

## Successful treatment of a challenging periprosthetic femoral fracture on a premenopausal patient with a long history of immunosuppression

### Case report

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### ABSTRACT

While immunosuppression provides relief and care in patients with rheumatic arthritis, the prolonged usage of steroids has been known to cause various and serious complications. While in older patients it is common to find those with a long history of immunosuppression, younger patients also suffer from its prolonged complications. We present a 38 year old heavily immunocompromised female patient with excellent compliance on which we operated on multiple occasions and have treated from 2019 to 2022. The patient was originally diagnosed with rheumatoid arthritis at age 7, and has been receiving high dose immunosuppressive medication. The patient received bilateral total hip arthroplasty during 2009 and 2013, and a Total Knee Arthroplasty (TKE) in 2011. Over the course of her postoperative recovery, she suffered from multiple cases of periprosthetic fractures. In October 2019, the patient again presented with spontaneous pain in her right thigh. She was then diagnosed with a Vancouver C type periprosthetic fracture on the right femur, and was referred and admitted to our level one Trauma Center in Szeged, Hungary. After multiple trials, the patient received a Locking Compression Plate (LCP) type Proximal Femoral Hook Plate (PFHP) with cable fixation, attachments and a bone allograft to reinforce stability and neutralize stress on the fractured area. Multiple and repetitive challenges can be expected in treating bony fractures of weight bearing lower limbs for heavily immunocompromised patients. The patient, despite her young age, had the osteological biology of an elderly patient, requiring us to take into consideration not only surgical components but biological components as well. With a multidisciplinary approach from osteological, biological, and surgical fields, successful results may be acquired even in these challenging cases.

### Keywords

**Arthroplasty, replacement, hip; Arthroplasty, replacement, knee; Immunosuppressive Agents; Osteoporosis; Periprosthetic fractures; Premenopause;**

## INTRODUCTION

While immunosuppression provides relief and care in patients with autoimmune disorders, the prolonged usage of steroids has been known to cause various and serious complications. While in older patients it is common to find those with a long history of immunosuppression, younger patients also suffer from its prolonged complications. While immunosuppression is a relative common therapy in the elderly, we rarely come across patients who are young and have a long history of its use, leading to pre-menopausal changes in osteobiology. Treatment of periprosthetic fractures is in itself relatively rare, and it poses multiple mechanical challenges. Combined with the complicated medication therapy of rheumatoid arthritis (RA), it gives surgeons a whole different dimension of challenges. Here we report a young patient with a 30 year history of immunosuppressive therapy who underwent multiple periprosthetic fractures, the challenges and consideration of its treatment.

## PATIENT INFORMATION

The patient was a 39 year old female with a 30 year history of immunosuppression (4 mg of methylprednisolone) due to Juvenile Rheumatoid Arthritis (JRA) from the age of 8. She had been prescribed and had been continuously using Methylprednisolone, Methotrexate (22.5 mg once a day), and Leflunomide. The patient gave birth in her mid 30s. She had been taking other osteoporotic medication from a young age as well, alongside her prosthetic surgeries; calcium, vitamin D (6000 International Units), Alendroate. For her advanced JRA, she later received tofacitinib therapy as well. She developed allergic reactions to numerous substances, such as phenobarbiturates, Iodine, metal, diclofenac etc. No known rheumatoid arthritis was reported in her family. The patient was extremely cooperative and compliant, and all medical treatment and rehabilitation instructions were followed.

## CASE PRESENTATION

Clinical findings, Timeline, Therapeutic intervention

The patient was originally diagnosed with rheumatoid arthritis at age 7, and has been receiving high dose immunosuppressive medication (Methylprednisone, Methotrexate, Leflunomide, biological therapy every 6 weeks) ever since. All immunosuppressive medication had been halted during the acute perioperative phase. By the time of admission at our clinic, the patient had already undergone right side total hip arthroplasty (THA) in 2010, left side total knee arthroplasty (TKA) in 2011 and left side THA in 2013 (*Figure 1*). Her acute postoperative course was uneventful.

