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Case report

PERIPROSTHETIC KNEE INFECTION: A CASE REPORT

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ABSTRACT

Periprosthetic joint infection (PJI) is one of the major complications resulting from prosthesis implantation. Staphylococci are responsible for more than 50% of PJI, 20% are polymicrobial, 15% are caused by gram-negative, and about 10% of cultures are negative. The complete eradication of PJI is challenging. For a correct treatment, it is helpful to perform clinical staging based on the anatomical location of PJI and the immune characteristics of the host. However, regardless of the area of infection, the surgeon's role is crucial, firstly in terms of timing and secondly in assessing the extension of the pathological process. The goal of the treatment is to eradicate PJI ensuring the maximum functional result. The reported case describes an extensive necrotic area on the right knee, with exposure to the prosthetic device, the treatment, and the available bibliography is discussed.

KEYWORDS: *joint, knee, infection, prosthesis, leg, bacteria*

INTRODUCTION

Periprosthetic joint infection (PJI) is one of the major complications resulting from prosthesis implantation. The incidence of PJI is 1-2%, which reaches 4% in revisions (1-3).

There is no universally accepted definition of a PJI. Clinically, it manifests itself in multiple forms, while classical signs of a phlogistic process such as fever leukocytosis or local signs may be absent, thus making the diagnosis difficult.

Staphylococci are responsible for more than 50% of PJI, about 20% can be polymicrobial, 15% are caused by gram-negative, and about 10% of cultures are negative (4, 5). However, failing to identify the pathogen does not rule out the diagnosis. Pathogens differ depending on the onset of the infection and when the prosthesis was inserted (6, 7).

It has been observed that PJI that develop within the first 4 weeks after surgery (e.g., early infection) is caused by highly virulent microorganisms (such as Staphylococcus aureus), while those that develop after 3 months are caused by

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low virulence organisms (such as coagulase-negative Staphylococcus, Propionibacterium acnes and Enterococci). In addition, infection rates are higher in the first 2 years after surgery due to the greater vascularisation of the peri-implant tissues, which favours the hematogenous spread of PJI (8).

The complete eradication of the infection is challenging, mainly because the biofilm, a complex environment formed by bacteria within their extracellular matrix, can evade the body's immune defences, thus creating a resistance to antibiotics that is 1000 times higher than normal (9). The most relevant points on PJI were discussed during the International Consensus held in Philadelphia in 2018 to give indications deriving from the latest publications.

To apply a correct treatment, it remains mandatory to perform a clinical staging based on the infection's anatomical location and the host's immune characteristics. However, regardless of the area of PJI, the surgeon's role is crucial, firstly in terms of timing and secondly in assessing the extension of PJI.

Few articles have been published on the management of exposed prostheses, and it seems that adequate and early soft tissue coverage allows the prosthesis to be saved (10).

Skin complications are common following knee replacement surgery, although they do not always lead to exposure to the implant. In case of exposure, the simple suture is ineffective, and only a vascularised graft makes it possible to heal the wound and save the prosthesis. The gastrocnemius muscle flap is the technique of choice since it is simple and safe, allowing good-quality coverage. In addition, it can be performed in a single step, and low morbidity and no residual scarring are reasons for doing it early (11-13). Other advantages of this method are early mobilisation and hospital discharge (11). It also reduces the rate of the arthrodesis with better functional results.

Here, we describe a case of an extensive necrotic area on the right knee with implant exposure. Moreover, the available bibliography is discussed to support our clinical management and the technique employed.

CASE REPORT

A lady, 74 years old, arrived at the hospital in February 2021 due to an evident and extensive necrotic area on the right knee that arose after a revision implant surgery in December 2020.

The patient reported a previous surgery for right knee arthroplasty in May 2017 as a result of a tri-compartmental arthrosis responsible for severe right knee pain, resistant to medical therapy and physiotherapy. After rehabilitation treatment, optimal knee range of motion recovery was reported, and recovery in normal daily activities. However, in August 2020, the patient had an accidental fall and presented a periprosthetic fracture on the right femur that was reduced and synthesised with a condyle plate.

In December 2020, due to a non-traumatic rupture of the implanted plate (Fig. 1), a second surgical treatment with implantation of mega-prosthesis revision (Fig. 2) was performed.

The patient was then admitted to a rehabilitation department where, about two weeks after admission, she reported an extensive wet necrotic ulcer on her right knee (7cmx7cm with 3 fistulous ulcers) with positive wound swab for Staphylococcus spp. (Fig. 3). Routine laboratory investigations showed C-reactive protein (CRP) 35 and erythrocyte sedimentation rate (ESR) 112.

