Antibiotic Loaded Cement Spacers for Two Stage Treatment of Periprosthetic Joint Infections

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Periprosthetic joint infections are devastating complications confronted by every orthopedic surgeon. Guidelines for treatment are constantly improving but several areas lack a consensus. Two stage revision is the current gold standard for deep joint infection following total knee and hip replacement. We present our experience with 12 cases and comment on current data from the literature. Based on the moment of treatment, most of our cases were chronic PJJ. Staphylococcus aureus was more common than CNS and the gram negative bacteria were also highly prevalent. Teicoplanin and Vancomycin were most commonly used for iv administration whereas Gentamicin was mostly used in the cement spacer. Periprosthetic joint infections continue to pose a great therapeutic challenge with high costs for the health care systems, high stress for the patient and frustrating results for the physician. With two stage revisions our patients had better results when the curative treatment was done early and in immunocompetent hosts.

Keywords: cement spacers, antibiotic elution, periprosthetic joint infection, revision arthroplasty, two stage treatment

After the initial implant is explanted, a thorough irrigation and debridement removes all devitalized tissue. A mobile of fixed lump of antibiotic loaded acrylic cement is placed to fill the articular gap, deploy antibiotic and provide temporary support. We present our experience and comment on current data from the literature.

Experimental part

A review of the cases treated in our Clinic over the last 5 years identified 12 total joint replacements treated by two stage revision for infection (table 1). All had the implant removed and replaced by a fixed PMMA (polymethylmethacrylate) antibiotic loaded cement spacer. Representative cases are presented in figures 1 to 4.

Fig. 1. Case 7 (table 1) early infection with Staphylococcus aureus after TKR; removal of implant at 2 mo and insertion of spacer, maintained for 3 months; revision arthroplasty using Zimmer LCCK with 6 weeks of iv Teicoplanin

Fig. 2. Case 3 (table 1) late infection with MRSA at 7 years, possibly hematogenous in a patient with RA and chronic immunosuppressive medication; the implant was removed and replaced by two consecutive spacers, held in place for a total of 9 months; infection and inflammation persisted and was fused on external fixator with no relapse at one year

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Osteoarthritis of the hip and knee are the most common locations treated by joint replacement. Worldwide, more than 1 in 5 people may be affected. Although infrequent (1%), periprosthetic joint infections are devastating complications confronted by every orthopedic surgeon. Guidelines for treatment are constantly improving but several areas lack a consensus [1-3].

Two stage revision is the current gold standard for deep joint infection following total knee and hip replacement. This is especially valid for chronic and acute late infections caused by biofilm forming organisms. The majority of knee infections are caused by coagulase negative and aureus Staphylococci and a big percentage are from the methicillin resistant subtype.

Case example 1
Results and discussions

Diagnosis of PJI is not always straightforward [4,5]. The presence of a sinus tract communicating with the joint is probably one of the most reliable signs. Several other possibilities exist, such as two positive cultures with the same pathogen, clinical signs of inflammation, elevated serum CRP and ESR or increased leucocyte count with PMN predominance in the synovial aspirate. In two stage revisions, CRP and ESR are also used to monitor evolution and decide upon the best moment for the new arthroplasty.

Onset of symptoms relative to index surgery usually classifies PJI into early (less than 6 weeks), mid term and late (over 6 months). Based on the moment of treatment, most of our cases were chronic PJI. Patient profile also plays an important role in development of an infection. RA treatment induces immunosuppression and predisposes to PJI both immediately postoperatively, as well as at a later time by hematogenous inoculation [6]. The most common pathogen is a gram positive biofilm forming Staphylococcus. In our series, Staphylococcus aureus was more common than CNS and the gram negative bacteria were also highly prevalent. This pathogen profile is somewhat different than the literature but may be caused by the small number of cases or the selection bias from including only two-stage revisions. For two cases we were unable to isolate the pathogen. The treatment was conducted empirically against the most likely candidate. Although probably not entirely cured, deep infections can be controlled with a combined approach in which parenteral antibiotics are a very important component. Most relapses after septic revisions are caused by the initial organism although the resistance profile may change. Therefore, these organisms should also be targeted together with the most common infecting agents. We had one case of multi resistant Pseudomonas arthritis that persisted through the primary TKR and revision. The extensive and prolonged treatment with Colistin proved safe [7].

PMMA cement is the workhorse for local antibiotic deployment in musculoskeletal infections [8]. Articulating spacers may provide better function and easier reimplantation especially if kept in place for several months. However, long term function and relapse are the same. Handmade ones are less expensive and more porous which leads to better antibiotic elution. The antibiotic release is dependent on dose, cement porosity and spacer surface. The highest concentrations are obtained in the first few days, with bactericidal local concentrations and safe systemic levels [9].

Many types of antibiotics can be used. The main requirement is that it should be chemically stable in order not to be destroyed by the exothermic PMMA polymerization. In our clinic gentamycin in one of the most used antibiotic for mixing into spacers. It is inexpensive and very efficient against gram negative bacteria such as E coli, Pseudomonas and Klebsiella. Normally 4 vials (80mg/2ml) are used for each pack of 40g of PMMA. It binds selectively to certain tissues which makes it potentially nefrotoxic. May lead to hearing loss and acute renal failure by tubular necrosis. Toxicity is dose related but may also be augmented by increased age, concomitant use of diuretics or cephalosporins. First generation cephalosporins (Cefazolin) are efficient against gram positive, second generation (Cefuroxime) have a more balanced activity and third (Ceftriaxonum) are active against gram negatives including Pseudomonas in doses of 2g per 40g of PMMA. Vancomycin 2-4 g/ 40 g PMMA is the main line of treatment for MR Staphylococcus aureus [1,10].

There are several issues with systemic prolonged high dose antibiotic administration which may be mitigated by local deployment via cement spacers. Excessive consumption of broad spectrum antibiotics can give saprophytes like Clostridium difficile an opportunity to take over normal intestinal flora. In frail, elderly population this can have serious consequences even with prompt diagnosis and treatment [11]. Therefore regimens should be selected wisely based on individual susceptibility and host tolerance. In our series Telipolplatin and Vancomycin were most commonly used for iv administration whereas Gentamicin was mostly used in the cement spacer. We did not use Tobramycin even if this is a popular aminoglycoside reported by studies in the literature [1,10]. The generalized use of antibiotic cement for primary arthroplasty cases, as well as cement spacers for two stage revisions may create resistance to those substances [12].

Future directions are aiming to reduce biofilm formation on the implant surfaces as well as use absorbable materials to deploy local antibiotics instead of PMMA cement [1, 13]. Furthermore, being able to develop ways to identify cases at risk or infections in an early stage may give a chance for curative treatment with implant retention. A multimodal approach should be aimed at decreasing incidence and deployment of individualized treatment from an early stage [1, 14].
Periprosthetic joint infections continue to pose a great therapeutic challenge with high costs for the health care systems, high stress for the patient and frustrating results for the physician. With two stage revisions our patients had better results when the curative treatment was done early and in immunocompetent hosts.

References

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