In June 2019, the patient presented with pain and discomfort in her right thigh during physiotherapy. She was admitted to her local Traumatology Department and was diagnosed with a right side femoral shaft fracture of which was surgically reduced by Open Reduction and Internal Fixation (ORIF) with plates.

In October 2019, the patient again presented with spontaneous pain in her right thigh. She was then diagnosed with a Vancouver C type periprosthetic fracture on the right femur, and was referred and admitted to our level one Trauma center in Szeged, Hungary. The patient received a Locking Compression Plate (LCP) type Proximal Femoral Hook Plate (PFHP) with attachments and a bone autograft to reinforce stability and neutralize stress on the fractured area (*Figure 2*). Unfortunately the patient suffered from left side brachial artery thrombosis on the first postoperative day. A Fogarty thrombectomy was performed immediately with successful revascularization. The patient was discharged 15 days later with no further complications.

The patient received Teriparatide therapy (Parathyroid hormone analogue) from her local hospital in November, 2019. The patient presented to our outpatient clinic for post-operative radiographic revision on the 6th week (41th postoperative days), and was instructed to commence partial weight bearing from 20kg, up to 7 kg per week. She later presented to the outpatient clinic on the 55th postoperative day due to local pain on

the operated limb during weight bearing, and was thus instructed to practice lighter partial weight bearing (10 kg, with a 5 kg increase in weight bearing every week). No radiographic anomalies were found and progressive ossifications were noticeable. By 2020.02.04 (111th postoperative day), the patient was able to complete weight bearing on the operated limb.

In 2020.06.25 the patient presented again to our outpatient clinic with pain in her operated right hip, while playing with her children. Radiology revealed that the right LCP PFHP component had been fractured (*Figure 3*). We surgically exchanged the LCP PFHP and further added a cadaver allograft component to the fractured area in hope of increased ossification (*Figure 4*). Cable fixation was utilized the stabilization of the allograft, as well as the distal end of the LCP PFHP, and completed a allograft strut osteosynthesis. The patient was observed post-operatively on our ward, with no unusual findings radiographically.

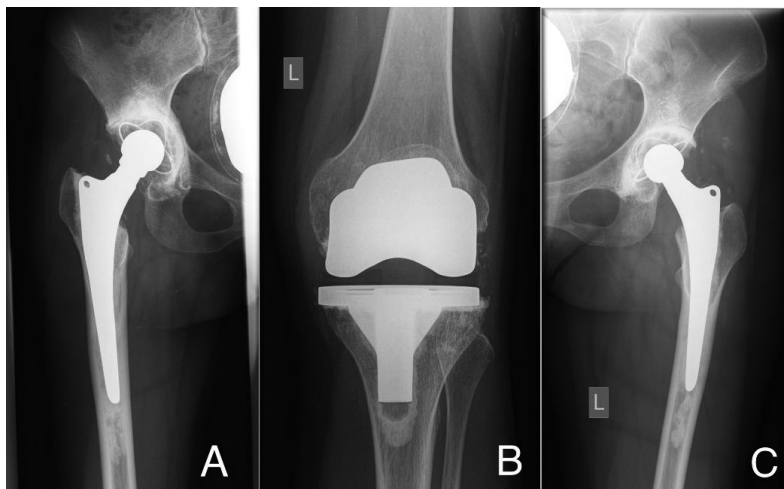
During 2020 September the patient presented with tachycardic episodes, hypertensive attacks, polyuria, and diarrhea. The patient was referred to an endocrinological institution in suspicion of pheochromocytoma. After no further improvement, approximately 3 months later evidence of pheochromocytoma had not been established. After careful

deduction, parathyroid hormone therapy was halted. The patient's condition had improved, and had only presented with fewer random tachycardic episodes due to this day.

After the suture removal on the 10th postoperative day, the patient was discharged and has been presenting to our outpatient clinic for follow-ups. On the latest radiographic followup on 2020.12.15 (168th postoperative day from the reoperation) no signs of novel periprosthetic injury had been found, and complete ossification could be seen on the operated right limb.

