identify patients at risk for PJI, propose effective standardised treatment guidelines and carry out all preventive measures at the onset to reduce this serious complication.

Pathophysiology

Adherence of bacteria over inert implant surface mediated by either physical and chemical actions or specific cell surface receptors is the first step towards the pathophysiology of PJI. Biofilm is a complex structure made of microcolonies of organism surrounded by extracellular polysaccharides and glycocalyx matrix. This provides a protective layer for the microbes preventing them from getting exposed to body defence mechanisms like neutrophils and macrophages[4]. The process of intracellular internalisation of staphylococcus is considered responsible for development of resistant infection as it facilitates invasion and growth of microbes within the host cells and protection from antibiotics. Most common organisms associated with PJI are gram positive cocci(Coagulase negative staphylococcus and Staphylococcus aureus)[5]. Gram negative organisms maintain a moderate (9-23%) proportion cases, which are more difficult to treat[6]. Some studies have reported polymicrobial growth in around 19% of cases[7].

Risk factors associated to PJI

The number of revision arthroplasty cases due to PJI are on the rise and it is necessary to identify at risk individuals so that timely preventive actions can be executed. These risk factors can be broadly classified as modifiable and non-modifiable. Patient related factors such as male sex, obesity, diabetes mellitus, inflammatory arthropathy, smoking, post op myocardial infarction or urinary tract infection, patients with diagnosis of osteonecrosis and post traumatic arthritis and bilateral arthroplasty are associated with increased incidence of PJI [8]. Procedure related factors such as high volume centres, long duration of surgery, need of quadriceps snipping or tibial tubercle osteotomy are also associated with high risk for PJI [8,9].

Definition

Even though the incidence of PJI is rising alarmingly, there appears to be no exact diagnostic criteria for PJI. A workgroup conveyed by the 'Musculoskeletal Infection Society'(MSIS) carried out thorough analysis of available data and proposed following recommendations for the diagnosis of PJI. This standardised definition of PJI is now universally accepted by treating surgeons, physicians and all authorities associated to PJI [10].

Based on the proposed criteria, definite PJI exists when:

1. There is a sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from at least two separate tissue or fluid

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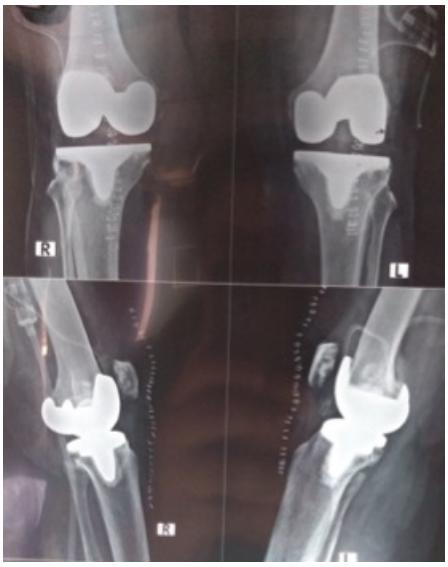

Figure 1: a-Pre-op infected left knee

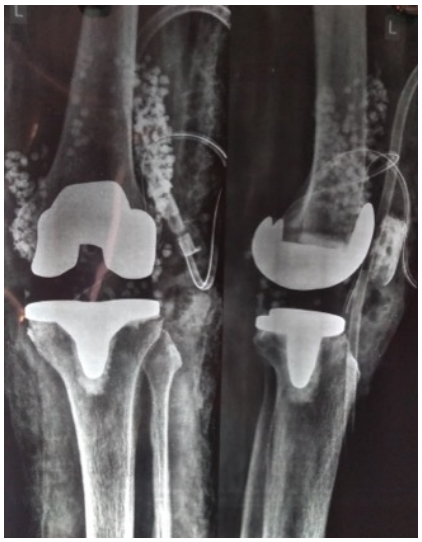

Figure 1: b- After DAIR, PE exchange &CaSO4 cement pellet insertion

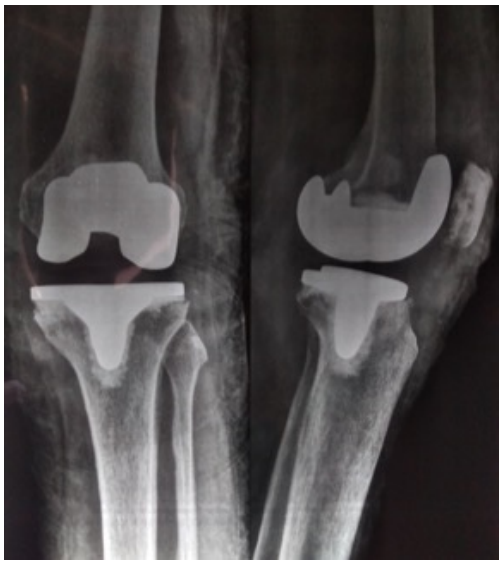

Figure 1: c-4 years follow-up

samples obtained from the affected prosthetic joint; or

3. Any four of the following six criteria exist:

a. Elevated serum erythrocyte sedimentation rate (ESR) (>30mm /hour) and serum C-reactive protein (CRP) concentration (>10mg/L)

