Trauma Case Reports 57 (2025) 101176

Contents lists available at ScienceDirect

Trauma Case Reports

journal homepage: www.elsevier.com/locate/tcr

Managing delayed union of fragility fractures of the pelvis successfully using romosozumab: A case report

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ARTICLE INFO

Keywords:
Fragility fracture
Pelvis
Romosozumab
Osteoporosis
Delayed union

ABSTRACT

Fragility fractures of the pelvis (FFPs) are typically caused by minor trauma or without any trauma in older individuals with osteoporosis. In recent years, FFP incidence has increased considerably owing to the increasing number of individuals in the aging population as well as impaired daily life. Surgeries are the main treatment options for some types of FFPs; however, the potential of the use of romosozumab, an FDA-approved humanized monoclonal antibody that can bind and inhibit sclerostin, is yet to be evaluated. Romosozumab substantially increases bone mineral density (BMD) in the spine and the hip, improves bone strength, and prevents the occurrence of new fractures. Previous studies have demonstrated the efficacy of romosozumab in promoting fracture healing, including the healing of nonunion in some fractures. Herein, we present a case of a 61-year-old woman who had FFP delayed union, after falling 4 months before visiting our hospital. She presented with bilateral buttock and leg pain. Baseline BMD measured using dual-energy X-ray absorptiometry revealed a T-score of −3.8 and −3.2 for the lumbar spine and total hip, respectively. As the patient's BMD indicated a high risk of fractures, romosozumab was administered. Her pain improved 3 months after the medication. Computed tomography taken after 3 months revealed that the fracture had healed, suggesting that romosozumab is an effective medication for treating FFP delayed union and nonunion.

Introduction

Pelvic fractures are caused by various factors, ranging from high-energy traumas such as traffic accidents to low-energy traumas, including falls from a standing position. Pelvic fractures caused by high-energy traumas have received considerable attention to date. However, the incidence of fragility fractures of the pelvis (FFPs), caused by the advancing age of the population, is yet to be sufficiently investigated [1]. Indeed, 64 % of FFPs are based on osteoporosis. In particular, 94 % of the patients, aged ≥60 years, have pelvis fractures caused by low-energy traumas [2]. Among all osteoporotic fracture types, the highest increase has been predicted in pelvic fractures, with the incidence rate increasing by 56 % and costs rising by 60 % between 2005 and 2025 [3].

Romosozumab is a monoclonal antibody that binds and inhibits sclerostin. Its efficacy was demonstrated in a large phase III clinical trial in postmenopausal women, where 1 year of romosozumab therapy led to a 13.3 % increase in lumbar spine bone mineral density (BMD) and a 6.8 % increase in total hip BMD. Romosozumab also increased bone formation markers and decreased bone resorption

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https://doi.org/10.1016/j.tcr.2025.101176
Accepted 14 April 2025
Available online 15 April 2025

markers, thereby rapidly increasing BMD via the dual effects on bone formation and resorption [4]. Clinical use of romosozumab was found to rapidly increase bone density, particularly in the lumbar spine [5,6]. These reports also showed differences in the effect of pretreatment of osteoporosis on BMD and the dynamics of bone metabolism markers. In some basic research, romosozumab has been reported to enhance bone healing [7–9]. Additionally, two case reports have demonstrated that romosozumab promoted bone healing of nonunion fractures in the distal radius and humerus, respectively [10,11].

Herein, we present a case of a 61-year-old woman with FFP delayed union successfully treated using romosozumab.

