Percutaneous autologous bone marrow injection as a substitute for operative grafting in delayed union and nonunion of long bone fractures

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Received 25 November 2015
Accepted 27 December 2013

Egyptian Orthopedic Journal 2015, 50:249–253

Background

Cells aspirated from bone marrow have been shown to provide stimulus for osteogenesis in animal experiments and in clinical evaluation of bone graft and bone substitutes. Despite this osteogenic characteristic, the clinical use of marrow as an osteogenic source has remained limited. The marrow is harvested by means of needle aspiration from the patient's pelvic bone and is then injected percutaneously at the nonunion site. This method offers the advantage of treating fracture-healing problems without operative exposure of either the donor or the recipient site.

Aim of the work

The purpose of this study was to ascertain the osteogenic potential of autologous bone marrow injection and its effectiveness in the management of delayed union and nonunion.

Patients and methods

Autologous marrow injection was used to stimulate healing in 21 patients with delayed union and nonunion of fracture of the long bones. Of these 21 cases, two patients had fracture shaft femur, one had fracture shaft humerus, and 18 patients had tibial shaft fractures during the period from January 2008 to April 2010 at Tanta University Hospital.

Surgical technique

Bone marrow aspirated from the posterior iliac crest was injected at the fracture site two to three times with an interval of 3 weeks.

Results

Marrow stimulated callus formation sufficient to unite 18 of 21 cases of delayed unions and nonunions immobilized with cast or intramedullary nails.

Conclusion

Bone marrow injection was as effective as open autogenous grafting but with considerably less complications. Thus, the technique provides a reliable source of osteogenic stem cells with numerous advantages compared with standard open grafting techniques.

Keywords:
bone marrow injection, delayed union and nonunion, long bone fractures

Egypt Orthop J 50:249–253

1110-1148

Introduction

Approximately two million long bone fractures occur each year in the USA; about 100 000 (5%) result in nonunions and an even larger number result in delayed unions. Unfortunately, problems with long bone fractures seem to be increasing rather than diminishing; because the better initial management of severe injuries to this bone has allowed limbs that would once have been amputated to be salvaged, the price now is, however, problems concerning fracture union and limb rehabilitation [1].

Numerous modalities have been advocated for the treatment of delayed union and nonunion of fracture, including plate osteosynthesis, intramedullary rod, external fixation, and electrical stimulation. Despite these advances, the time-tested technique of grafting the fracture site with autogenic bone has been and continues to be the standard clinical practice. When normal biologic responses to fracture prove insufficient, corticocancellous bone grafting is thought to succeed because of its osteoconductive and osteoinductive properties and because of the introduction of new osteogenic bone marrow cells [2].

The search for a new osteoinductive substance has been the subject of great interest from the dawn of fracture management. Current research in basic science provides an understanding of the factors needed for osetogenesis in bone substitutes. The osteoblast is very well known as the chief bone-forming cell, but now it has been shown that osteoblasts, fibroblasts, and reticular cells have common precursor cells, and these common precursor cells are found in the bone itself, in bone marrow, and in certain areas of connective tissue framework [3].

The successful use of bone marrow for hematologic and oncologic clinical problems and for the treatment of congenital osteoblastic deficiencies has stimulated interest in the use of bone marrow to supply cells for osteogenesis [4].

Patients and methods

A diagnosis of nonunion is unjustified until there is evidence, either clinical or roentgenographic, that healing has ceased and union is highly improbable. A fracture of the shaft of a long bone should not be considered nonunion until at least 6 months after the injury, because often union requires more time, especially after local complications such as an infection. This study approved by the Ethical committee of Tanta University.

Twenty-one cases of delayed union and nonunited long bone fractures were treated with marrow injection since January 2008 up to April 2010 at Tanta University Hospital. Of these 21 cases, two patients had fracture shaft femur, one had fracture shaft humerus, and all other 18 patients had tibial shaft fracture. Six cases were of closed fractures, seven were of Gustilo's grade I, five were of grade II, two were of grade IIIa, and one was of grade IIIb. Both femoral fractures were closed and treated with interlocked nailing. Fracture humerus was of grade I and treated with interlocked nail after debridement. Four cases with closed fracture shaft tibia were treated by means of closed reduction and interlocked nail. Twelve cases with open fracture shaft tibia were treated with reduction and above knee cast application after surgical debridement. Two cases with open tibial fractures were put on external fixator initially, which was changed to either above knee cast or cast after healing of the wound.