b. Elevated synovial leukocyte count

c. Elevated synovial neutrophil percentage (PMN%)

d. Presence of purulence in the affected joint,

e. Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or

f. Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at X400 magnification.

It is recommended to collect at least three and no more than five periprosthetic tissue samples for aerobic and anaerobic culture. Identification of single low virulent microorganism such as Propionibacterium acnes, coagulase negative staphylococcus, Corynebacterium without other associated criteria cannot be classified as PJI [10].

Classification

Based on the duration of symptoms, periprosthetic joint infection can be classified into four types: [11,12]

A. Positive intraoperative culture: more than two positive intraoperative culture reports.

B. Early postoperative infection: onset <30 days after primary arthroplasty.

C. Acute haematogenous infection: characterised by acute symptoms in a previously well-functioning joint.

D. Chronic(late) infection: infection present for >30 days.

Diagnostic workup

Establishing the diagnosis of PJI is often difficult causing rising numbers of cases with delayed diagnosis and increased morbidity. The cardinal signs of fever, chills, elevated blood WBC levels, discharging sinuses may not be present in all cases of PJI. An accurate diagnosis will aid the treating surgeon in decision making and selecting appropriate management option for a particular patient. The tests for diagnosis of PJI detect either the causative organism or the host response to infection and sepsis. Serological tests (ESR & CRP) are standard screening tests for any patient undergoing revision arthroplasty due to PJI. Cut-off values of ESR>30 and

