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Case Report

Successful Treatment of Nonunion Following Periacetabular Osteotomy Using Teriparatide: A Case Report

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Abstract

Case: Two cases of osteotomy site nonunion after periacetabular osteotomy in healthy patients. Treatment with teriparatide (Forteo; Eli Lilly and Company, Indianapolis, IN) was initiated between 5-6 months post-operatively resulting in successful union, bony remodeling and symptom relief.

Conclusion: Teriparatide is a safe, effective and non-invasive means of aiding treatment of a relatively common complication following periacetabular osteotomy.

Keywords: Periacetabular Osteotomy (PAO); Parathyroid Hormone (PTH); Femoral-Acetabular Impingement (FAI)

Introduction

First described in 1988 by Ganz., *et al*. the periacetabular osteotomy (PAO) remains a popular and successful option to preserve hip function in patients with symptomatic hip dysplasia [1]. Through osteotomy sites in the superior pubic ramus, ischium, ilium and posterior column, the periacetabular region can be manipulated to increase femoral head coverage, medialize the hip center and adjust acetabular version [2]. Despite the technical demands of the procedure, it is typically quite successful at reducing pain and improving hip function [3-7]. It has also been found to be quite durable, with reported survival rates ranging from 78-95% at 10 years [3,6].

Despite the aforementioned success, complications associated with PAO have been found to occur in 6-37% of cases [4,7,8]. Within this subset, nonunion at one or more osteotomy sites is one of the more common complications, occurring in 1-17% of cases [9,10]. As with most fractures, patient factors including advanced age, smoking, diabetes mellitus and obesity have been implicated as risk factors for nonunion [9]. Additionally, more severe pre-operative dysplasia may also be associated with nonunion as greater displacement at the osteotomy site is necessary in order to achieve a desired correction.

Despite the frequency of nonunion, there have been few reliable solutions to this problem shy of the morbidity involved with revision fixation and bone grafting. While necessary in some cases, reoperation has been avoided in similar fracture nonunion cases by off-label utilization of teriparatide (Forteo), a parathyroid hormone (PTH) analog. We now present two cases in which Forteo aided in the successful recovery of patients with symptomatic nonunion following PAO.

Both patients were made aware that information regarding their care was being submitted for publication and have given consent to do so.

Case 1

32 year-old female, non-smoker, with history of asthma, Ehlers-Danlos Sydrome, BMI 24 kg/m^2, who presented with right hip pain.

She was found to have bilateral hip dysplasia with more severe undercoverage of the right femoral head (Figure 1). She underwent combined hip arthroscopy with synovectomy, chondroplasty, labral repair and decompression of femoral-acetabular impingement (FAI) and PAO in a non-staged fashion. Her hospital course was unremarkable and she was discharged home on post-operative day (POD) 5 with non-weight bearing restrictions.

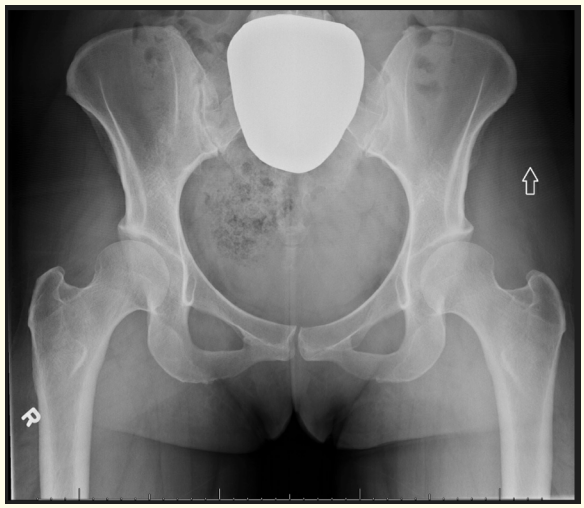

Figure 1: Pre-Operative Anteroposterior (AP) Pelvis X-Ray for Case 1 demonstrating right sided hip dysplasia and undercoverage of the femoral head. Acetabular index measured 33 degrees and center-edge angle measured 9 degrees.