On February 2021, the patient arrived at our hospital's emergency department presenting a wide skin loss on the implant (Fig. 3). Clinically, the patient was apyretic and in good general condition.

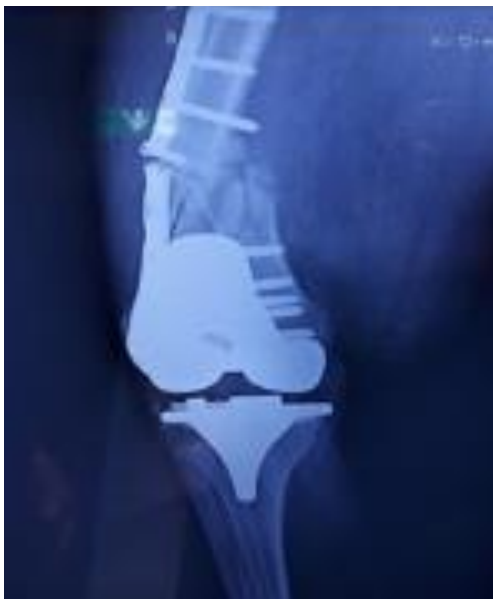


Fig. 1. *Non-traumatic rupture of the implanted plate.*

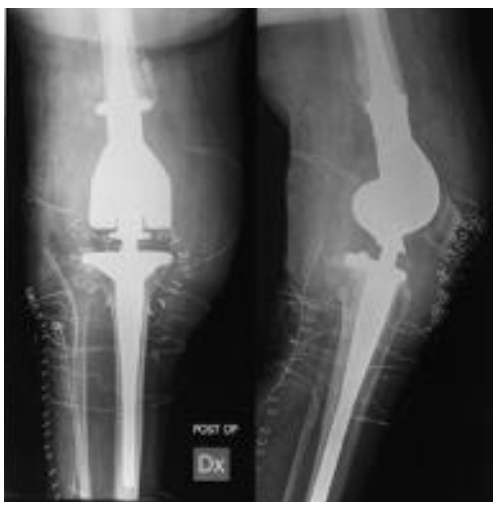


Fig. 2. *Second surgical treatment.*

On admission, intravenous therapy with Augmentin 2 gr x 3/day and Bactrim 60 mg 1 fl x 3/day was performed, as well as a new wound swab, while the advice from the plastic surgeon was to apply a tissue coverage of the wound after an accurate debridement and intraoperative evaluation of the depth extension of the necrotic area and the type of surface (e.g., bone or prosthesis) exposed.

The wound swab was positive for Proteus Mirabilis, so Augmentin was stopped, and Tazocin 4.5 gr x 3/day was administered. The radiographs showed no signs of detachment or mobility of the prosthetic components (Fig. 4).

Computed tomography (CT) scan revealed the presence of subcutaneous bullae at knee level with an abscess in the vastus intermedius muscle at the proximal third of the femoral prosthetic taproot; the positron emission tomography (PET) scan performed about one week after admission showed the presence of tissue with high glycidic metabolism compatible with a phlogistic process. During hospitalisation, CRP, ESR and presepsin values showed progressive improvement.

We discussed with the patient and relatives the possibility of amputation, but the patient refused. Finally, in agreement with the plastic surgeons, it was accepted to do Vacuum Assisted Closure (VAC) therapy in polyurethane foam to be replaced every 5 days and to continue the antibiotic treatment. On March 2021, the patient voluntarily resigned and continued antibiotic and medical treatment at home.

On May 2021, the patient returned to the hospital. She was apyretic, in good general clinical condition and with CRP values <2.9. Following medical treatment with VAC therapy, the necrotic area was reduced by at least 2 cm compared to those at previous admissions (Fig. 5).

CT scan showed the presence of minimal intra-articular effusion with a small collection on the lateral side of the knee extended in the subcutaneous region with a diameter of 4x2 cm. We discussed again with the plastic surgeon about therapeutic options, and the patient agreed to perform a surgical debridement of the wound and placement of a dermo-epidermal graft.

