IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 1 Ver. III (Jan. 2015), PP 07-13
www.iosrjournals.org

Role of Percutaneous Autologous Bone Marrow Injection in Treatment of Delayed Union and Non Union of Long Bones

Dr. Karma Uden Bhutia[1], Dr. Ashik A Bary[1], Prof. Arun Kumar Singh[2], Prof. A Mahendra Singh[2], Dr. Raghvendra Raghuvanshi[1], Dr. Christopher Hmar[1]

1 Post Graduate Trainee, 2 professor, Department of Orthopaedics, Regional institute of medical sciences, Manipur University, Lamphelpat, Imphal, 795004, Manipur, India

Abstract:

Background: *Bone marrow contains osteoprogenitor cells that can be obtained with aspiration and appear to arise from a population of pluripotential connective-tissue stem cells.*

Objectives: *The purpose of the study was to evaluate the efficacy of autologous bone marrow injection in the treatment of delayed union and non union of long bones.*

Methods: *Thirty patients, twenty five delayed union and five non union of long bones were treated with this procedure. Of these, 23 had fracture tibia, 4 fracture ulna, 2 fracture humerus and 1 fracture femur. The average time duration between injury and procedure was 25.53±10.75 weeks (range 14 to 46 weeks). The bone marrow was aspirated from the anterior iliac crest and injected percutaneously in the fracture site under guidance of II tv.*

Results: *Union was achieved in 26(86.67%) out of 30 cases. The average time of clinical union was 11.31±4.52 weeks and radiological union was 14.92±4.62 weeks.*

Conclusion: *Bone marrow injection technique is simple technique which has high osteogenic potential. This minimally invasive procedure is safe, easy, simple, economical and short procedure*

Keywords: *Bone marrow injection, delayed union, non union, osteoprogenitor cells*

I. Introduction

Bone healing is a simple but endlessly complex biologic phenomenon.[1] Fracture healing requires the recruitment of appropriate cells(fibroblasts, macrophages, chondroblasts, osteoblasts, osteoclasts) and the subsequent expression of the appropriate genes (genes that control matrix production and organisation, growth factors, transcription factors) at the right time and in the right anatomical location.[2]

The major complications in fracture treatment were delayed union and non union. Union is considered delayed when healing has not advanced at the average rate for the location and type of fracture (usually 3 to 6 months). Non union is defined by US FDA as established when a minimum of 9 months has elapsed sine injury and the fracture shows no visible progressive signs of healing for 3 months.[2]

There are various factors used to enhance union, such as drugs, electromagnetic fields, distraction and compression osteogenesis by ilizarov, autogenous bone graft and bone graft substitutes like bone morphogenetic protein.[3]

The concept of percutaneous bone graft was introduced by Herzog in 1951.[4] McGaw and Habin were among the first to demonstrate the osteogenic activity of the bone marrow.[5]The osteogenic precursor cells which are capable of producing bone have been demonstrated among the stromal and endosteal cells of the bone marrow which are the key element in the process of bone formation and fracture healing.

Since percutaneous bone marrow injection is a simple and easy technique, we have taken up this study to ascertain its effectiveness in treatment of delayed union and non union.

II. Materials And Methods

The present study was conducted in the Department of Orthopaedics, RIMS, Imphal, Manipur over a period of two years from September 2012 to August 2014. This was a prospective study in which thirty (30) cases of delayed and non union of long bones, irrespective of sex and age, fitting in the inclusion criteria was subjected to percutaneous autologous bone marrow injection after obtaining written informed consent.

Inclusion Criteria

- Both genders were eligible.
- Age of fracture more than 12weeks.

- Clinically –abnormal mobility at the fracture site
  -tenderness at the fracture
  -pain on applying bending stresses.

Radiologically-insufficient amount of callus -sclerosis of fracture ends.
-obliteration of bone marrow cavity at the fracture site.

Exclusion Criteria

- Infected fracture.
- Malignancy.
- Hepatitis B, Hepatitis C, HIV at the time of screening.
- Segmental bone loss.
- Smoking.
- Other major comorbidity.

Method

Ethical approval was taken from Institution Ethical Committee, RIMS, Imphal, Manipur. Informed consent were taken from all participants. All details of participating individuals were recorded**.** The fractures were assessed by antero-posterior and lateral radiographs of the long bone and clinically in delayed or non union. All routine investigations were done on all patients.