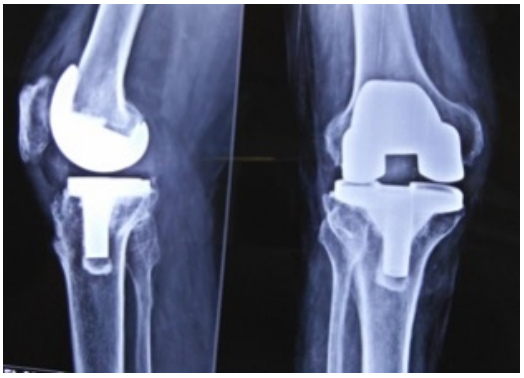

Figure 2: a-Pre-op X-ray of Rt. Infected Knee

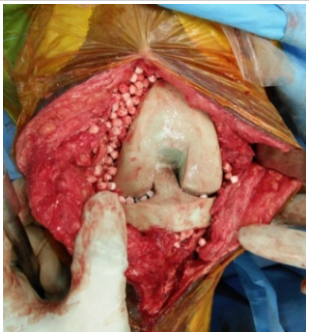

Figure 2: b-Articulating spacer prepared with Polysiloxan templates

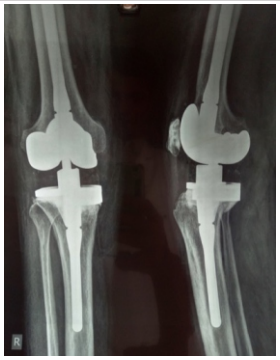

Figure 2: c-Follow-up 7 years after reimplantation

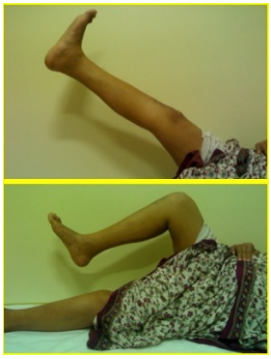

Figure 2: d-Follow-up function

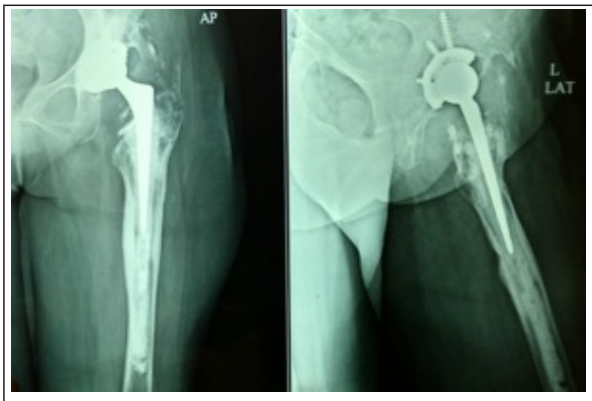

Figure 3: a-Pre-op X-ray of Infected Hip

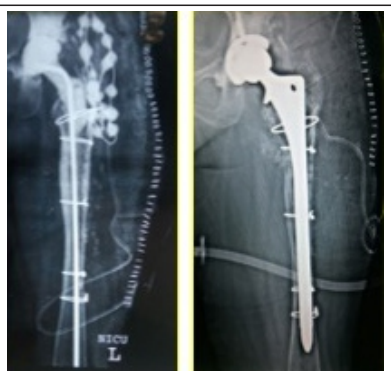

Figure 3: b-Spacer using polysiloxan template & reimplantation

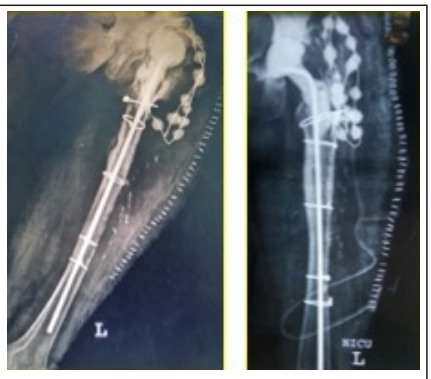

Figure 3: b-Spacer using polysiloxan template

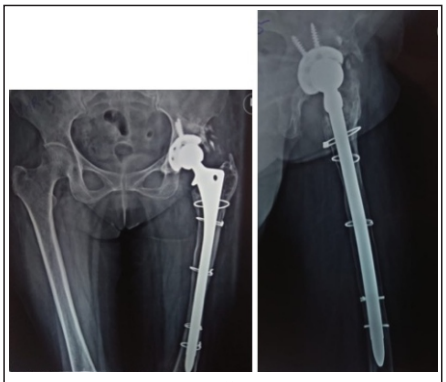

Figure 3: c-Follow-up 3years

CRP>10 have sensitivity of 94.3% and 91.1% and combined ESR & CRP have a sensitivity of 97 % respectively[5,13]. The levels of synovial fluid WBC count and PMN % in infected joint arthroplasties vary in different clinical scenario. Acute PJI are characterised by synovial WBC >20000 with >89% neutrophils whereas chronic PJI are defined by WBC count >1700 and PMN % > 65% [10,14]. Feldman et al.15concluded that ESR of >50 mm/hr had a sensitivity of 79%, a specificity of 78%, and an accuracy of 81% for the detection of periprosthetic infection. Both ESR and CRP are excellent screening tools due to high negative predictive value.

One the most important diagnostic tools is the culture of aspirated joint fluid. It provides the surgeon with adequate data on the virulence of the organism, the guide to antibiotic to be added to cement and the choice of treatment (single stage vs two staged). It is recommended to take three to five intraoperative samples around the prosthesis to increase likelihood of growth. Zywiel et al[16] demonstrated a low sensitivity (7%), high specificity (99%), positive and negative predictive values of 92% and 57% respectively for gram staining to be used as a diagnostic tool for PJI. Fungal and mycobacterial cultures are not routinely done and reserved for high risk cases. However, in our country fungal and mycobacterial infection should always be kept in mind especially in low immune patients[17].Culture negative PJI are reported in 7% cases [18].

The use of frozen section for diagnosis of PJI is well established. A recent meta-analysis of twenty-six studies involving 3269 patients found a positive likelihood ratio of 12 and negative likelihood ratio of 0.23 concluding that intraoperative frozen sections is helpful to detect culture positive periprosthetic joint infection[19]. FDG-PET scan relies on detection of neutrophils and macrophages at the site of infection showing increased glucose uptake. Parvizi et al.[2] showed that FDG-PET scanning had a positive predictive value of 80% and a negative predictive value of 98.5% for the diagnosis of infection at the site of total hip arthroplasty showing increased uptake around the implant-bone interface.

Leucocyte esterase is another enzyme secreted by neutrophils at the site of inflammation. Parvizi et al[20] showed a sensitivity of 80.6% and a specificity of 100% for diagnosing a PJI by this method. This method is quick, requires small amount of synovial fluid but can give erroneous results if there is contamination by blood and is not cost-effective for a single patient diagnosis.

