Use of teriparatide in preventing delayed bone healing in complex biosseous leg fracture: a case report

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ABSTRACT

Fracture nonunion is one of the greatest challenges for orthopedic surgeons. We present the case of a young man with a complex open biosseous fracture of the leg who underwent surgery and early systemic pharmacological treatment with teriparatide. Teriparatide is widely used in the treatment of osteoporosis as its anabolic effects promote the deposition of new bone tissue. Associated tibia and fibula fractures have relatively high rates of nonunion and poor long-term outcomes. In this particular case, the fracture had further negative prognostic factors, such as exposure. Two months after the trauma, the radiological healing signs were insufficient, therefore it was decided to use teriparatide, prior to the possible onset of pseudarthrosis, in order to enhance bone healing and promote adequate callus formation. Complete healing of the fracture was achieved after 99 days of treatment. The authors believe that the use of pharmacological aids may be desirable, especially in the presence of risk factors such as complex and open fractures that could seriously slow down the natural regenerative processes of the fractured bone. In this scenario, teriparatide could have an important role in preventing delayed consolidation and improving the healing of nonunion fractures.

KEYWORDS

Nonunion, fracture healing, teriparatide, complex fractures, open fractures.

Introduction

Teriparatide is a synthetic polypeptide hormone that contains the 1-34 amino acid amino-terminal fragment of recombinant human parathyroid hormone (PTH 1-34). It is an interesting research topic, being one of the few drugs approved by the Food and Drug Administration [1] for obtaining bone mass increase in cases of poor bone mass, due to its anabolic effects. Teriparatide showed positive modulation of anabolic metabolism in bone tissue, promoting the deposition of new bone tissue [2-5]. Endochondral ossification improvement and bone remodeling have both been observed in animal models [6-8]. After fracture, this molecule is thought to improve callus volume, mineralization and mechanical strength of the bone. Nowadays, the efficacy of teriparatide in treating osteoporosis is widely accepted. Instead, the debate on its use to enhance fracture healing has yet to lead to a consensus, although it has been described as effective in numerous case reports and is a promising treatment to improve the healing of nonunion fractures [9-15]. In this report, we present the case of a patient with a complex open biosseous fracture of the leg which was addressed through surgery and early systemic treatment with teriparatide 20 mcg/day for 3 months, in order to prevent delayed union of the fracture.

Clinical case presentation

This report complies with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

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The patient gave written consent. It concerns a 27-year-old Caucasian man, 5'9" (1.75 m) tall and weighing 160 pounds (73 kg), with no previous disease or pharmacological therapy at the time of hospitalization. In a road accident in November 2019, he suffered an exposed both-bone fracture of his right leg (Fig. 1), classed as 42B3-b according to the AO Trauma Fracture Classification and IIIA according to the Gustilo open fracture classification system [16]. Within a few hours of the traumatic event, the fracture was treated surgically through osteosynthesis with external fixation. After the surgical treatment, hyperbaric oxygen therapy was performed in order to improve wound healing and prevent soft tissue complications such as infections; the patient received adequate anti-thromboembolic, antibiotic, gastroprotective and analgesic therapies. In this first phase, weight-bearing on the injured limb was not allowed. 40 days after the trauma and first surgery, there were no radiological signs of bone callus in the fracture site, while slight procurvation and valgus deviation of the tibia were observed. For these reasons, a revision external fixation surgery was carried out. Physical therapy (ultrasound and magnetotherapy) was also prescribed in order to promote soft tissue restoration and improve bone healing.

Figure 1 Pre-operative X-Rays.

Since healing signs were still insufficient at X-ray follow-up 60 days after the trauma (Fig. 2), implant dynamization was carried out and it was decided to start pharmacological treatment, consisting of calcifediol 0.15 mg/dl (30 drops per week), calcium carbonate 500 mg (taken every evening after dinner) and teriparatide 20 mcg (one ampule every day) as adjuvant treatment. One month after the patient started the pro-anabolic bone therapy, new X-rays showed a little progression in bone healing: the bone callus appeared wider and its density increased. The patient was allowed to begin progressive partial weight-bearing on the affected leg; no significant pain or discomfort and no local signs of irritation or infection were observed. Over the following weeks, in consideration of both the clinical and the radiological improvements, we allowed full weight-bearing on the right limb. The external fixation was finally removed one month later after X-rays demonstrated an advanced stage of bone healing, with satisfactory size and density of the bone callus. At the latest clinical follow-up, after 99 days of therapy with teriparatide, the X-rays showed complete callus formation and healing of the fracture. The patient did not complain of weight-bearing pain in the right leg. His skin scars appeared fully recovered, without any signs of dehiscence or superficial infection. The muscles

Figure 2 X-Rays after surgical treatment.