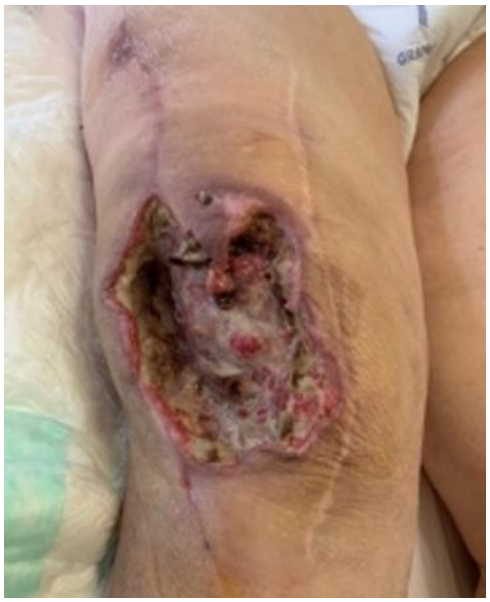


Fig. 3. *Skin loss on the implant.*

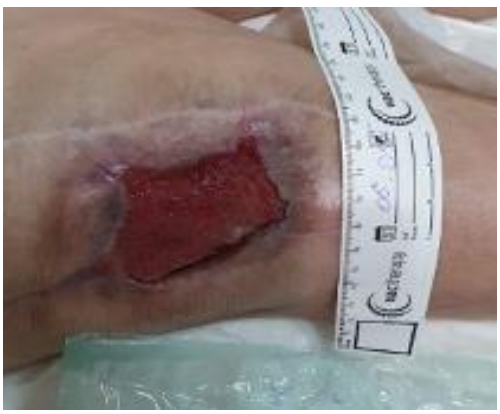


Fig. 5. *After medical treatment with VAC therapy, the necrotic area was reduced by at least 2 cm compared to those at previous admissions.*

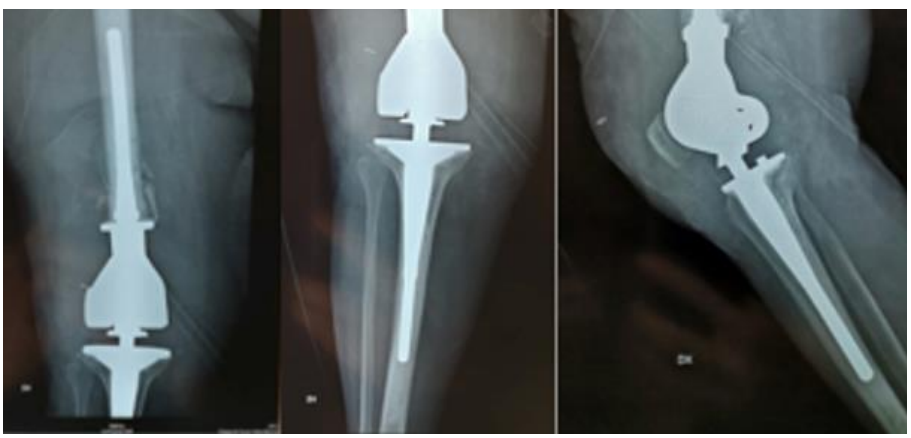


Fig. 4. *The radiograph of the prosthetic components.*

First surgical procedure

Two grams of Cefazolin were administered as antibiotic prophylaxis and 1 gram of Tranexamic acid to decrease bleeding. The patient was placed in the lateral position, and spinal anaesthesia plus sciatic nerve block was done. After 15 minutes, the patient was placed in supine decubitus, and a sterile surgical field with alcoholic chlorhexidine was done. The edges of the loss of substance were recentered, and medial parapatellar access was performed. Prosthetic components were exposed, and their stability was tested. Debridement of periprosthetic tissues was performed, and multiple samples were taken for microbiological evaluation. Washing with 4 litres of Bactisure ® solution and 2 litres of Ringer Lactate was performed as well as with 2 litres of saline solution. Finally, suturing of the arthrotomy was done.

Second surgical procedure

In ischemia, a skin incision was made cranially-caudally at the level of the lateral margin of the right leg. Identification of the body of the lateral gastrocnemius muscle, dieresis of the soft tissues and access to the vascular space between that muscle and the peroneal muscle was made. Detachment of the flap at the level of the insertion of the lateral gastrocnemius muscle, identification of the vascular peduncle was performed, and the flap was tunnelled (Fig. 6, 7). Finally, partial-thickness dermo-epidermal grafting was done from the ipsilateral thigh (Fig. 8). Two suction drains were placed at the level of the leg. Suturing and dressing were done.