Patient were primarily treated for the fracture by external fixators, plating, plaster cast and nailing . The bone marrow injection was performed under spinal or local anaesthesia or general anaesthesia with monitoring by Image intensifier Television (IITV).

Under aseptic precautions, patient was kept in supine or lateral position. Painting was done around the site of aspiration i.e. over the iliac crest and injection site i.e. over the fracture site followed by draping. Bone marrow was be aspirated from the patient's iliac crest with a bone marrow aspiration needle connected to a 20ml syringe. Required amount (10-30ml) of bone marrow was aspirated and injected immediately at the site of delayed or non union with a 16G spinal needle under the guidance of Image Intensifier. After bone marrow injection, the recipient site was either immobilised by a Plaster of Paris cast or the primary treatment was continued.

III. Assessment Of Results

All cases were followed after an interval of 4 weeks post injection for 6 months. The union was assessed clinically and radiologically.

Clinically-No abnormal mobility at the fracture site.
-No tenderness at the fracture sites on applying bending stresses.
Radiologically-No gap at the fracture site.
-Sufficient amount of callus.

The final results were based on whether union was achieved clinically and radiologically or not.

Results

Between September 2012 to August 2014, thirty patients, 25 with delayed union and 5 with non union of long bones were subjected to percutaneous autologous bone marrow injection in the Department of Orthopaedics, RIMS, Imphal. In 15 patients bone marrow injection was done under local anaesthesia, 10 patients under spinal anaesthesia and 5 patients under general anaesthesia.

Bone marrow aspiration was done from anterior iliac crest and injected percutaneously at the fracture site. Patients were followed up at 4weeks interval till 6 months in the outpatients department of Orthopaedics, RIMS.

The mean age of the patients was 36.43±11.04 years with the range of 18 to 54 years. There was 18 males and 12 females. The study subjects comprised of higher percentage of male (60%) as compared to female (40%). Majority of the fractures were due to Road Traffic Accident which accounted for 80% (24), 13.33% (4) had injury following fall and 6.67% (2) had occupational injury. 23 out of 30 cases i.e. (76.67%) were of tibia, 4 (13.33%) were of ulna, 2 (6.67%) were of humerus and 1(3.33%) of femur. 14(46.67%) were closed fractures and 16(53.33%) were open fractures. The initial treatment given was plating in 10(33.33%) patients, external fixation in 9(30%) patients, casting in 9(30%) patients and nailing in 2(6.67%) patients. The mean time interval between injury to bone marrow injection was 25.53±10.75 weeks in the range of 14 to 46 weeks. The amount of bone marrow injected was 20-30 ml for tibia and femur, 15-20 ml for humerus and 10-15 ml for ulna. The mean time for callus formation was 5.92±1.87 weeks ranging from 4 to 11weeeks. It is represented in Table 1

and Figure 1. The mean time for clinical union was 11.31±4.52 weeks ranging from 6 to 22 weeks. It is represented in Table 2 and Figure 2. The mean time for radiological union was 14.92±4.62 weeks ranging from 8 to 24 weeks. It is represented in Table 3 and Figure3. Union was achieved in 26(86.67%) out of 30 cases. 2 out of 25 delayed union and 2 out of 5 nonunion(3 hypertrophic and 2 atrophic) failed to achieve union as shown in Table 4 and Figure 4. The two non union cases which failed to achieve union were atrophic type (one in ulna and other in tibia both initially treated by casting). Both the delayed union cases that failed to achieve union was in tibia(both type III open treated by external fixators).The two non-union cases were then managed by plating and interlocking nail with bone grafting for ulna and tibia respectively. The two delayed union cases were later managed by plating and bone grafting.