After the initial procedure, partial weight bearing was allowed between 8 and 16 weeks as soon as the fracture became sticky. Tibial fractures were mobilized in a PTB cast, whereas femoral fractures were mobilized after removing one set of locking screws. These patients were mobilized for a mean of 12.6 weeks (7–38 weeks) before being subjected to bone marrow injection. The time from injury to bone marrow injection ranged from 5 to 11 months, with the median being 5.78 months. Fractures with acceptable alignment and good bone apposition at the fracture site were included in the study. The ages of the patients ranged from 37 to 58 years, with a median of 45.6 years. Fifteen of these fractures were considered delayed union and the remaining six were considered nonunited fractures. In most cases the bone marrow could be injected percutaneously with the aid of image intensifier as a day case under general anesthesia. Most patients received three injections with marrow at 3 weeks interval, but two cases received only two injections.

Surgical technique

The most productive source of bone marrow was the posterior iliac wing.

The patient was placed supine with a sandbag under the desired iliac bone.

The aspiration marrow needle was inserted in the posterior part of the iliac crest between the two cortices.

A volume of 3–5 ml was aspirated from three different sites.

Simultaneously with the marrow aspiration, a second marrow needle was inserted into the site of nonunion under image intensifier control. The needle was placed into a well-vascularized region of muscle attachments (in the posterolateral aspect of the tibia).

The marrow injection was supplemented using the basic fracture stabilization technique.

Results

Eighteen of the 21 fractures healed with the technique of marrow injection combined with adequate fracture stabilization (Table 1).

Eleven of the 14 fractures treated with external cast immobilization healed, whereas all seven cases treated with intramedullary nailing eventually united. Figs. 1 and 2 show ununited fracture of the tibia and healing after bone marrow injection within 5.5 months. Figs. 3 and 4 show ununited fracture of the femur and healing after bone marrow injection within 5 months. Figs. 5 and 6 show delayed union of fracture of the humerus and healing after bone marrow injection within 4.5 months. The time of union ranged from 4 to 7 months, with a mean time of 5.76 months (Table 1).

Complications

Most patients had discomfort at the donor site for 1 or 2 days after multiple needle aspiration. Despite this discomfort, none had problems of persistent pain or unsightly scarring, or other complications associated with operative bone grafting.

Table 1 Types of fractures, stabilization technique, and time of union after bone marrow injection

Case	Type of fracture	Type of stabilization with marrow injection	Union time
1	Open tibia (type II)	Cast	4 months
2	Open humerus (type I)	Interlocked nail	4.5 months
3	Open tibia (type II)	Cast	5 months
4	Closed tibia	Interlocking nail (dynamized)	6.5 months
5	Open tibia (type I)	Cast	7 months
6	Closed tibia	Interlocked nail	5 months
7	Open tibia (type I)	Cast	7 months
8	Closed femur	Interlocking nail	5 months
9	Closed tibia	Interlocking nail+fibulectomy	5 months
10	Closed tibia	Interlocking nail+fibulectomy	4.5 months
11	Open tibia (type II)	Cast	4.5 months
12	Open tibia (type IIIa)	External fixator then cast	Nonunion
13	Open tibia (type I)	Cast	6.5 months
14	Open tibia (type IIIa)	External fixator then cast	Nonunion
15	Closed femur	Interlocked nail	5.5 months
16	Open tibia (type I)	Cast	4.5 months
17	Open tibia (type I)	Cast	5 months
18	Open tibia (type I)	Cast	6 months
19	Open tibia (type II)	Cast	5.5 months
20	Open tibia (type II)	Cast	6 months
21	Open tibia (type IIIb)	Cast	Nonunion