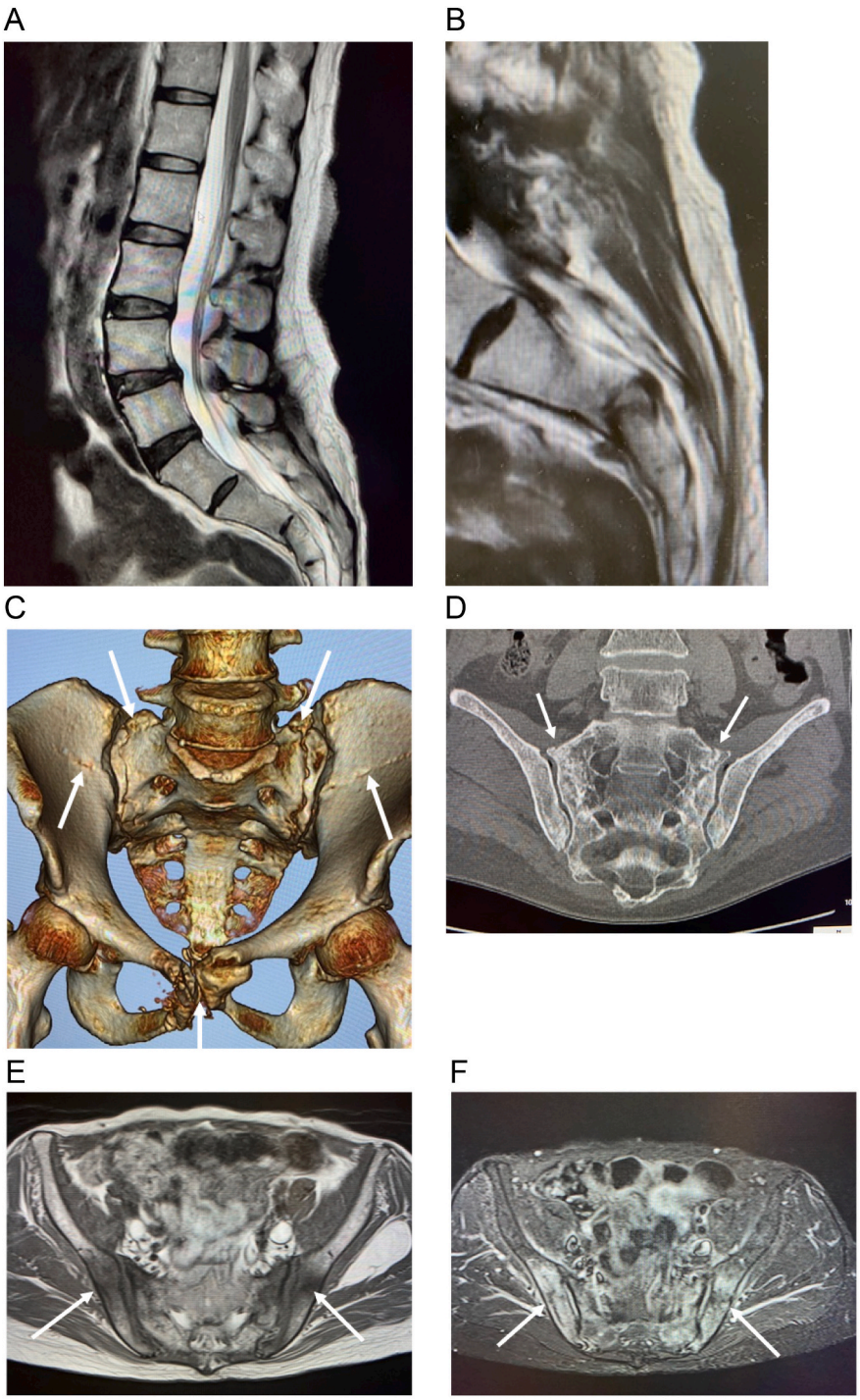

Fig. 1. Sagittal MRI of the lumbar spine showing slight spinal canal stenosis at L4/5 (a) and sacrum fracture (b). CT (c, d) and MRI (e, f) showed fractures of the bilateral sacrum, ilium, and pubis (white arrows).

Case report

A 61-year-old woman with bilateral buttock pain presented to our hospital. She had been treated for rheumatoid arthritis (RA) with 3 mg of tacrolimus hydrate, 50 mg of iguratimod, and 5 mg of prednisolone daily as well as 6 mg of methotrexate weekly. In addition, 0.5 μg of alfacacidol was prescribed. Four months before visiting our hospital, she fell and visited another hospital where she was diagnosed with stenosis of the lumbar spinal canal. Her magnetic resonance imaging (MRI) findings of the lumbar spine taken at the previous hospital showed no severe spinal canal stenosis, but a sacrum fracture was discovered (Fig. 1a, b). Therefore, further radiography of the pelvis such as computed tomography (CT) and MRI was performed, which showed fractures of the bilateral sacrum,