IV. Discussion

In this study 30 patients of which 25 cases were of delayed union and 5 cases were of non union were given percutaneous bone marrow injection. Patients were between 18 to 54 years of age, with a mean age of 36.43 ± 11.04 years. This is similar to the findings of Sim R et al[6] where the mean age was 38 years (range, 19-62 years). Braley Houston L et al[7] reported reported a mean age of 40.1 years (range, 24-51 years). There were 12 female and 18 male patients (m:f = 1.5:1). Majority of other studies showed marked male predominance. The study showing findings similar to ours was of Singh Ashok K[8] where the male to female ratio was 1:1. The mean time between injury and bone marrow injection in this study was 25.53±10.75 weeks ranging from 14 to 46 weeks. This is similar to Bhargava R et al[9] where the mean time was 25 weeks (range, 14-53 weeks). According to Padha Vikas et al[10] the mean age was 28.1 weeks (range, 4-52 weeks). The fracture site involved in this study was tibia in 23 out of 30 patients (76.67%), ulna in 2 patients (6.67%), humerus in 2 patients (6.67%) and femur in 1 patient (3.33%). The findings were similar to Sim R et al[6] where tibia comprised 72.7 % of the total fracture sites. In study by Bhargava R et al[9] also tibia comprised majority of the bone involved i.e. 25 patients had fracture tibia out of 28 patients. In this study of 30 cases, there were 14 closed (46.67%) and 16 open (53.33%) out of which 4 were type I, 8 type II and 4 type IIIa. In the study by Ismaeel Firas T et al[3], 50% were open and 50% were closed fractures. In study of Bhargava Rakesh et al[5] also 8 patients had type II open fracture out 28 cases. In this study the initial treatment given was plating in 10 patients (33.33%), external fixators in 9 (30%), POP casting in 9 (30%) and nailing in 2 (6.67%). In other studies also these were used as initial forms of treatment but the percentage of different types of treatment varied. In this study 15 patients (50%) were given local anaesthesia, 10 patients (33%) were given spinal anaesthesia and 5 patients (17%) general anaesthesia. In study by Bhargava R et al[9] also majority of patients (76.67%) were given local anaesthesia. The amount of bone marrow injected in this study was 20-30 ml in tibia and femur, 15-20 ml in humerus and 15-30 ml in ulna. No definitive conclusion can be made regarding the amount of marrow to be injected because different investigators have injected different amounts of bone marrow with good results but now it has been shown that the efficacy of injected marrow is directly related to the number of progenitor cells.[11] Larger volume aspirates contribute little to the overall number of bone marrow cells and result in unnecessary blood loss.[12] In our study volume of injection depended mostly on the space available at the fracture site. Space had to be created in most cases by the inserted needle by breaking up the fibrous tissues between the fragments of bone. Only one injection was given like in studies of Padha V et al[10], Bhargava R et al[9], Braley H et al[7], Srivastav R et al[13] and Sim R et al[6]. In studies by Braley H et al[7], Srivastav R et al[13] and Sim R et al[6] heparinised syringes were used. Heparin was not required in our study because of short interval between aspiration and injection, thereby avoiding the potential impairment of bone healing associated with heparin reported by Stinchfield et al[14]. In this study bone marrow was injected directly. According to Conolly et al[15] osteogenenic capacity of marrow is related to cell density and that concentration of marrow by simple centrifugation can enhance the rate and amount of bone formation. In this study the time taken for callus formation was 5.92 ± 1.87 weeks ranging from 4 to 11 weeks. 77% of successful cases showed callus between 4 to 6 weeks. In study by Singh Ashok K et al[8], the time taken for callus formation was 5.8 weeks (range, 3-10 weeks). The mean time taken for clinical union in this study was 11.31 ± 4.52 weeks ranging from 6 to 22 weeks. 38.5% of successful cases showed clinical union between 9 to 11 weeks. According to Sim R et al[6]'s and Ahmed HH et al[16] studies the time taken for clinical union was 10 weeks (range, 4-23 weeks). The mean time for radiological union in this study was 14.92 ± 4.62 weeks ranging from 8 to 25 weeks. Among other studies the ones that matched to ours closely were study of Sim R et al[6] and Ahmed HH et al[16] where mean time for radiological union was 17 weeks (range, 9-29 weeks) . Goel A et al[17] showed bony union following percutaneous injection in an average time of 14 weeks.

In this study union was achieved in 26 (86.67%) out of 30 cases. In delayed union cases union was successful in 23 (92%) out of 25 cases. In non union cases union was successful in 3 (60%) out of 5 cases. Similar findings were found by Shrivastav R et al[13] where union was achieved in 87.87% of cases, Garg et al[18] where union was achieved in 85% of cases, Singh Ashok K et al[8] where where union was achieved in 83.33%

cases and Sim R et al[6] in 81.8% of cases. The 2 failed non union cases were of atrophic type. Husseini et al[19] has observed that atrophic type of non union shows lower success rate to achieve union.