Many new diagnostic tools have been developed and studied for accuracy in detecting PJI including synovial fluid CRP, sonification of explanted materials, interleukin-6 and molecular methods such asPCR. Berberi et al[21], in a study involving 3909 revision total hip and knee arthroplasties, concluded that the diagnostic accuracy for PJI was best for interleukin -6, followed by CRP, ESR and WBCcount in that order. They found the diagnostic odds ratio of 314.7 for interleukin-6, 13.1 for serum CRP level, 7.2for ESR, and 4.4 for white blood-cell count. Although studies to assess diagnostic accuracy of interleukin-6 were limited and needed further investigations.

Management

It is a challenging task to make an accurate diagnosis and effective treatment of an infected joint. There is a significant debate regarding the ideal management of PJI and as a result of which there is no standardised algorithms /guidelines to this devastating complication. Treatment of PJI requires amulti-disciplinary approach involving the orthopaedic surgeon, infectious disease expert and microbiologist. The final goals of treatment are to eradicate infection,

provide pain-free mobility to the patient with minimum morbidity and mortality. In this section, we would review different management options available to the operating surgeon and their expected clinical outcomes.

A)DAIR procedure (Debridement, Antibiotics, Implant Retention)(Fig. 1a-c)

DAIR procedure is effective in eradicating infection in early onset PJI (< 3 months) as the formation of impenetrable glycocalyx biofilm by the organism is still inadequate. The success of DAIR largely depends upon appropriate patient selection and identifying the organism on culture with known antibiotic sensitivity. Healthy patients (with no associated comorbid conditions) with acute symptoms and a stable joint are ideal candidates for this procedure.

Absolute contraindications include patients with implant loosening, periosteal reaction, bone loss and poor soft tissue coverage which may need a staged revision in future. Relative contraindications are immuno compromised patients, patients with rheumatoid arthritis, elevated ESR (>60), elevated CRP (>100), presence of sinus track, chronic symptoms(>3 weeks) and infection by highly virulent organisms (e.g. MRSA) [22].

The key steps to successful result include thorough debridement following open arthrotomy, removal of all necrotic and suspected inflamed tissues, obtain sufficient and representative tissue and fluid samples for culture, irrigation of the joint with pulse lavage, change of all modular components (polyethylene liner in TKR, femur head and acetabulum liner in THR)leaving the fixed components intact. All antibiotics are stopped prior to surgical interventionto facilitate the growth of infecting organism and appropriate culture sensitivity patterns. A post -op regime of 6 weeks of antibiotic is considered adequate. Arthroscopic debridement is not advisable and associated with poor outcomes [23].

B) One-staged exchange arthroplasty

The therapeutic goal in one or two staged revision surgery is complete eradication of infection with maintenance of joint function. Although two or more staged revisions are considered as gold standard for treating PJI, one stage removal of infected prosthesis along with thorough debridement followed by reimplantation can provide successful outcome in selected group of patients. It is to be emphasized that patients with healthy soft tissue cover, minimum bone loss and less than two previous failed surgeries can be considered fora one staged procedure[24].

An absolute requirement for one staged exchange arthroplasty is a preoperative joint fluid aspirate showing exact identification of bacteria with a complete antibiotic sensitivity pattern [25]. Removal of cemented prosthesis is comparatively simpler than a well osteointegrated uncemented implant causing excessive loss of native bone during the procedure. Of late, surgeons have shown encouraging results in one stage procedure by keeping antibiotic soaked mops inside the joint after explantation and then converting it to definitive prosthesis after redraping during same surgical setting.

C) Two staged exchange arthroplasty (Fig.2a-d & Fig.3a-c)

A two staged revision surgery is the gold standard for treating PJI and produces good clinical outcomes. The key elements of surgical procedure are radical debridement and local delivery of high concentration of antibiotics. Late onset PJI (>12 weeks), infection with highlyvirulent organisms (MRSA), polymicrobial infection, inability to obtain exact causative organism on culture with ambiguous antibiotic sensitivity patterns are ideal candidates for a two staged procedure.

It is an essential prerequisite to educate the patient regarding the diagnosis, possible treatment options with expected results, long duration of treatment, multiple hospital admissions, higher economic burden with associated morbidity. Preoperative surgical planning can be discussed with microbiologists, theatre assistants and infection specialist to have a complete knowledge regarding the choice of antibiotic, dosage, route of administration (oral, IV, local drug delivery). Good clinical assessment including appropriate history, history of previous surgery with implant details (for intraoperative assistance during explantation), local surrounding soft tissue condition (need for plastic surgery intervention in the event of extensive soft tissue loss), location of scars and sinuses allows for an accurate planning for a staged procedure.