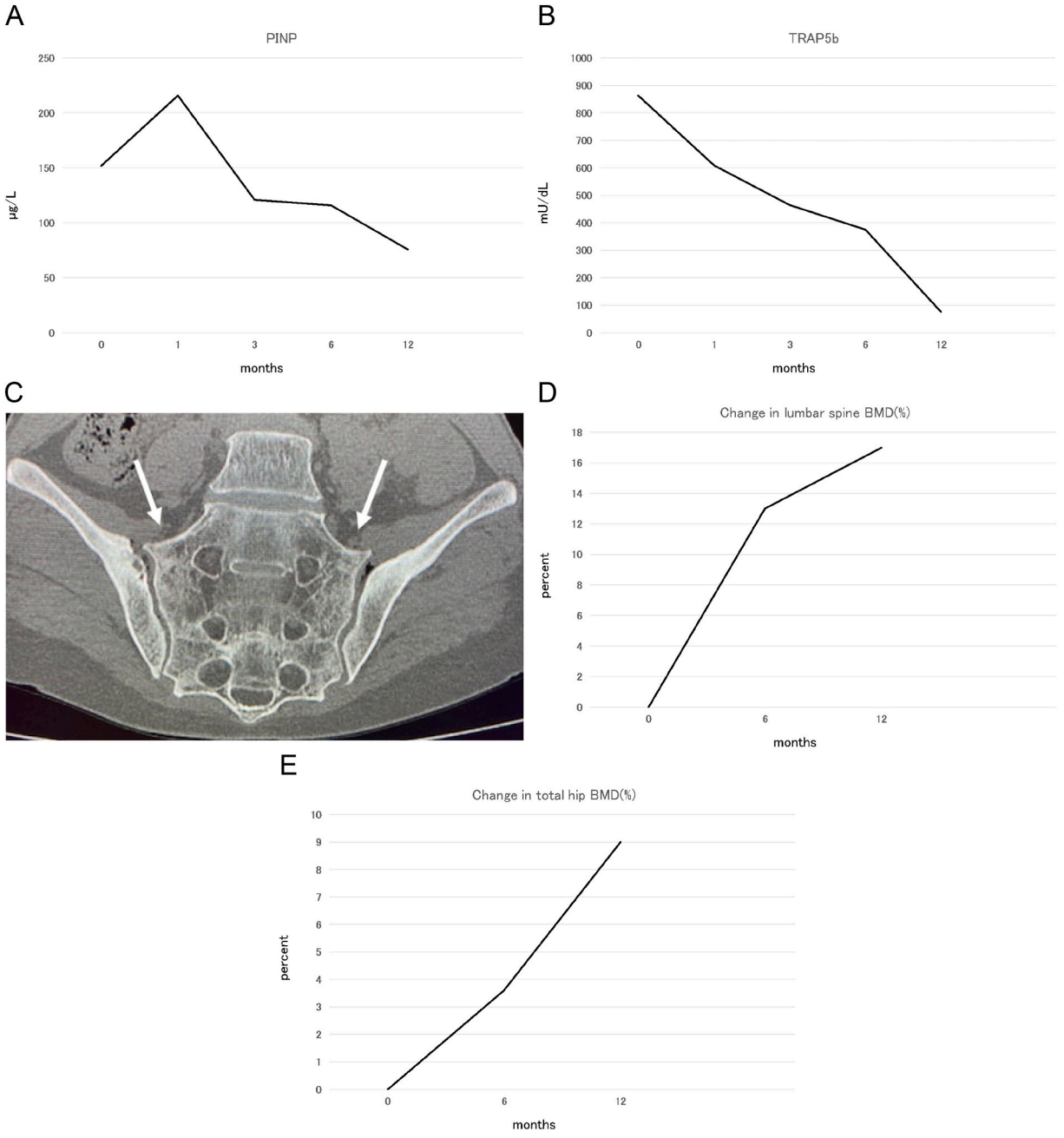

Fig. 2. Changes of bone metabolic markers. P1NP rose to 216 μg/L and gradually dropped at 3, 6, 9 and 12 months (a). TRAP5b decreased to 609 mU/dL at 1 month and continuously dropped at 3, 6, 9, and 12 months (b). CT was performed 3 months after romosozumab administration. Bone union was observed (white arrows) (c). Percent change in the BMD at the lumbar spine (d) and total hip (e) at 6 and 12 months. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

ilium, and pubis (Fig. 1c–1f). Based on Rommens' classification, the FFP was classified as type IV [12]. Although she had been treated for RA, the BMD had never been measured. Thereafter, the BMD was measured using dual-energy X-ray absorpiometry. The T-scores of lumbar spine and total hip were − 3.8 and − 3.2, respectively. No abnormalities in the biochemical results were found in the liver and renal functions such as serum calcium, phosphate, alkaline phosphatase, thyroid-stimulating hormone, and parathyroid hormone and urine analysis. Her initial 25-hydroxy vitamin D was 16 ng/mL, whereas the serum procollagen type I N-terminal propeptide (P1NP) and tartrate-resistant acid phosphatase 5b (TRAP5b) levels were 152 ng/L and 864 mU/dL, respectively. Total spine X-ray imaging showed no previous vertebral fractures.

