The deleterious relationship of Pseudomonas aeruginosa and Induced Membranes in infected non-union treatment

Thiyagarajan U, Senthil Loganathan*, Raghavendar, Pradeep P

Department of orthopaedics, Sri Ramachandra institute for higher education and research, Porur, Chennai-600116, Tamil Nadu, India

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ABSTRACT

The Masquelet technique was originally described for the treatment of an infected non-union with an extensive bone defect where a staged protocol was needed to first eliminate an infection then secondarily bone graft a defect. Though this is a versatile technique, certain limitations/ complications must be recognized. The study was done between 2012 to 2019 at SRIHER university. 19 patients in whom the Masquelet technique has failed is taken into study. 17 male and two females, with a mean age of 31 years (range of 13 yrs. – 51 yrs.) with a mean follow up of 12 months. The 19 patients who presented with Pseudomonas aeruginosa infected non-union of the tibia and femur with bone defects underwent the Masquelet technique. All patients failed to form adequate induced membrane at the non-union site. Infected non-union with a bone defect is difficult to treat. Bone defects of 2cms can be treated by cancellous bone grafting. Defects more than 4-5cms will require specialized reconstructive procedures to prevent amputation. The two common techniques used are Ilizarov technique with bone transport and bone graft into an induced membrane as described by Masquelet. This study shows a high failure rate of the Masquelet technique with Pseudomonas infection. The most difficult issue faced by the surgeon in treating P. aeruginosa is its ability to develop resistance to multiple classes of antibiotics during the course of treating the patient. Masquelet technique is used extensively for the treatment of infective non-union. Pseudomonas secretes a slime layer that may lead to a weak or deficient formation of the induced membrane. And the elution of antibiotics may not be adequate for intramedullary osteomyelitis with pseudomonas growth. This limits the Masquelet technique in the management of infected non-union with pseudomonas infection.

INTRODUCTION

The Masquelet technique was originally described for the treatment of an infected non-union with an extensive bone defect where a staged protocol was needed to first eliminate an infection then secondarily bone graft a defect (Pelissier et al., 2002). Post-traumatic segmental bone defects remain a challenge for the orthopaedic surgeon. These complex lesions are difficult to treat and lead to significant morbidity. This technique has the theoretical advantage of providing an infected site with a scaffold, that is the induced membrane, to protect the bone graft...
from resorption. The induced membrane not only contains the bone graft and prevents its resorption at the early stages; it plays a vital role in angiogenesis and bone formation throughout the regeneration process (Pelissier et al., 2002, 2004).

This is a two-staged procedure, and soft tissue reconstruction is essential for the formation of healthy membrane (Pelissier et al., 2004; Flick et al., 1987). Though this is a versatile technique, certain limitations and complications must be recognized. Overall, the union rate was achieved in 88% of the cases and infection cured in 93% (Morelli et al., 2018).

The study was done between 2012 to 2019 at SRI-HER university. 19 patients in whom the Masquelet technique has failed is taken into study. 17 male and two females, with a mean age of 31 years (range of 13 yrs. — 51 yrs.) with a mean follow up of 12 months. The anatomical locations included the Tibia (14 patients) and the femur (5 patients). The diagnoses were infected non-unions (18 patients) and one pseudoarthrosis of the tibia. The initial presentation of the patients was open fractures, which proceeded to infected non-unions from different fixation methods. 14 patients included in our study were initially treated by intramedullary nailing, of which 8 patients were with a femur fracture, and six patients were tibial fracture.

Five patients with tibial open fracture were treated by Ilizarov ring fixator and later removed and converted to a functional cast bracing for the tibia. Pseudomonas aeruginosa was grown by culture from a deep swab for all the patients. The mean size of the defect was 6.3cm on the AP and 6.5cm on the lateral view. Surgical technique — In the first stage as per the technique used by Masquelet et al. Pelissier et al. (2002), a thorough debridement was done initially after removal of the implant or Ilizarov. The area of fracture non-union site was carefully debrided and irrigated.

Non-viable tissue and sclerotic bone at the non-union site were removed. Method of fixation was decided based on the level of the fracture and location. After achieving alignment of the limb, an intramedullary nail or external fixator was applied to stabilise the fracture. Antibiotic coated PMMA spacer was placed in the bone defect. This was placed in a such a way as to overlap the bone ends by 2cm and as per culture sensitivity, Meropenem (3 vials – 500mg/vial) were mixed into a single pack of palacos cement.

Wound closure by primary suturing was possible in all the patients. The patients who underwent application of external fixator were mobilized with strict non-weight bearing while the patients who underwent intramedullary nailing were mobilized with partial weight-bearing.

All patients were treated with a sensitive or broad-spectrum antibiotic for 2 weeks and then received oral antibiotics for 2-3 weeks. Erythrocyte sedimentation rate and C-reactive protein were done on a weekly basis and showed no significant elevation (ESR stayed below 16mm/hr and CRP was <0.6mg/dl). X-ray was done prior to the second stage procedure of bone grafting.