V. Conclusion

Delayed union and non-union are rare but well known complications of long bone fractures which present a major challenge to an orthopaedic surgeon despite continued advances in their treatment. For long, autologous cancellous bone grafting has been the standard of treatment. But this bone grafting has not been without complications such as painful scar, hematoma, infection, fracture or subluxation and gait disturbances. Various methods of treating delayed and non-unions have been described such as Onlay bone grafting with or without internal fixation (Campbell, 1939; Phemister, 1947), cancellous insert grafts (Nicoll, 1956), subcortical iliac bone grafts (Forbes, 1961), dual only bone grafts (Boyd, 1941), stimulation by direct current through implanted electrodes (Peterson and Lewis, 1980) and by an electro magnetic field about the site of fracture (Sharrard et al., 1982). In bone grafting, the bone grafts mainly act as a scaffold with most of the cellular elements dying out and being replaced by creeping substitution (Charls, 1992).

Although there are several treatment options for patients with delayed and non union, bone marrow injection is a simple technique which has high osteogenic potential and can be grafted percutaneously. This minimally invasive procedure is safe, easy, simple, economical and short procedure. It is both patient as well as surgeon friendly procedure. In short, it is an easy substitution of a complex problem.

Our study has established that bone marrow has high osteogenic potential and can be grafted percutaneously successfully. Our study showed success rate of 86.67%. In two cases of atrophic non union and two cases of delayed union, union was not seen. This procedure can be used as an early intervention , whenever one suspects a delay in healing of fracture. This procedure can be done on an outpatient basis and even under local anaesthesia with minimal donor and recipient site morbidity.

References

[1]. Bolhofer BR, Ricci WM. Principles of nonunion treatment. In: Bucholz Heckman J, editor. Rockwood and Green's Fractures in Adults. 7th ed. Philadelphia: Lippincott-Wolters; 2010. p. 641-57.

[2]. Cleveland KB. Delayed union and non-union of fractures. In: Canale and Beaty, editors. Campbells Operative Orthopaedics. 12th edition. Philadelphia: Mosby Elsevier: 2013. p. 2578-79,2982-83.

[3]. Ismaeel FT. Bone marrow injection in patients with delayed union and non-union of long bone fracture. Tikrit medical Journal 2008; 14(2): 131-4.

[4]. Herzog K. Verlangerungosteoto mic unter Vernen dungdes percutan gezeit Verriegelten Markangels. Unfallheikunde 1951; 42: 226-30.

[5]. McGraw WH, Harbin M. The role of bone marrow and endostium in bone regeneration : an experimental study of bone marrow and endosteal transplants. J Bone Joint Surg 1934; 14: 816-21.

[6]. SimR, Liang TS, Tay BK. Autologous bone marrow injection in the treatment of delayed and non-union in long bones. Singapore Medical Journal 1993; 34: 412-7.

[7]. Braly HL, O'Connor DP, Brinker MR. Percutaneous autologous bone marrow injection in the treatment of distal meta-diaphyseal tibial nonunions and delayed unions. J Orthop Trauma 2013 September; 27(9): 527-33.

[8]. Singh AK, Shetty S, Saraswathy JJ, Sinha A. Percutaneous autologous bone marrow injections for delayed or non-union of bones. Journal of Orthopaedic Surgery 2013; 21(1): 60-4.

[9]. Bhargava R, Sankhla SS, Gupta A, Changani RL, KC Gagal. Percutaneous autologous bone marrow injection in treatment of delayed or non-union. Indian J Orthop 2007 Jan-Mar; 41(1): 67-71.

[10]. Padha V, Mahajan N, Kalsotra N, Salaria A, Sharma S. Role of percutaneous bone marrow injection in delayed union and non-union. The Internet Journal of Orthopaedic Surgery 2010. 18(1). DOI: 10.5580/13b.

[11]. Hernigou P, Mathieu G, Poignard A, Manicom O, Beaujean F, Rouard H. Percutaneous autologous bone marrow grafting for non-unions. Surgical technique. J Bone Joint Surg Am. 2006 Sep; 88 Suppl 1 pt 2: 322-7.

[12]. Muschler GF, Boehm C, Easley K. Aspiration to obtain osteoblast progenitor cells from human bone marrow: The influence of aspiration volume. J Bone Joint Surg Nov 1997; 79(11): 1699-1710.

[13]. Rakesh S, Sapolia A, Balaji G, Parmar S. Percutaneous autologous bone marrow injection in the treatment of delayed and non-union of long bones. NJIRM 2013 March-April; 4(2): 39-42.