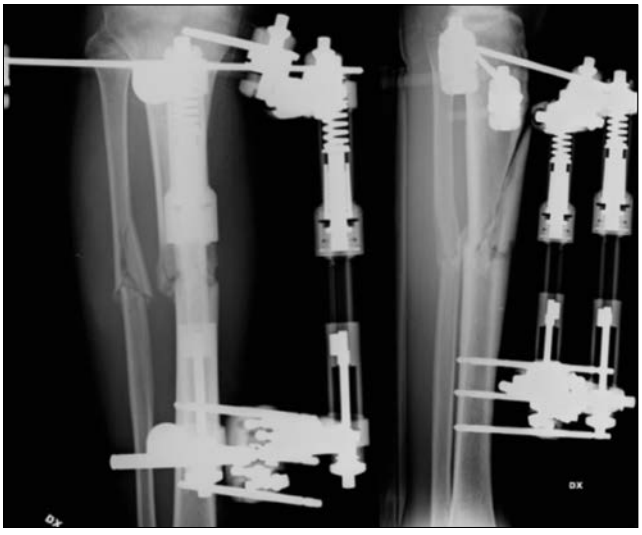
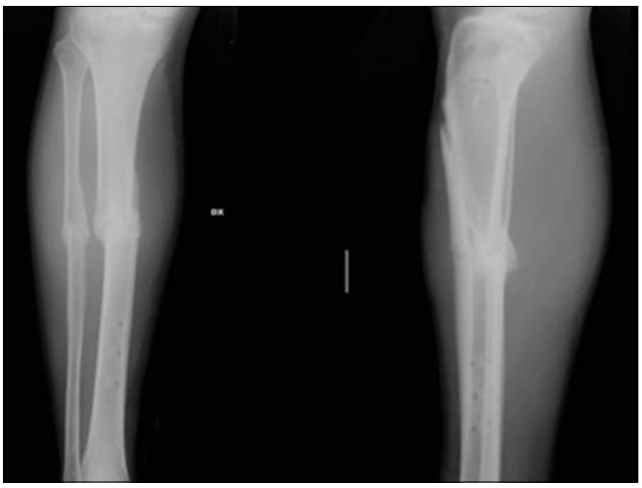


Figure 3 X-Rays 5 months after the trauma.



of the right lower limb showed mild hypotrophy (subsequently treated with a program of muscle-strengthening exercises), but without any significant repercussion on their functionality. No side effects attributable to the drug were observed during the treatment (Fig. 3).

Discussion

Fractures of the tibia and fibula are very common in clinical practice. Although most are closed, open fractures of the leg are relatively common (between 12% and 47%) and are often due to high-energy mechanisms [17-19]. There is still no consensus on the best treatment strategy for severe open tibial fractures, and further studies are therefore required in the years to come. From the surgical point of view, some reports have advocated the use of modern external fixators for severe Gustilo type IIIA, IIIB, and IIIC open fractures, particularly in the presence of bone defects [17,20]. The management of tibia and fibula fractures is largely influenced by the associated soft tissue injury. Severe open fractures of the tibia are generally associated with higher complication rates and poorer long-term outcomes. The SPRINT study (the largest prospective study of tibia fractures) found that open tibial diaphyseal fractures had poorer overall outcomes than closed injuries, showing twice the rate of reoperation or autodynamization within the first year (26.5%) [18]. Fracture nonunion is among the most dreaded complications after a both-bone fracture of the leg and represents one of the greatest challenges for the orthopedic surgeon. In general, approximately 10% of all fractures can result in fracture nonunion, and many more show signs of delayed union or improper tissue restoration. Compared with fractures at other sites, associated tibia and fibula fractures are plagued by relatively high rates of malunion (39% to 48%) and nonunion (between 5.3% and 24%), while the average time to union is significantly higher than average at 10.7 months [17,21,22]. Pseudoarthrosis is the macroscopic consequence of a post-fracture lack of efficiency of the biological bone healing processes and it represents a major challenge in orthopedic surgery, being associated with increased economic management costs and major social consequences. The healing mechanism is a cascade of a complex series of multiple inter-related factors. Some of these are patient-dependent such as

age, osteoporosis, menopause, use of tobacco or alcohol, regular use of corticosteroids and malnutrition. Others depend on the trauma experienced and the stability of the fracture [23]. In our case the fracture did not show sufficient healing signs at the first two X-ray follow-ups, and the fracture itself had bad prognostic factors, such as exposure. We opted to use systemic therapy with teriparatide prior to the possible onset of pseudoarthrosis, simultaneously with mechanical stimulation obtained through dynamization, in order to enhance the bone healing, achieve an adequate callus, and prevent delayed bone healing. The positive effect of teriparatide on fracture healing is observed in animals, but several case reports also describe a positive effect in humans, although more studies are necessary to confirm this [6-15,24]. The effect of teriparatide is due to its capacity to stimulate bone progenitor cells [25,26]. Together with teriparatide, local therapies were also applied, such as bone stimulation with magnetic fields, in order to utilize all the available non-surgical treatment options. The fracture showed a progressive positive evolution and healed in 99 days, allowing the patient to walk without any discomfort or pain at the end of the treatment.

Conclusion

Once surgery has been performed, in order to maximize the chances of good and quick bone healing, it is mandatory to remove all potential risk factors. At the same time, the use of pharmacological aids may be desirable, especially in the presence of serious risk factors that could slow down or even abolish the natural regenerative processes of the fractured bone. Among the drugs proposed to enhance the deposition of new bone tissue, teriparatide is one of the most innovative and fascinating. It can be used both in cases of full-blown pseudoarthrosis and cases of potential delayed fracture, in order to prevent treatment failure.

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