The early post-operative course was unremarkable and the patient was made weight bearing as tolerated roughly 11 weeks after surgery. At this same visit, it was noted radiographically that the superior ramus osteotomy was healing at a slower rate than the remaining osteotomies (Figure 2). 17 weeks post-operatively the patient presented to clinic with increased groin pain with imaging demonstrating persistent delayed union at the superior ramus. Vitamin D level was found to be 57.6 ng/mL (30-80 ng/mL). Teriparatide (Forteo) was initiated 22 weeks post-operatively at a dose of 20 µg/day, with plans for a 4-month course. Radiographic signs of healing at the nonunion site were noted as soon as 3 weeks after starting treatment, with symptomatic improvement noted 8 weeks after initiation (Figure 3). This improvement facilitated more aggressive rehabilitation and complete recovery.

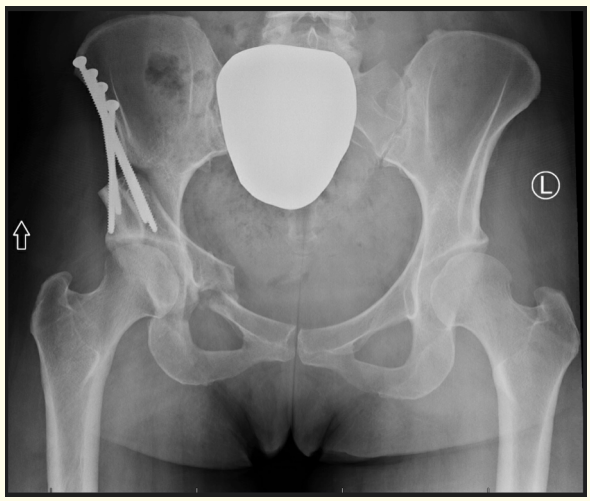

Figure 2: AP X-Ray demonstrating slow healing at the superior ramus 3 months post-operatively.

Figure 3: AP Pelvis X-Ray obtained 7 months post-operatively, after 2 months of treatment with Forteo. Increased callus formation is noted at the superior ramus osteotomy site.

The patient presented back to clinic 1 year post-operatively, 3 months after Forteo completion, inquiring about symptomatic screw removal. Her X-Rays demonstrated sufficient bony healing to facilitate this and she underwent implant removal 2 months later (Figure 4). The patient was last seen 18 months from her index procedure and was noted to be doing well without complaints.

Figure 4: AP Pelvis X-Ray at 15 months post-operatively. Union and early remodeling are noted at all osteotomy sites. Interval screw removal is observed.

Case 2

45 year-old female, non-smoker, with history of migraines, BMI 31 kg/m^2, who presented with right hip pain. She was found to have right hip dysplasia with under coverage of the femoral head (Figure 5). She underwent staged hip arthroscopy, synovectomy, chondroplasty, labral repair and decompression of FAI with subsequent PAO 26 days later. Her post-operative course was unremarkable and she was cleared to discharge home on POD 4 with non-weight bearing restrictions.

Figure 5: Pre-operative AP Pelvis X-Ray for Case 2. Right sided hip dysplasia with femoral head undercoverage is displayed. Acetabular index measured 20 degrees and center edge angle measured 15 degrees.

The early post-operative course was unremarkable and the patient was advanced to weight bearing as tolerated 11 weeks from her PAO. Imaging at this time revealed delayed union at the superior ramus and iliac osteotomy sites, yet the patient remained asymptomatic and continued to progress with physical therapy. She returned to clinic 23 weeks status post PAO with new concerns of groin and deep gluteal pain. Radiographic appearance of the superior ramus and iliac osteotomies remained unchanged (Figure 6). Vitamin D level was noted to be 40 ng/mL (30-60 ng/mL). Forteo was initiated 10 days later at a dose of 20 µg/day. The patient's pain started to improve clinically near the end of her 3-month course. Radiographic improvement was first noted nearly 11 weeks after initiation of treatment (Figure 7). Symptoms continued to improve at her 1 year post-op visit, allowing for further progression with physical therapy. The patient was last seen nearly 2 years after her index surgery and was found to have effectively remodeled her osteotomy sites (Figure 8). At the time of this visit, her primary concerns were regarding the contralateral hip, which eventually went on to require total hip arthroplasty. Her right hip continued to do well.