[14]. Stinchfield FE, Sankaran B, Samilson R. The effects of anticoagulant therapy on bone repair. J Bone Joint Surg 1956; 38-A: 270-6.

[15]. Connolly J, Guse R, Lippiello L, Dehne R. Development of an osteogenic bone marrow preparation. J Bone Joint Surg Am 1989; 71: 684-91.

[16]. Ahmed HH. Management of tibial non-unions using autologous bone marrow injection as a substitute for operative grafting. Pan Arab J Orth Trauma 2002 July; 6(2): 203.

[17]. Goel A, Sangwan SS, Siwach RC, Ali AM. Percutaneous bone marrow grafting for treatment of tibial non union. Injury 2005; 36: 203-6.

[18]. Garg NK, Gaur S, Sharma S. Percutaneous autologous bone marrow grafting in twenty cases of ununited fracture. Acta Orthop Scand. 1993 Dec; 64(6): 671-2.

[19]. Timour F, El-Husseini. Percutaneous bone marrow autotransplantation in the treatment of delayed and non union of long bones. Department of orthopedic surgery, Ains Shams University, Cairo. 1997.

VI. Tables

Table 1: Showing time for appearance of callus in successful cases:

Period in weeks	No. of cases	Percentage(%)
4 to 6	20	76.92
7 to 9	4	15.38
10 to 12	2	7.69
Total	26	100

Table 2: Showing time taken for clinical union in successful cases:

Period in weeks	Delayed union cases	Non union cases	Percentage(%)
6 to 8	7	0	26.92
9 to 11	10	0	38.46
12 to 14	3	0	11.53
15 to 17	1	0	3.84
18 to 20	3	0	11.53
21 to 23	0	2	7.69
Total	24	2	100

Table 3 : Showing time taken for radiological union in successful cases:

Period in weeks	Delayed union cases	Non union cases	Percentage(%)
8 to 10	5	0	19.23
11 to 13	5	0	19.23
14 to 16	10	0	38.46
17 to 19	1	0	3.84
20 to 22	2	0	7.69
23 to 25	1	2	11.53
Total	24	2	100

Table 4 : Showing overall result:

	Delayed union	Non union	Percentage(%)
Union achieved	23	3	86.67
Union not achieved	2	2	13.33
Total	25	5	100

