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Modified Masquelet technique using allogeneic umbilical cord-derived mesenchymal stem cells for infected non-union femoral shaft fracture with a 12 cm bone defect: A case report

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ABSTRACT

INTRODUCTION: Non-union due to large bone loss often causes significant long-term morbidity. We incorporate the use of allogeneic umbilical cord-derived mesenchymal stem cells (UC-MSCs) as part of the diamond concept of regenerative medicine in a case of infected non-union fracture.

PRESENTATION OF CASE: We reported a 54-year-old female patient presenting with pain on the right thigh. She was previously diagnosed with a closed fracture of the right femoral shaft and underwent four surgeries before finally being referred to Dr. Cipto Mangunkusumo General Hospital with infected non-union of the right femoral shaft. The patient was treated with a combination of UC-MSCs, bone morphogenetic protein-2 (BMP-2), Hydroxyapatite (HA), and mechanical stabilization using Masquelet Technique. The combination of allogeneic MSCs, BMP2, HA, and Masquelet Technique was successful in creating new bone with no apparent side effects.

DISCUSSION: Bone loss might be caused by external factors (true defects), or structural loss of the existing bone. The combination of allogeneic UC-MSCs, BMP-2, HA and an induced membrane technique pioneered by Masquelet allowed for faster regeneration process and more optimal bone healing. This paper aims to assess and compare the result of such procedures with the previous four surgeries done to the patient, which did not yield satisfactory results.

CONCLUSION: The application of allogeneic UC-MSC, BMP-2, HA and Masquelet technique as proposed in the diamond concept is a viable method in treating critical-sized bone defect and provides an effective way to overcome non-union caused by large defect.

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1. Introduction

Bone loss often resulted in extended healing period, higher complication rates with its associated hospital costs, and in turn resulted in significant long-term morbidity. The various factors expressed in the diamond concept of regenerative medicine plays an important role in determining bone fracture healing. Moreover,

the inoculation of microbial pathogens at the time of initial trauma, during the initial fixation surgery or during the healing process, represent additional factors that may lead to delay of fracture union, loosening of fixation, and chronic osteomyelitis [1–3].

Non-union cases usually involve a complex management strategy, often requiring a number of surgical stages. Recently, Masquelet proposed a simple method of treating bone defect by combining autologous bone grafting that is placed within induced granulation tissue membranes and is applicable to both aseptic and septic conditions. This technique requires no advanced skills in microvascular surgery [1,3,4].

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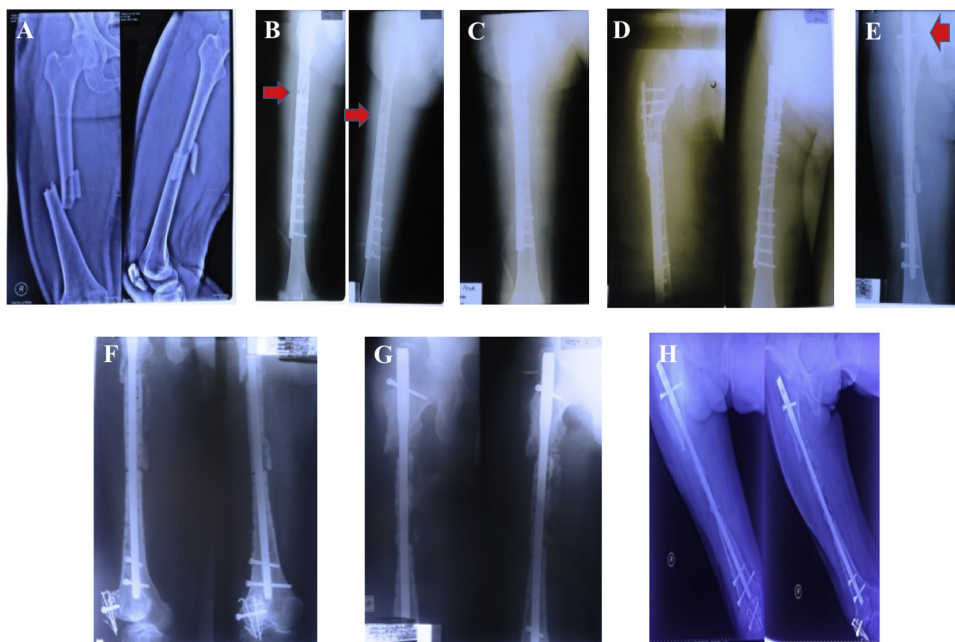


Fig. 1. AP and Lateral Femur X-rays before presenting to our hospital; **A:** Initial presentation; **B:** Post Operative-1 showing missing plate and screw in fixing the proximal fracture above the plating; **C:** Two weeks Post Operative-2 showing another proximal plating; **D:** Post Operative-3 showing proximal plating failure; **E:** Intramedullary nailing conversion showing improper nail insertion and locking fixation; **F:** Femur nailing has been revised and patellar fracture was fixed with screw and wire; **G:** Three months post-operative; **H:** Five months post-operative showing infected and sequestered middle segment of femoral shaft.