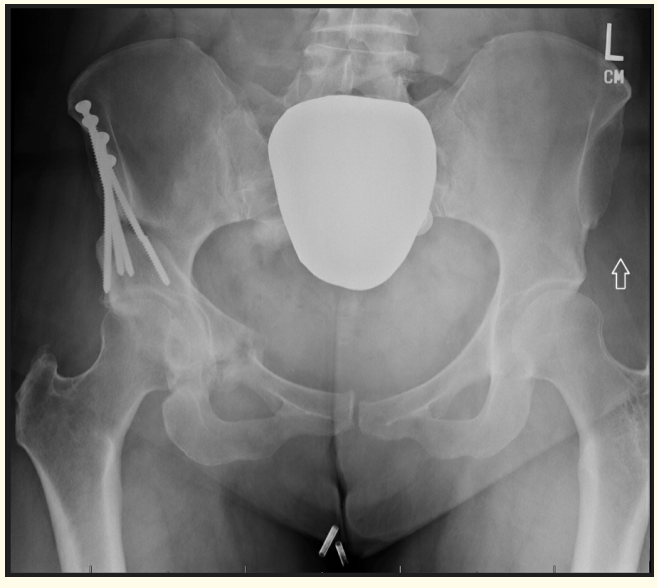

Figure 6: AP X-Ray 5 months post-operatively demonstrating delayed healing at the iliac and superior ramus osteotomy sites.

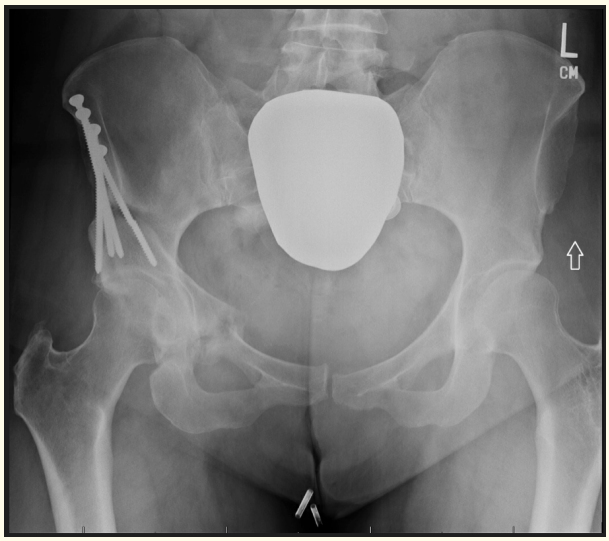

Figure 7: AP Pelvis X-Ray obtained 8 months post-operatively and 3 months after initiation of treatment with Forteo. Interval callus formation is noted at the iliac and superior ramus osteotomy sites.

Figure 8: AP Pelvis X-Ray obtained 19 months post-operatively. There has been successful union and early evidence of remodeling at all osteotomy sites.

Discussion and Conclusion

We present two cases of nonunion following PAO in which teriparatide was utilized for successful nonoperative management. In both cases, teriparatide was initiated at standard dosing [11] between 5 and 6 months post-operatively and continued for 3 to 4 months. Both patients experienced bony union and symptom relief by one year from PAO and neither experienced side effects from the medication.

In both cases the superior pubic ramus osteotomy site was involved. This is one of the more common sites where nonunion is observed, likely secondary to the amount of displacement with rotation and correction of the periacetabular region [10]. Some would argue that, in asymptomatic patients, nonunion at the superior ramus can be treated with observation [1,9], however this was not the case in our symptomatic patients. Etiology of nonunion remains unclear in both cases as, aside from older age and an elevated BMI in Case 2, minimal risk factors were present.

In a 2020 study by Selberg., *et al*. the incidence and outcomes of nonunion in PAO patients were investigated in 245 patients. 55% of their cohort demonstrated nonunion of at least 1 osteotomy site at 6 months, which dropped to 8% by one year [9]. Due to this stark change, they concluded that aggressive treatment of nonunion at 6 months is not indicated as most will resolve spontaneously. However, they also make this comment with reference to reoperation, noting that no reliable alternatives existed. With demonstrated success of non-operative management utilizing teriparatide, there may be a role for treatment at this time point in symptomatic individuals, though further studies are needed to definitively discern this.