VII. Figures

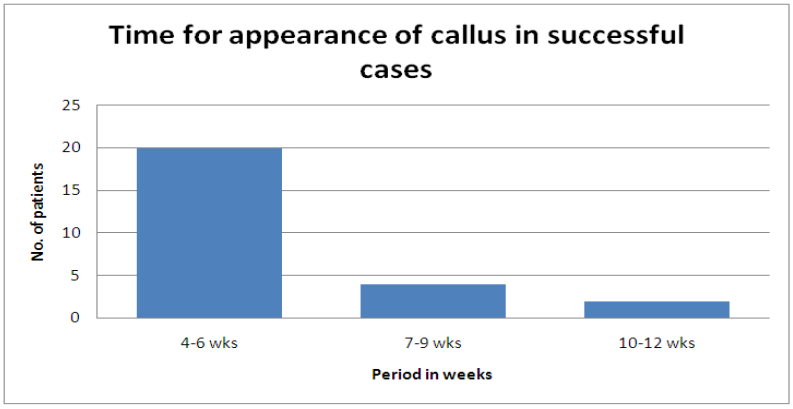


Figure 1 : Showing time for appearance of callus in successful cases

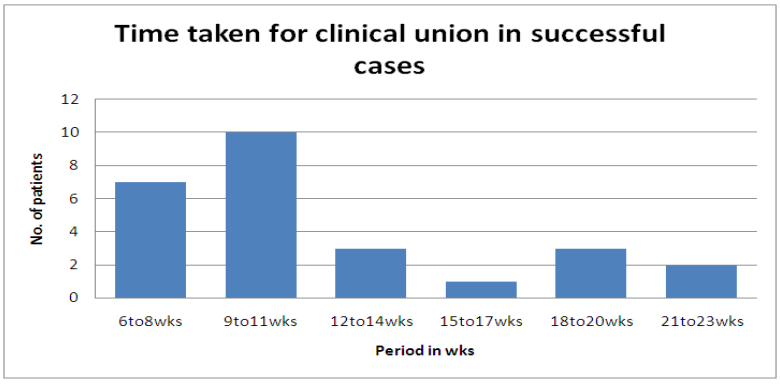


Figure 2 : Showing time taken for clinical union in successful cases

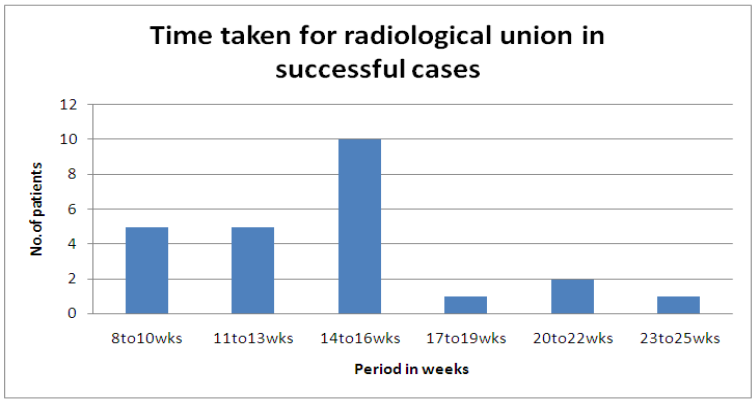


Figure 3 : Showing time taken for radiological union in successful cases

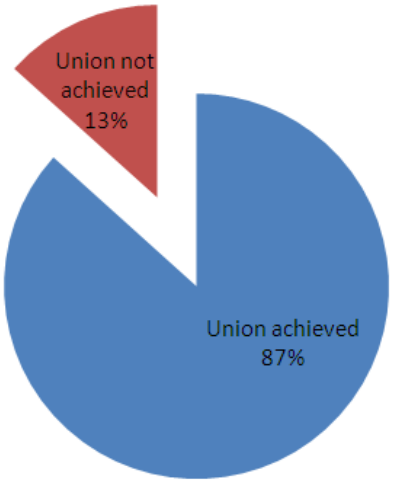
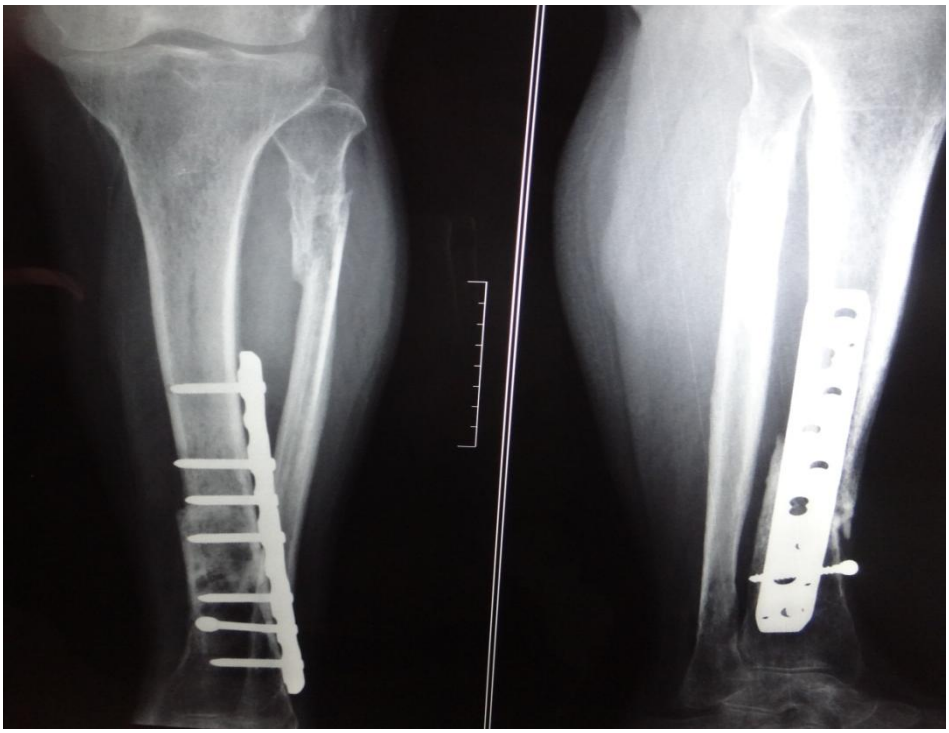
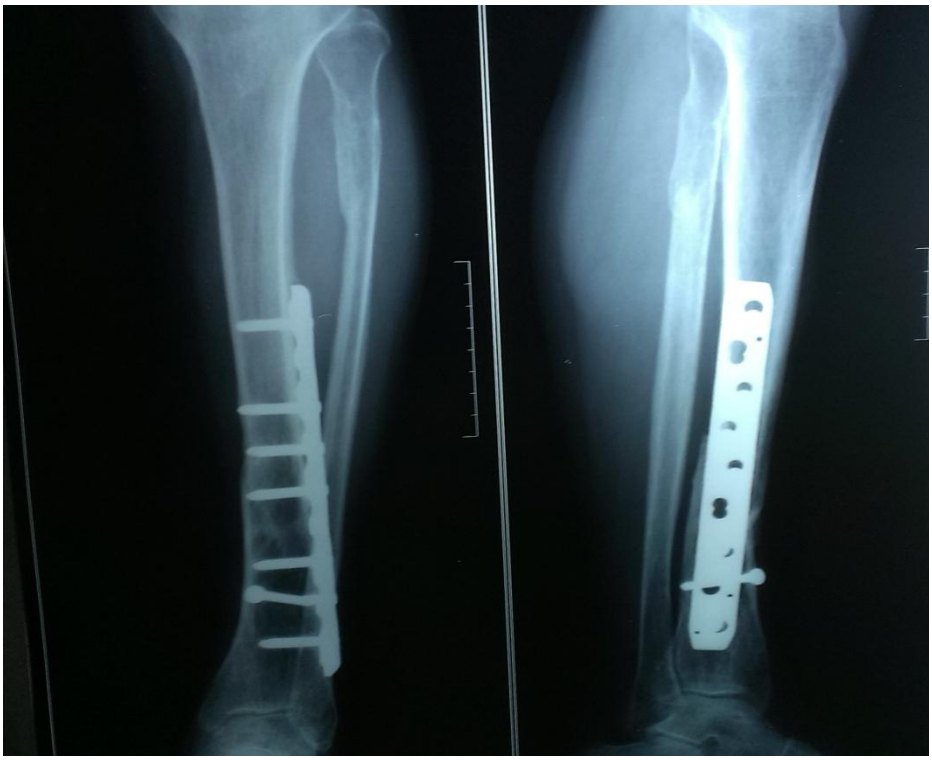