Because of the size of the defect, we opted for a rotation flap of the lateral side of the gastrocnemius muscle, formed by two muscle bellies. The two heads originate respectively from the two femoral condyles, run in the posterior region of the leg divided by a median raphe and insert through their common tendon on the tendon of the soleus muscle forming the calcaneal or Achilles tendon. The lateral head is vascularised by the lateral sural artery that originates from the popliteal artery at the level of the articular surface of the knee. The lateral gastrocnemius rotation range allows it to cover an area up to about 5x12cm, unlike the medial wound area, which was about 7x7cm. It should be considered during lateral head rotation not to compress the peroneal nerve. The most significant disadvantage of using the lateral gastrocnemius is a cosmetic deformity from the donor site.

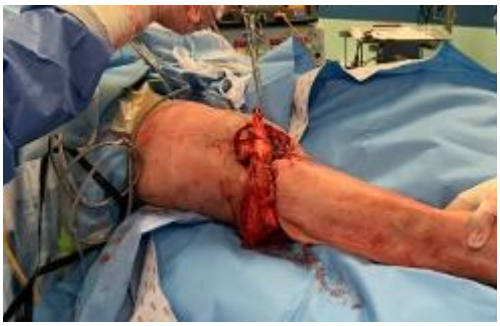


Fig. 6. *Detachment of the flap.*

In the post-operative period, there was a partial failure of the lateral skin flap with localised necrosis (Fig. 9-12); treated with VAC therapy. However, after 5 months, there was a complete healing of the wound and the normalisation of infection (Fig 10- 13).

Special attention was given to masks to control the COVID-19 infection during the surgical treatment (14, 15) and to the decontamination of the operating room (16).

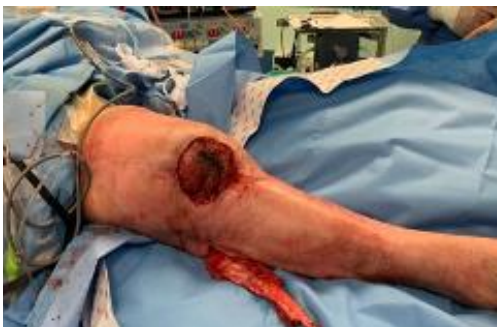


Fig. 7. *Tunnelling of the flap.*

DISCUSSION

The diagnosis of PJI represents a challenge, although new criteria and scores have been developed to facilitate the diagnosis. Nevertheless, proper PJI diagnosis remains critical to choose the optimal treatment option (17). In 2011, the Musculoskeletal Infection Society proposed some criteria to standardise the diagnosis of PJI (18), which were revisited in 2013 during the International Consensus Meeting (19).

Recently, national and international workgroups have established standardised diagnostic protocols for suspected PJI. In 2018, a new evidence-based PJI definition was published, which improved performance for diagnosing hip and knee PJI (20). In addition, in 2020, the European Joint Infection Society gave the latest definition of PJI, a practical guide for clinicians based on a three-level approach (21).

In the presence of a fistula, or in case of prosthesis exposure, the total

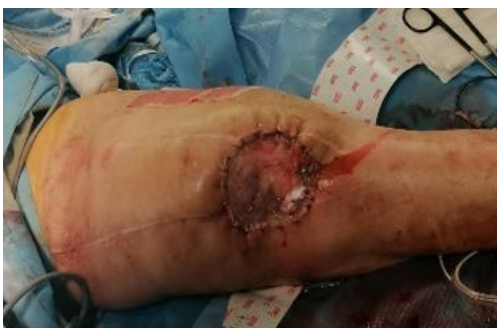


Fig. 8. *Dermo-epidermal grafting from the ipsilateral thigh.*

knee arthroplasty is considered infected. In occult cases, local signs of infection or fever can lead to suspicion of PJI, and pain is the most relevant symptom in over 90% of cases. X-rays in two projections, blood tests and arthrocentesis must be performed. X-rays may show prosthesis loosening and femoral or tibial osteolysis (radiolucent lines). To date, there is no clinical sign able to make a 100% diagnosis.

Usually, levels of CRP and/or D-dimers and ESR are increased, but recent studies on the sensitivity of CRP and ESR have demonstrated about 20% of false negatives (22). In case of fever (> 38 ° C), a blood culture is recommended to diagnose early-stage bacteremia and avoid worse complications such as septic shock, systemic inflammatory response syndrome,e or multi-organ failure. Another essential diagnostic step is knee arthrocentesis. If possible, any antibiotic therapy should be suspended for at least 14 days prior to sampling to increase the test's sensitivity (23).