Usually, Rommens' type IV fracture is recommended for surgical treatment [12]. However, the patient refused to undergo surgery because she could walk without any assistance. Therefore, surgery was not performed, and conservative treatment was chosen. Because she was taking 0.5 μg of alfacacidol alone and her BMD indicated a high risk of fracture, romosozumab was administered. One month after the initiation of romosozumab therapy, P1NP rose to 216 μg/L and gradually dropped at 3, 6, 9, and 12 months after (Fig. 2a). TRAP5b decreased to 609 mU/dL at 1 month and was dropping continuously at 3, 6, 8, and 12 months thereafter (Fig. 2b). Three months after the initiation of romosozumab, her buttock and leg pain improved, and CT confirmed bone union (Fig. 2c). Romosozumab was administered until 12 months. The BMD was measured at 6 and 12 months. Percent changes in the BMD of the lumbar spine and total hip were 17 % and 9 % at 12 months, respectively (Fig. 2d, e).

Discussion

We presented a case of FFP delayed union that was successfully treated with 3 months of romosozumab. The number of FFP cases has increased alongside the aging society. FFPs usually occur in women aged >80 years, and multivariate statistical studies have confirmed that FFPs were an independent risk factor of mortality in older patients [13]. The primary goal in the treatment of older patients is to restore mobility and independence.

In our case, although the fracture was classified into type IV, we did not choose surgical treatment because she was relatively young for FFPs and refused to undergo surgery because she could walk even with buttock and leg pain 4 months after the trauma. A drug therapy for FFPs using teriparatide, which is also a bone formation-promoting drug, has been reported. A previous report indicated that although teriparatide administration does not positively affect fracture union, pain is relieved after 8 weeks [14]. However, no studies have described the effectiveness of romosozumab for FFPs. Some basic studies have revealed the effectiveness of romosozumab for bone healing [15]. Two phase II clinical trials have reported the efficacy of romosozumab in adult fresh fractures. Moreover, these studies reported bone-healing effects of romosozumab on tibial and femoral fresh fractures treated by fixation surgeries. Both studies have concluded that romosozumab did not improve fracture healing in those patients [16,17]. Previous case reports have demonstrated that romosozumab was effective for nonunion cases of humerus shaft and distal radius fractures [10,11]. To date, in clinical settings, the bone-healing effect by romosozumab has not been proven. After the commencement of romosozumab therapy, the bone metabolic marker of bone formation P1NP increased at the peak of 1 month and gradually dropped to baseline by 6 months [4]. Conversely, bone resorption markers such as type 1 collagen cross-linked C-terminal telopeptide (CTX) and TRAP5b dropped 1 month after the initiation and continued at low level until the end of the treatment [4]. Speculatively, bone-healing effect exists during the early stage of romosozumab therapy when the levels of bone formation markers increased. In a bone biopsy study performed 2 months after romosozumab initiation, romosozumab accelerated modeling-based bone formation while remodeling-based bone formation was maintained [18]. Accordingly, during the early phase of romosozumab therapy, it showed a positive effect on bone union. Our patient had RA, although only 0.5 μg of alfacacidol was prescribed, BMD had never been checked. The T-scores of the lumbar spine and total hip were − 3.8 and − 3.2, respectively. Her BMD values were at the risk of imminent fractures, coupled with the presentation of FFPs, romosozumab was prescribed to rapidly increase BMD. In this case, PINP peaked at 1 month and gradually declined, falling below baseline after 3 months. TRAP5b values fell rapidly in the first month and continued to fall until the 12th month. BMD increased in percent change by 17 % and 9 % in lumbar spine and total hip at 1 year. After 3 months of romosozumab therapy, the patient's pain disappeared, and bone union was completed. Considering the delayed union of FFPs 4 months after the trauma, which was healed with 3 months of romosozumab therapy in this case report, we believe that the romosozumab therapy had some positive effect on bone healing.

Conclusions

Our findings revealed that 3 months of romosozumab therapy is effective for the management of FFP delayed union by rapidly increasing the BMD in the lumbar spine and total hip. Although these findings are not based on clinical trials, the present case report suggests a possibility that romosozumab promotes bone fusion.

CRediT authorship contribution statement

K. Wada: Writing – original draft, Writing – review & editing. **A. Tominaga:** Data curation. **M. Naruo:** Visualization. **K. Okazaki:** Supervision.

Consent for publication

All authors approved.

Ethics approval and consent to participate

The study design and protocol were approved by the institutional review board of our hospital. The patient was informed that information involving this case would be presented for publication and gave informed consent.

Funding

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

None.

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