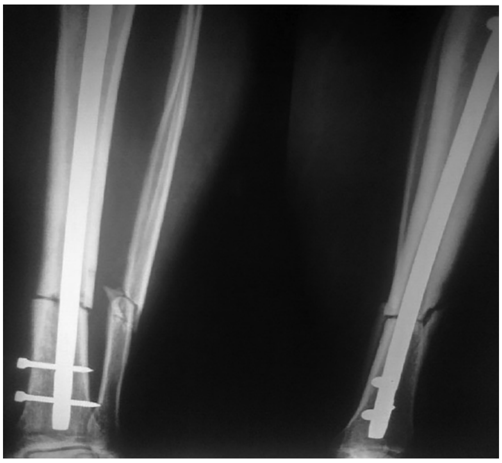
Discussion

Skeletal healing is primarily a biological process and depends upon cellular response. The most productive source of cells that influences osteogenesis is considered to be autologous marrow. In treating nonunited fractures, the orthopedic surgeon can choose from a vast number of surgical and nonsurgical methods that vary greatly in their invasiveness and propensity for minor and catastrophic complications.

Faced with equal risks and benefits, the simplest, most easily tolerated method should be chosen [5].

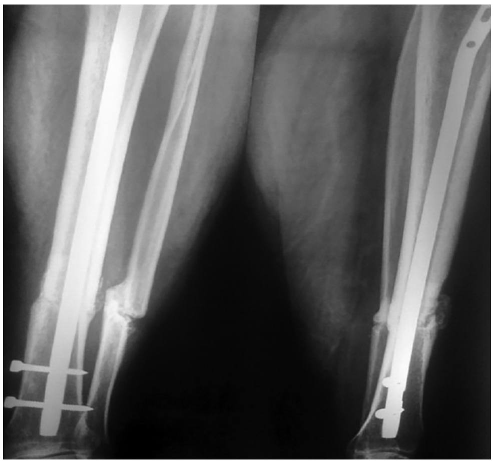
Successful treatment of a nonunion rarely consists of only one method or surgical technique, and the surgeon must anticipate the next step that may be necessary. Operation for nonunions are relatively extensive and

Figure 1



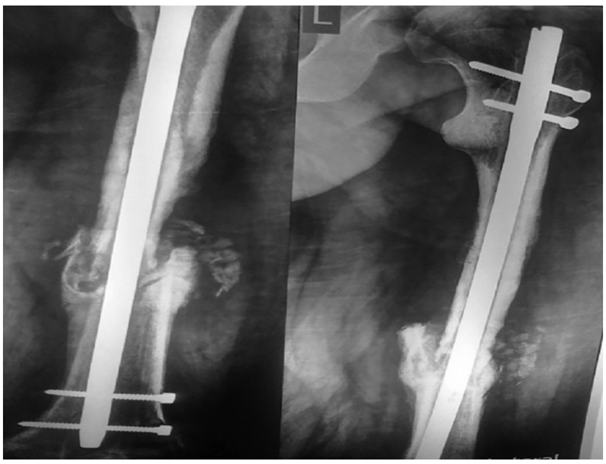
At 6 months postoperatively.

Figure 2



At 5.5 months after marrow injection.

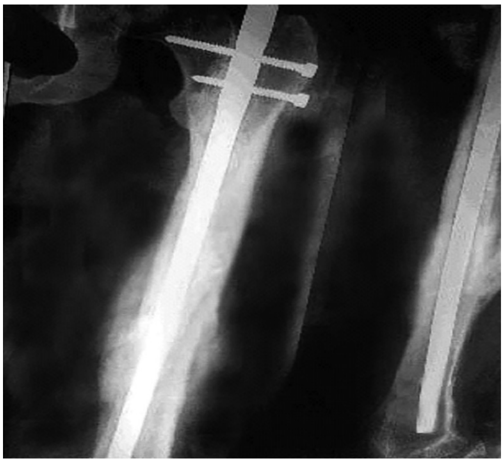
Figure 3



At 5 months postoperatively.