A synthetic/recombinant form of parathyroid hormone, teriparatide plays an active role in bone health via calcium/ Vitamin D metabolism, early callus formation and also having anabolic properties [12-15]. On a molecular level, teriparatide induces the kidney to convert Vitamin D to its active form, facilitating calcium reabsorption from the kidney and intestinal tract. For this reason, it is important to ensure patient's Vitamin D levels are repleted or supplementation is occurring concurrently. In its pathologic form, hyperparathryroidism, too much PTH may have a detrimental effect on bone, though this has not been

found to occur with shorter pulses of treatment using teriparatide [14]. From a bone healing perspective, teriparatide plays an early role in chondrocyte differentiation, contributing to robust callus formation and accelerated endochondral ossification. Lastly, teriparatide displays its anabolic effect through stimulation of osteoblasts as well as reduction of osteoblast apoptosis. This tilts the balance of bone metabolism towards formation, however, through osteoblast activity indirect activation of osteoclasts occurs leading to remodeling of this newly formed bone [15].

Teriparatide is delivered through subcutaneous injection and is generally well tolerated by patients. Potential side effects include nausea, dizziness, headache and leg cramps. A theoretical concern for development of osteosarcoma has been identified in animal models, however has not been observed in humans. Treatment for longer than 2 years is not recommended [13].

FDA approved teriparatide in 2002 for use in osteoporotic patients at risk for fracture. Off-label usage of teriparatide for nonunion has gained some traction in the orthopaedic community, though opinions on the efficacy of the drug remain split [15]. Two 2020 systematic reviews favor usage, concluding teriparatide allowed for successful union in upwards of 95% of cases, shorter time to union, decreased pain scores and increased functional scores [11,16]. Included were patients with nonunion following fractures of the femur [17], femoral neck [18], humerus [19], sternum [20] and odontoid [21]. Further favorable evidence exists for treatment of nonunion seen in periprosthetic femur fractures [22], acromion stress fractures [23], post-operative foot and ankle arthrodesis patients [24] and of perhaps greatest relevance, pelvic fractures [25]. These results are refuted by a 2020 meta-analysis on randomized controlled trials in which teriparatide was compared to placebo to determine the efficacy in decreasing risk of treatment failure. While this analysis focused more on osteoporotic patients, opposed to nonunion patients, nonunion was included as a means of treatment failure. 4 out of 5 studies included concluded no significant difference between the groups [26].

While further research is certainly needed to identify the true efficacy of this medication, we feel that teriparatide was able to catalyze healing in our cases. It is our opinion that its non-invasive nature, mild and seldom-experienced side effect profile and largely successful history make teriparatide a promising alternative to hasty, morbid revision surgery in nonunion patients.

Bibliography

1. Ganz R., *et al*. "A New Periacetabular Osteotomy for Treatment of Hip Dysplasias. Technique and Preliminary Results". *Clinical Orthopaedics and Related Research* 232 (1988): 26-36.

2. Sanchez-Sotelo J., *et al*. "Surgical Treatment of Developmental Dysplasia in Adults: I. Nonarthroplasty Options". *Journal of American Academy of Orthopaedic Surgeons* 10.5 (2002): 321-333.

3. Larsen J., *et al*. "14-year hip survivorship after periacetabular osteotomy: a follow-up study of 1,385 hips". *Acta Orthopaedica* 91.3 (2020): 299-305.

4. Clohisy J., *et al*. "Periacetabular Osteotomy: A Systematic Literature Review". *Clinical Orthopaedics and Related Research* 467 (2009): 2041-2052.

5. Holleyman R., *et al*. "Periacetabular Osteotomy for Developmenta Dysplasia of the Hip and Femoroacetabular Impingement". *The Journal of Bone and Joint Surgery* 102 (2020): 1312-1320.

6. Cho Y., *et al*. "Long-Term Results of Periacetabular Rotational Osteotomy Concomitantly with Arthroscopy in Adult Acetabular Dysplasia". *The Journal of Arthroplasty* 35 (2020): 2807-2812.