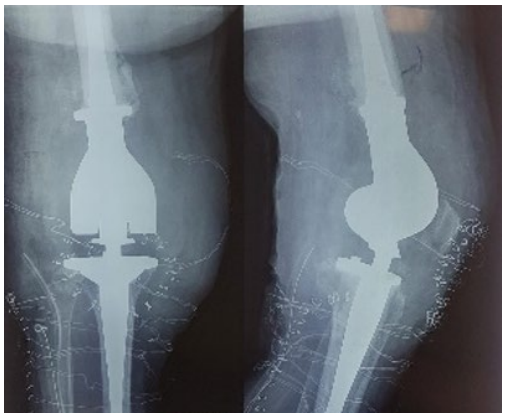
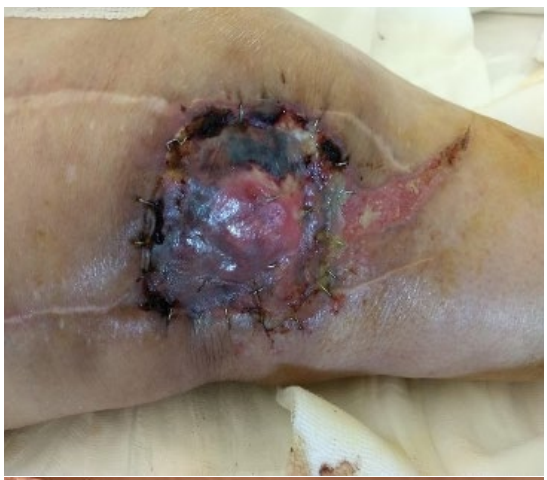


Fig. 9. *Post-operative X-ray.*



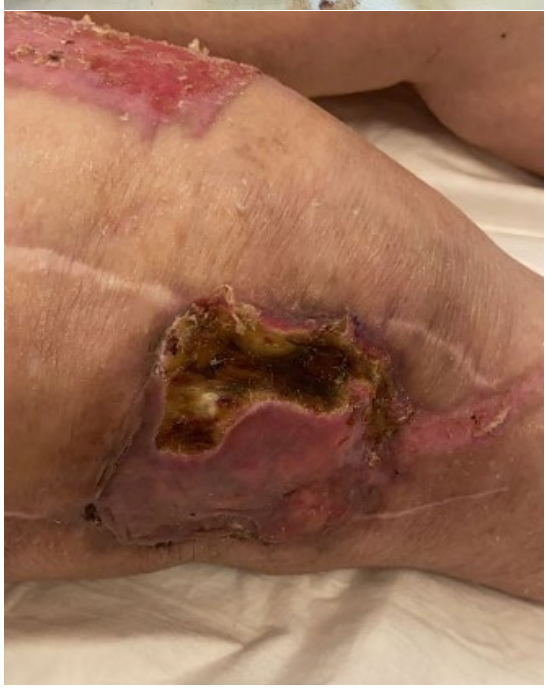


Fig. 10. *June 2021*

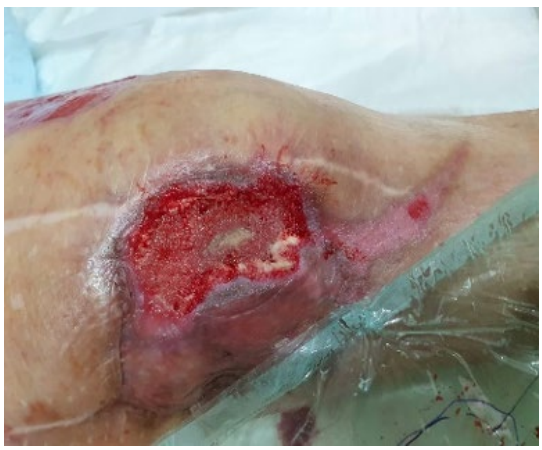


Fig. 11. *July 2021*

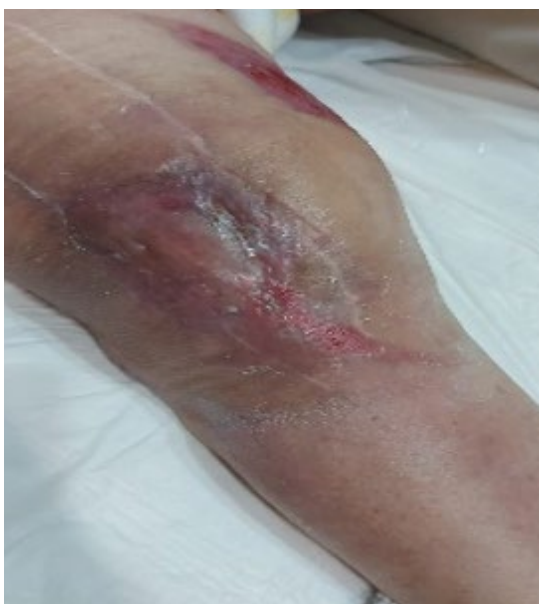


Fig. 12. *November 2021*

It would be recommended to take at least 2 mL of liquid to perform the various tests: alpha-defensin test and dosage of white blood cells (WBC), leukocyte esterase (LE), CRP and PMN in the synovial fluid.