We reported a case of 54-year-old female with infected non-union of the right femoral shaft, who underwent a modified Masquelet technique in combination with umbilical cord-derived mesenchymal stem cells (UC-MSCs), bone morphogenetic protein-2 (BMP-2) and bone matrix substitute (Hydroxyapatite (HA), Bongros® -HA, Daewoong), in exchange of the autologous bone graft. This case report represents the application of diamond concept of healing, in line with the SCARE guidelines [5], which was done in Dr. Cipto Mangunkusumo General Hospital, a national top referral academic hospital.

2. Presentation of case

A 54-year-old Indonesian female was referred to Dr. Cipto Mangunkusumo General Hospital with a chief complaint of pain on right thigh since one year ago. One year ago, patient was involved in a motor vehicle accident, and diagnosed with closed fracture of the right femoral shaft (Fig. 1A) and patella. Patient initially presented to a local hospital and underwent open reduction and internal fixation (ORIF) of the femoral fracture using plate and screw. The orthopaedic surgeon opted not to operate on the patella.

Three days after the first operation, patient was informed that the ORIF was insufficient (Fig. 1B) and went for a second revision surgery for another proximal plating. An X-ray was done one-month post-op to evaluate the healing process which showed a new fracture line and proximal plating failure (Fig. 1C). No history of trauma was reported and patient was sent for a third operation for revision of the internal fixation with intramedullary interlocking nail (Fig. 1D).

Two weeks following the third surgery, patient complained of pain during exercise. X-ray showed improper nail insertion and fracture of the patella (Fig. 1E). Revision of intramedullary nailing and tension band wiring was performed for the patellar fracture (Fig. 1F). Unfortunately, three months after the revision surgery, the middle segment of the femoral shaft fracture developed infection and sequestered (Fig. 1G and H). Patient had an uneventful post-op, was able to walk using axillary crutch and was referred

to physiotherapist for range of motion (ROM) exercises. A serous turned purulent discharge was noted at the site of the operation one-month after the final surgery, wound dressing change and antibiotic were prescribed. Patient did not remember the type of antibiotic consumed. Over the next 3 months, no improvement was seen and patient decided to ask for a second opinion.

At the second surgeon, patient was diagnosed with infected non-union femoral shaft fracture with bone defect and was referred to in Dr. Cipto Mangunkusumo General Hospital. The previous physical examinations and baseline data, including the physiotherapy programs were not available and could not be retrieved at the time of presentation. Patient reported no previous history of diabetes, hypertension or smoking.

On physical examination, a sinus producing purulent discharge from the previous operation scar was noted (Fig. 2). There was pain on palpation, Visual Analog Scale (VAS) of 3–4 and good distal neurovascular function. The knee and hip joint movement was limited due to pain. Lower Extremity Function Scale (LEFS) was calculated to be 27.5% and there was a leg length discrepancy of 5 cm. The discharge was cultured and patient was given oral Cefixime 2 × 200 mg for one month.

From the clinical examination and imaging gathered from previous hospitals, we diagnosed the patient with an infected non-union right femoral shaft fracture with significant bone loss and was planned for a modified Masquelet Technique.

The modified Masquelet Technique for treatment of segmental bone defects with the addition of UC-MSCs was done (Fig. 3A and B). The operation began with debridement, removal of sinus tract and intramedullary nail, followed by bone cement spacer nailing insertion and coil wire. The surgery was performed by a senior orthopaedic surgeon specializing in trauma and adult reconstruction. Patient was positioned in left lateral decubitus position under spinal anesthesia. Incision was made on the previous scar. Sinus discharge was collected and sent for culture. A sequestrum from the femoral bone was removed and debrided. Intramedullary nail was removed from the tip of the femur followed by flushing of the femur using saline and hydrogen peroxide. A bone spacer consisting

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