The second procedure of autologous bone grafting was planned for all the patients at 4-8 weeks after the first surgery (average 5.2 weeks). On opening the fracture non-union site with PMMA, we observed a deficiency or total absence of induced membrane. Hence, the second procedure of autologous iliac crest bone grafting was abandoned. A deep culture was again sent, which revealed the presence of Pseudomonas aeruginosa.

RESULTS

The 19 patients who presented with Pseudomonas aeruginosa infected non-union of the tibia and femur with bone defects underwent the Masquelet technique. The average age of the patients was 31 years (range 13-51). The site of bone defect: 14 cases of middle third tibia and 5 cases of femur middle third infected non-union. One month after the first stage, wound dehiscence and superficial wound infection were seen in 2 patients. All the other patients had good wound healing after the primary procedure of cement implantation. All patients failed to form adequate induced membrane at the non-union site.

A: X-ray appearance showing the non-union with a bony defect. B: Intra-op picture showing the defect. After IMIL nail removal. C: 8 weeks post-op after application of the PMMA cement showing deficient formation of induced membrane (Figure 1).

All the patients were then treated with an Ilizarov ring-fixator and bone transport. 17 patients went in for bone healing with distraction osteogenesis using the Ilizarov method. Two patients subsequently
DISCUSSION

Infected non-union with a bone defect is difficult to treat. Bone defects of 2cms can be treated by cancellous bone grafting. Defects more than 4-5cms will require specialized reconstructive procedures to prevent amputation (Pelissier et al., 2002, 2004). The two common techniques used are Ilizarov technique with bone transport and bone graft into an induced membrane as described by Masquelet (Pelissier et al., 2002, 2004; Flick et al., 1987). There are few case reports which has shown the failure of the Masquelet technique. This study shows a high failure rate of the Masquelet technique with Pseudomonas infection. Pseudomonas aeruginosa is a ubiquitous organism present in many environmental settings, and it can be isolated from various living sources, including plants, animals, and humans.

Serious infections by Pseudomonas aeruginosa are found to be predominantly hospital-acquired and can be isolated from respiratory therapy equipment, antiseptics, soaps, sinks and medicines. Danielle et al. and Scott C P et al. have shown the ability of Pseudomonas to produce biofilm and slime layer over bone cement (Scott et al., 1999). They showed that enhanced slime production on antibiotic-loaded bone cement together with the formation of small colonies variants resulted in decreased susceptibility to antibiotics leading to persistent infections (Scott et al., 1999; Rezzouk et al., 2005). Various studies have shown the failure of antibiotic-loaded bone cement in treating pseudomonas infection, but none of the studies has shown the relationship of pseudomonas and induced membrane. In our study, one patient underwent Masquelet technique for congenital pseudoarthrosis of the tibia. A: Pre-op X-ray showing bone loss and implant failure. B: Immediate post-op X-ray showing the reduced fracture with cement in-situ. C: 8weeks post-op showing some lucency in the cement with loosening inferiorly. D: Intra-op photo at 8 weeks showing failure to form induced membrane. (Figure 2)

Though preliminary results of the induced membrane in CPT showed promising results in many studies (Korompilias et al., 2009), our patient had pseudomonas infection at the non-union site and hence did not respond to the Masquelet technique. Tobramycin, Meropenem and Imipenem have shown to have good efficacy against pseudomonas when used with bone cement (Rezzouk et al., 2005; Korompilias et al., 2009). In our study meropenem was used in all patients based on culture sensitiv-
ity. The most difficult issue faced by the surgeon in treating P. aeruginosa is its ability to develop resistance to multiple classes of antibiotics during the course of treating the patient. This has been attributed to the way this organism regulates its AmpC, OprD and efflux pumps (Rezzouk et al., 2005; Gouron, 2011). Though in our study, P. aeruginosa isolated in culture throughout the study appeared to be sensitive to Meropenem the development of resistance experienced in the form of absence of membrane formation was suspected. Through the pioneering work of Masquelet et al., large post-traumatic bone defects have been bridged through this technique. Gerber et al. stated that this membrane prevents connective tissue infiltration and acts as a ‘bone-forming chamber’ with osteoinductive and osteoconductive properties (Hertel et al., 1994).

Welby et al. stated that this technique could be successfully used in patients who have had the limb irradiated or in the presence of infection (Welby et al., 2004). Even though the mean size of the defect in our study (6.5cm) was much less than the defect bridged by Masquelet et al., membrane formation. The bacterial biofilm formed are the root of many persistent and chronic bacterial infections (Coster-eton, 1999). We suspect that the presence of Pseudomonas Aeruginosa with its biofilm production and slime layer formation in bone cement played a major role in preventing the formation of the induced membrane.

CONCLUSIONS

Masquelet technique is used extensively for the treatment of infective non-union. The development of induced membrane requires adequate soft tissue cover and proper technique. Bone cement induced tissue necrosis may also lead to compromised soft tissue cover at the non-union site-specifically at the tibial shaft region. Pseudomonas secretes a slime layer that may lead to a weak or deficient formation of the induced membrane. And the elution of antibiotics may not be adequate for intramedullary osteomyelitis with pseudomonas growth. This limits the Masquelet technique in the management of infected non-union with pseudomonas infection. Further studies are needed to establish a relation between pseudomonas and induced membranes.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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