Alpha-defensin is an antimicrobial peptide produced by neutrophils and, together with CRP, represents one of the new markers included in the diagnostic criteria. Alpha-defensin is a very sensitive test but presents some disadvantages, such as the high costs and the possibility of giving false positives for metallosis.

Stone et al. (24) proposed an algorithm combining the alpha-defensin test with the CRP assay to reduce false positives and negatives.

Tests can be done directly at the patient's bedside. The cheapest and fastest is the leukocyte esterase test (LET). A differential diagnosis should be made with other inflammatory arthropathies (e.g., gout, rheumatological diseases) if positive. In a meta-analysis of 1011 patients, a sensitivity of approximately 90% and a specificity of approximately 97% were shown (25**)**.

However, tests performed on synovial fluid samples, centrifuged to remove blood traces, are more reliable. In a recent study, the cut-offs considered for the diagnosis of PJI are 1630 leukocytes / microL (estimate sensitivity - SE 83.6%, specificity - SP 82.2%) and PMN (%) of 60.5% (SE 80.3%, SP 77.1%) (26). It is now recognised that swab culture tests provide a high percentage of false positives. The gold standard for diagnosing PJI is bacterial cultures, which should be grown in a microbiology laboratory for at least 14 days. Two positive cultures for the same microorganism are indicative of infection. Based on these tools, a scoring system for diagnosing PJI was created at an international meeting in Philadelphia in 2018 (Table I, II). This new score system facilitated the preoperative diagnosis and, compared to the Musculoskeletal Infection Society criteria, demonstrated an improvement in results with a sensitivity of 97.7% and a specificity of 99.5%. The last frontier for diagnosing PJI is represented by next-generation sequencing (NGS), a new application of genetic sequencing with lower costs and faster times than the classical techniques (27). NGS has proved extremely sensitive in detecting bacterial DNA (28).

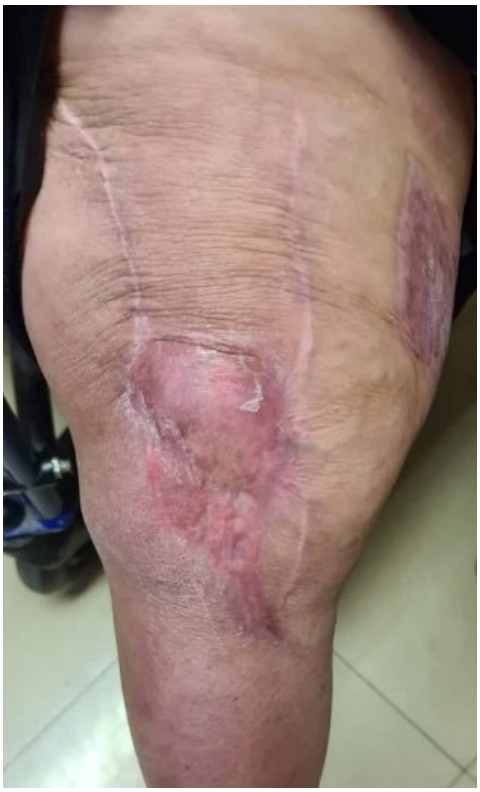


Fig. 13. *February 2022*

The treatment of PJI must take into account several aspects, such as the timing of the onset (early/ delayed/ late infection), the condition of the soft tissues and the clinical objectivity (i.e. the functionality of the extensor apparatus) (29, 30) the patient`s comorbidities, laboratory (i.e. inflammation indices) and microbiological data (i.e. the agent and relative antibiotic sensitivity), the stability of the prosthetic implant, the patient's expectations and the functional needs.

The treatment aims to eradicate the infection, ensuring maximum functional results. It includes antibiotic therapy as the only treatment or in combination with surgical therapy.