7. Clohisy J., *et al*. "Patient-Reported Outcomes of Periacetabular Osteotomy from the Prospective ANCHOR Cohort Study". *The Journal of Bone and Joint Surgery* 99 (2017): 33-41.

8. Biedermann R., *et al*. "Complications and patient satisfaction after periacetabular pelvic osteotomy *International Orthopaedics* 32 (2008): 611-617.

9. Selberg C., *et al*. "What Proportion of Patients Undergoing Bernese Periacetabular Osteotomy Experience Nonunion, and What Factors are Associated with Nonunion?" *Clinical Orthopaedics and Related Research* 478 (2020): 1648-1656.

10. Wells J., *et al*. "Are Complications After there Bernese Periacetabular Osteotomy Associated with Subsequent Outcomes Scores?" *Clinical Orthopaedics and Related Research* 477 (2019): 1157-1163.

11. Canintika A and Dilogo I. "Teriparatide for treating delayed union and nonunion: A systematic review". *Journal of Clinical Orthopadics and Trauma* 11 (2020): S107-S112.

12. Pietrogrande L and Raimondo E. "Teriparatide in the treatment of non-unions: Scientific and clinical evidences". *Injury* 44 (2013): S54-S57.

13. Lindsay R., *et al*. "Teriparatide for osteoporosis: The importance of the full course". *Osteoporosis International* 27 (2017): 2395-2410.

14. Quattrocchi E and Kourlas H. "Teriparatide: A Review". *Clinical Therapeutics* 26.6 (2004): 841-854.

15. Bukata S and Puzas J. "Orthopedic Uses of Teriparatide". *Current Osteoporosis Reports* 8 (2010): 28-33.

16. Yoon B and Kim K. "Does Teriparatide Improve Fracture Union?: A Systematic Review". *Journal of Bone Metabolism* 27.3 (2020): 167-174.

17. Giannotti S., *et al*. "Atrophic femoral nonunion successfully treated with teriparatide". *European Journal of Orthopaedic Surgery and Traumatology* 23 (2013): S291-S294.

18. Mitani Y. "Effective treatment of a steroid-induced femoral neck fracture nonunion with once-weekly administration of teriparatide in a rheumatoid patient: A case report". Archives of Osteoporosis 8 (2013): 131-133.

19. Oteo-Alvaro A and Moreno E. "Atrophyc humeral shaft nonunion treated with teriparatide: A case report". Journal of Shoulder and Elbow Surgery 19 (2010): e22-e28.

20. F Marin. "Treatment of Chronic Nonunion of a Sternal Fracture With Teriparatide". *Annals of Thoracic Surgery* 111 (2021): e41-42.

21. Rubery P and Bukata S. "Teriparatide May Accelerate Healing in Delayed Unions of Type III Odontoid Fractures: A Report of 3 Cases". *Journal of Spinal Disorders and Techniques* 23 (2010): 151-155.

22. Ramani A and Wagner R. "Periprosthetic Femoral Stress Fracture After Bisphosphonate Treatment Resulting in Nonunion Successfully Treated with Teriparatide". *JBJS Case Connect* 6.2 (2016): 1-5.

23. Lipof J., *et al*. "Treatment of an Acromial Stress Fracture After Reverse Total Shoulder Arthroplasty With Teriparatide". *JBJS Case Connect* 10.2 (2020): 1-7.

24. Lee H., *et al*. "Effects of teriparatide on fusion rates in patients undergoing complex foot and ankle arthrodesis". *Foot and Ankle Surgery* 25 (2020): 766-770.

25. Peichl P., *et al*. "Parathyroid Hormone 1-84 Accelerates Fracture-Healing in Pubic Bones of Elderly Osteoporotic Women". *The Journal of Bone and Joint Surgery* 93 (2011): 1583-1587.

26. Moon N., *et al*. "Effects of Teriparatide on Treatment Outcomes in Osteoporotic Hip and Pelvic Bone Fractures: Meta-analysis and Systematic Review of Randomized Controlled Trials". *Hip and Pelvis* 32.4 (2020): 182-191.