During the first stage, radical debridement of infected and necrotic tissue and taking appropriate and representative tissue samples for culture needs to be emphasised. It is advised to have a low threshold to carry out extended trochanteric osteotomy (ETO) or tibial tubercle osteotomy (TTO) to facilitate complete removal of implants and cement. Antibiotic impregnated PMMA cement beads over a stainless-steel wire/K-wire have been shown to elute high local concentration of antibiotics.

Many designs of cement spacers are used in the management algorithm of PJI. They are broadly classified as non-articulating (static) and articulating[26]. Static spacers are more commonly used in the knee and are known to produce complications such as restriction ofmotion, soft tissue contracture and bone loss. Mobile or articulating spacers are known tobe more patient friendly as they permit movement and prevent joint stiffness. Since the function relies on the remnant healthy host bone, significant bone loss may be a deterrent to

articulating spacers. They are available as metal on poly, ceramic on poly, cement on cement and unipolar varieties. PROSTALAC (prosthesis with antibiotic loaded acrylic cement)was quite popular for revision cases of infected THR. We have our own templates designed from polysiloxan (100% medical grade silicone), which is autoclavable and reusable available in different sizes.

The choice to antibiotics to be used while preparing these spacers largely depends on the sensitivity patterns after consultation with the microbiologist. The antibiotics selected should be bactericidal, water soluble, thermodynamically stable and should evoke minimum local responses. Glycopeptides (vancomycin) and aminoglycosides (gentamicin) are commonly used as they produce less systemic toxicity due to poor penetration from bone to vascular system. A routine practice involves adding two grams (max 8 grams) of vancomycin powder to 40 grams cement packet with preadded one gram gentamicin.

There is controversy regarding the ideal time interval between spacer insertion and final definitive surgery. A period of 8-12 weeks provides adequate time for local soft tissue healing and rest from active sepsis. There is no confirmatory test for complete eradication of infection. A 6-8 weeks course of IV antibiotics is generally practiced followed by 2-3 weeks of drug holiday. Decreasing titres of serological markers (ESR, CRP) and repeat joint aspirate culture after the period of antibiotic holiday can be assumed as deemed candidates fora definitive surgery.

The final stage is considered as an aseptic surgery and all methods to restore the bone loss and attain maximum stable and mobile joint should be attempted. Modular prosthesis, long stem implants, trabecular mesh and augments, revision cups with multiple screw options, antibiotic impregnated cement and local drug delivery systems (calcium sulphate granules with vancomycin) are kept available during second stage surgery to attain complete eradication of infection and reliable clinical outcome.

D) Non-salvageable infection:

In case of failure of two stage exchange arthroplasty, intractable infection, immunosuppressive patients, drug addicts, uncooperative/medically unfit/mentally impaired patients, inadequate musculature, hip excision arthroplasty or knee arthrodesis remains procedure of choice.

Preventive measures

The first step in the measures to prevent PJI is to identify the risk factors which are modifiable and develop strategies to minimise these risks. Screening for symptoms of infection at remote sites (UTI), optimum glycaemic control, modification of immunosuppressive drugs, weight loss, cessation of smoking & alcohol intake and regular preoperative screening for MRSA carriers by nasal swabs have been effective in reducing the burden of PJI. Prophylactic preoperative antibiotics administers within 30 mins prior to skin incision is recommended. The importance of theatre etiquettes, laminar airflow, optimum surgical site preparation, shorter duration of surgery in prevention of PJI is well established. It is important to increase awareness among the patient and the entire hospital team regarding their participation in preventive efforts.

Conclusions

Prosthetic joint infection is a devastating postoperative complication that compromises the long term outcome of the surgery. Prevention of PJI is crucial and involves preoperative optimization of the patient by controlling high risk factors. The incidence of PJI continues to be between 1-4%.

Early diagnosis of infection is crucial. Pain, out of proportion to that expected following surgery, increasing pain or progressive loss of joint motion are some features that may point towards a PJI. No single laboratory investigation is diagnostic of PJI. However, total WBC count, ESR, CRP and interleukin-6 are some parameters that may in isolation or together, aid the diagnosis of a PJI. Obtaining a fluid or tissue sample from the joint for microbiological examination is crucial in diagnosing the organism, starting targeted antibiotics and planning appropriate surgical course.

Depending on the stage at which the patient presents with a PJI, the organism cultured and its sensitivity to antibiotics, the stability of the implant and the medical comorbidities, surgery can range from aggressive irrigation and debridement with retaining of implant to single or two stage implant exchange to arthrodesis or even amputation. Decision making regarding treatment must be made on a case to case basis as there is no universally accepted algorithm for management of this devastating complication.

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