Antibiotic therapy

Antibiotic therapy is one of the two fundamental pillars in treating PJI. However, in the case of infection, the efficiency of eradicating the PJI with antibiotic therapy alone is limited, mainly due to the bacterial biofilm on the prosthetic implant. Therefore antibiotic therapy alone should be limited to specific circumstances, such as high operative risk, in the medically

Table I. *Scoring system for the diagnosis of PJI created at an international meeting held in Philadelphia in 2018.*

Major criteria (at least one of the following)	**Decision**
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

Table II. *New scoring system definition for PJI (Philadelphia ICM 2018).*

		Minor criteria	Score	Decision
Preoperative Diagnosis	Serum	Elevated CRP or D-Dimer	2	≥6 Infected **2-5 Possibly Infected** 0-1 Not Infected
		Elevated ESR	1	
		Elevated synovial WBC count or LE	3	
	Synovial	Positive alpha-defensin	3	
		Elevated synovial PMN (%)	2	
		Elevated synovial CRP	1	

	Inconclusive pre-op score or dry tap	Score	Decision
Intraoperative Diagnosis	Preoperative score	-	≥6 Infected **4-5 Inconclusive** ≤3 Not Infected
	Positive histology	3	
	Positive purulence	3	
	Single positive culture	2	

stable patient (absence of an ongoing septic picture), the presence of low virulence microorganisms sensitive to antibiotics and mechanically stable prosthesis (31). Based on the antibiogram, a specific antibiotic should be selected. Broad-spectrum antibiotics should be prescribed and used in case of an acutely PJI of the patient showing signs of sepsis (32).

Monitoring the patient during treatment and deciding the type and course of the antibiotic should be determined by specialists (e.g., microbiologists and virologists). A post-surgical protocol has to define the duration and route of antibiotic delivery.

Surgical treatment

Treatment must consider the degree of exposure of the prosthetic implant, in addition to PJI. In association with the antibiotic treatment, the surgical treatment has several options with different clinical outcomes: from rescue procedures (arthrodesis, amputation) to procedures with preservation of joint function (one/two-stage revision) and DAIR (debridement, antibiotic and implant retention).

DAIR

In early infection, the debridement and irrigation with antiseptic solutions, without implant removal, are usually the choices for surgical treatment in the absence of X-rays pictures of mobilisation of the prosthetic implant (to be confirmed intraoperatively) or of heterotrophic bone formation (radiographic signs of chronic infection) (31). The tissue removed during surgical debridement is sent to a microbiological laboratory. The application of a drain facilitates the expulsion of intra-articular blood/serum, and the local application of antibiotics in beads, in association with the systemic one, can ensure better post-operative antibiotic coverage.

In the presence of a moving prosthesis, the treatment should include replacing each modular component of the prosthetic system (32). DAIR is a valid surgical option even in the presence of mega-prostheses if sufficient covering tissue to ensure adequate post-operative wound closure is present. DAIR should be performed within 4 weeks after surgery before the biofilm is formed onto the prosthetic implant. Contraindications are chronic infections with signs of implant loosening, covering defects and patients not eligible for reoperation.

Two-stage revision

The prosthetic implant and any other foreign material are removed. Next, aggressive debridement of all necrotic tissues is performed, and an antibiotic spacer is implanted to allow the healing of the injured tissues and the total or partial preservation of joint motility. The second stage involves the removal of the antibiotic spacer and the implantation of a new prosthesis after the eradication of PJI (31).

The two-stage revision is indicated in the case of chronic infections with mobilisation of the implant and for infections caused by virulent organisms such as Methicillin-resistant Staphylococcus aureus (31).

Single stage revision

A single-stage revision is recommended in patients with a known aetiologic organism and sensitive to an antibiotic, when no abscess is present, when the patient is not immunocompromised, and if there is no radiological evidence of prosthetic implant loosening or ongoing osteitis (31). This type of revision is considered when the pathogen is sensitive to antibiotic treatment, and a specific antibiotic has to be given 2-3 weeks prior to surgery (33) when there is good coverage of healthy soft tissues onto the prosthesis and with little or moderate bone loss. Technically, the one-step revision procedure includes removing the implant and all foreign material and replacing with a new prosthesis.

Rescue Operation

Unfortunately, for some patients, it is not possible to perform a prosthetic re-implantation since it might lead to the patient death; thus, rescue surgeries such as arthrodesis, resection arthroplasty and amputation are needed (34). In addition, a rescue procedure is to be considered in case of a failure in the revision treatment, in case of a multi-operated knee or if the patient is debilitated (31).

Arthrodesis

The potential indications for knee arthrodesis are the failure of other surgical options, patients with extensive deformities, advanced alterations of the extensor mechanism, major soft tissue deficits, immunosuppression or infections with highly virulent bacteria. Arthrodesis stabilises the joint, irreversibly compromising its flexion-extension movement, allowing it to be loaded and making it painless. The surgical procedure can be performed using an intramedullary nail, a plate or an external fixator (31).