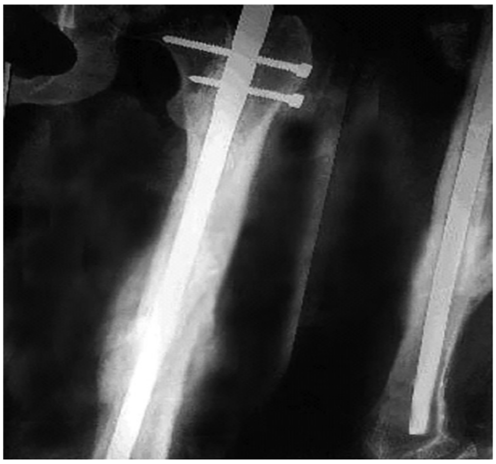
should be recommended only after nonunion has been demonstrated both clinically and radiographically and when union is obviously impossible without a change in treatment.

Figure 4



At 5 months after marrow injection.

Figure 5



At 4 months postoperatively with delayed union.

Figure 6

At 4.5 months after bone marrow injection with solid union.

This series represents clinical experience using autologous marrow injection as a substitute for standard open grafting techniques in the treatment of delayed union and nonunited long bone fractures.

Many authors experienced promising results using autogenous marrow injection as a substitute for standard open grafting techniques in the treatment of nonunited fractures.

The work of Paley *et al.* [6] showed experimentally that marrow produces optimal effect when used early in the fracture-healing process, with the poorest results encountered when used in the treatment of nonunion. Connolly and Shindell [7] also stated that 'autogenus bone marrow can be used as a preventive treatment of nonunion by early injection of delayed union'. He also said that the ideal time for bone marrow injection should be after the initial inflammatory and osteoclastic resorption period of fracture repair has subsided, which is usually by 6–12 weeks. Thus, it can be inferred that the procedure should be performed as soon as possible, when it is presumed that the union is not going to occur in the expected time duration. Although marrow by itself does not serve as an osteoconductive agent and therefore cannot fill a large gap, it has been used by various investigators as composite graft with demineralized bone matrix [8,9], xenograft [10], or porous ceramic materials in these situations. The use of marrow as composite graft with demineralized bone matrix for nontraumatic conditions such as spinal fusions has also been described [11].

Connolly *et al.* (1991) [12] reported the results of autogenous marrow injection in treating 20 ununited tibial fractures over a 5-year period with union of 18 of the 21 cases.

Garg *et al.* (1993) [13] grafted autogenous bone marrow percutaneously to stimulate healing in 20 ununited long bone fractures, all of which were immobilized in a plaster cast; 17 united in 5 months.

Sim *et al.* (1993) [14] studied the use of autogenous bone marrow injection for the treatment of delayed and

Table 2 Comparison between our results and those of other authors

Cases	This study	Connolly *et al.* [12]	Garg *et al.* [13]	Sim *et al.* [14]	Bhargava *et al.* [4]
United cases [*n* (%)]	18 (85.7)	18 (90)	17 (85)	9 (81.8)	25 (89.3)
Ununited cases [*n* (%)]	3 (14.3)	2 (10)	3 (15)	2 (18.2)	3 (10.7)
Total	21	20	20	11	28

nonunion of long bones at the orthopedic department, Singapore General Hospital, from 1990 to 1991.

There were 10 patients with 11 fractures, and nine fractures were united. The median time to clinical union was 10 weeks (4–23 weeks) and that for radiological union was 17 weeks (9–29 weeks).

The use of autogenous bone marrow injected percutaneously to stimulate osteogenesis of nonunions has several advantages. It is a relatively simple technique that can be performed on an outpatient basis, and therefore it is cost-effective; the complications at the donor and recipient sites are significantly diminished [15].

Most importantly, the method encourages early treatment of nonunion to minimize fracture disease — that is, muscle and joint functional impairment consequent to prolonged healing.

Many surgeons have recognized the merit of early bone grafting for fracture-healing problems, which ideally should be performed no later than 6 months after injury [16].

From this study, we noticed that our results are more or less similar to the results of other authors (Table 2).

Conclusion

Thus, the method of percutaneous bone marrow injection is a simple, safe, and less-expensive method in treating delayed and nonunited fractures. The median time to healing after injection in this series was 5.76 months, almost the same time required for operative grafting technique.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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