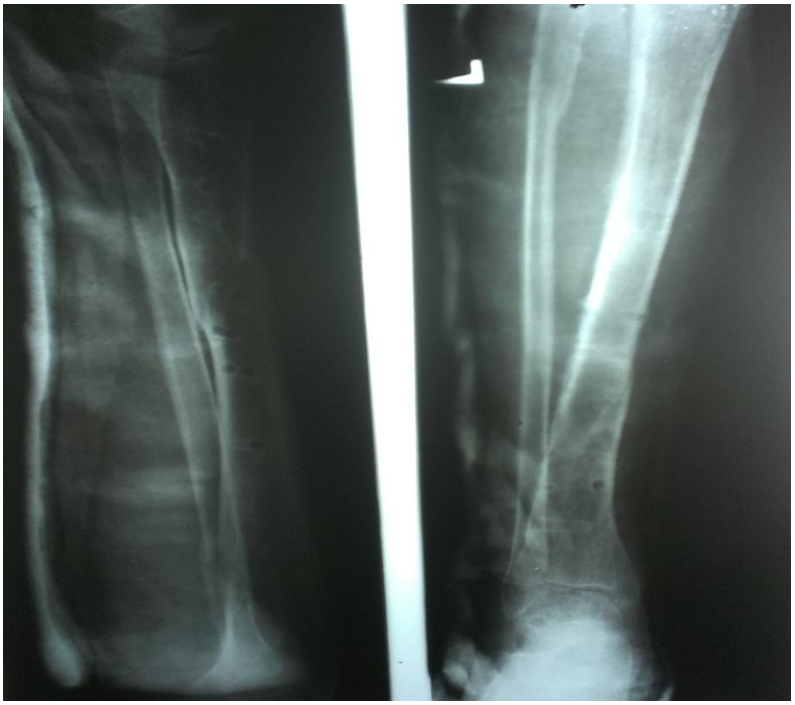
Figure 4 : Showing final result of union



X ray showing delayed union(6 months) of tibia with plating as the initial treatment



X ray taken 8 weeks after bone marrow injection



X ray showing united tibia after removal of plate