Arthrodesis is the most common rescue procedure in severe knee instability after removing a total knee prosthesis for infection. However, in some cases, it may not ensure joint stability, especially in cases where a constrained prosthesis has been explanted, which causes major bone resection. The arthrodesis's success also depends on the type of prosthesis.

Of 45 cases of arthrodesis, Brodersen et al. (35) recorded an 81% cessation following the failure of total knee arthroplasty with a condylar prosthesis, compared with a rate of 56% following the failure of a constrained implant. Similar results were recorded by Knutson et al. (36) out of a total of 85 cases of arthrodesis, the success rate after the removal of a semi-constrained knee prosthesis was 50%, compared with a success rate of 20% after the removal of a constrained prosthesis.

Furthermore, a stable arthrodesis is more challenging to achieve in those cases where implantation involves a more significant bone resection, such as in the case of the implantation of a mega-prosthesis.

Resection arthroplasty

Resection arthroplasty removes the implant and the cement associated with local debridement without re-implanting any device. This technique aims to create a false joint that ensures minimum mobility. The candidates for this type of treatment are patients with low functional demand (31).

After the resection arthroplasty, the limb is immobilised for three to six months. During this time, there is a retraction of the soft tissue at the level of the bone stumps subject to resection arthroplasty, which will ensure a certain degree of movement.

Resection arthroplasty can provide a viable alternative to arthrodesis, especially in severely disabled patients who may benefit from some degree of joint motility, especially if forced to be sedentary. A stiff knee in post-arthrodesis extension may be a factor that reduces rather than increases the chances of movement, especially in patients with severe disabilities (24).

Amputation

Amputation is a surgical rescue option to be considered when an uncontrollable local infection, reduced bone stock and significant loss of soft tissues that do not allow the wound to close are present (31).

Above-knee amputation also represents a valid alternative in those patients whose functionality of the extensor apparatus has been lost with consequent non-functional joint (27).

Treatment of surgical wound complications

After a knee arthroplasty, hemarthrosis can arise when drainage is reduced. The presence of persistent bleeding inside

the joint promotes bacterial growth. If bleeding is excessive, it can lead to a dehiscence of the surgical wound.

Rest and suspension of rehabilitation therapy can reduce the stress on the surgical wound and must therefore be considered in the presence of complications.

Surgical wound healing can be affected by several patient-related factors, such as nutritional status, pre-existing vascular disease, rheumatoid arthritis and/or diabetes mellitus, smoking and previous complications. In case of superficial dehiscence of the surgical wound after total knee arthroplasty and the absence of local signs and laboratory indexes of infection, the constant dressing of the surgical wound and its constant monitoring can represent the proper measures to ensure healing.

Much more serious is the presence of a large ischemic area around the surgical wound that can predict full-thickness tissue loss. A decision must be made on whether to surgically remove this area and then cover it with a skin graft, muscle flap or both. Timing is crucial in making this decision; surgery as early as possible ensures a greater chance of healing without further complications (27).

CONCLUSIONS

Identifying the patient's risk factors, adequate preoperative planning and correct surgical execution, antibiotic prophylaxis and early management of the potential complications reduce PJI risk.

In the presence of signs and symptoms and/or laboratory tests suggestive of infection, early diagnosis and aggressive treatment increase the rate of PJI eradication.

The most important factors to be considered when choosing the best protocol for treating a PJI include the following:
the time between the first surgery and the development of the infection;
the nature of the patient's symptoms;
the radiographic findings;
the etiological agents involved and their sensitivity to antibiotics;
what type of prosthesis is present;
if the bone-cement and bone-prosthesis interface is involved in the infectious process;
whether the prosthesis has any mobilisation findings;
if replanting is possible;
how much healthy bone remains after prosthesis removal;
the presence of complications affecting the surgical wound and/or soft tissue;
the functional needs of the patient.

In consideration of these variables, rational management can be planned. Early diagnosis of PJI can ensure less invasive surgical management. In this case, surgical debridement associated with antibiotic therapy can ensure implant retention, especially in the presence of a low-virulence infectious agent.

When these criteria are absent, the prosthesis must be removed, and the implant must be replaced after debridement and local antibiotic therapy. In case the infection cannot be controlled or in the presence of important skin and soft tissue loss, arthrodesis may be the best approach. Resection arthroplasty and amputation are reserved when neither re-implantation nor arthrodesis is possible. However, it is possible to perform implant retention with DAIR in selected cases, as reported.

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