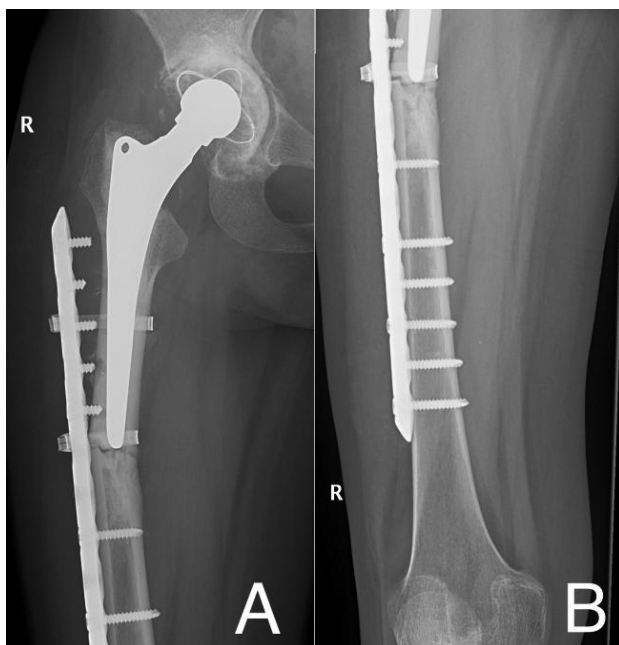
Around October 2020, the patient presented to our clinic with the inability to move her left wrist. X ray examination revealed a subluxation of the carporadial joint (*Figure 5*), but due to the history of arterial thrombosis, conservative treatment was recommended for the time being. After multiple consultations and careful consideration, an arthrodesis and tendon reconstruction was performed on 2021.01.20. (*Figure 6*). A cast was applied postoperatively, and no apparent complications were noticeable under postoperative observation.

In our most recent revision (15 months post FHL implantation, 10 months after arthrodesis), the patient presented with full ambulatory function and with no complications neither on the femoral components nor on the wrists (*Figure 7*).



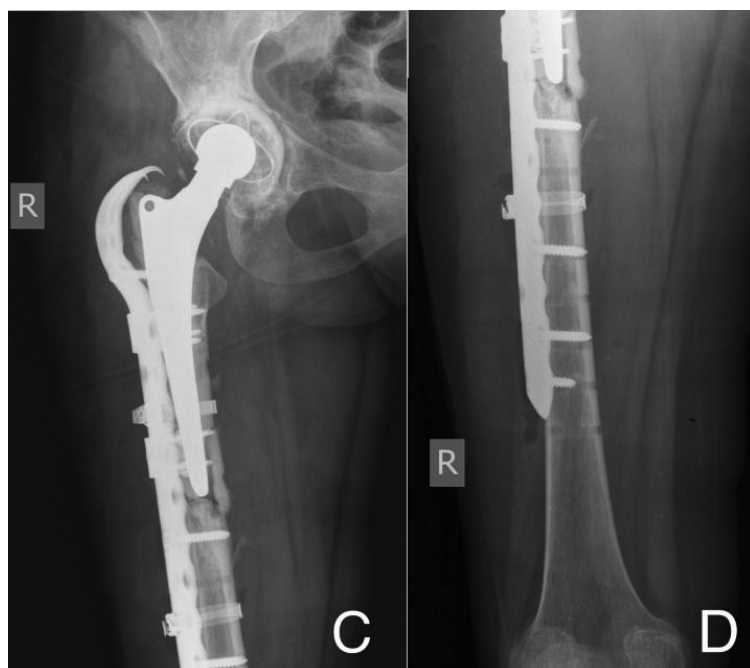
**Figure 1**

(A) X ray of the right side THA (2010); (B) Left side knee TKA (2011); (C) Left side THA (2013)



**Figure 2 (A, B)**

*Preoperative X rays of left side periprosthetic femoral shaft fracture on October 2019*



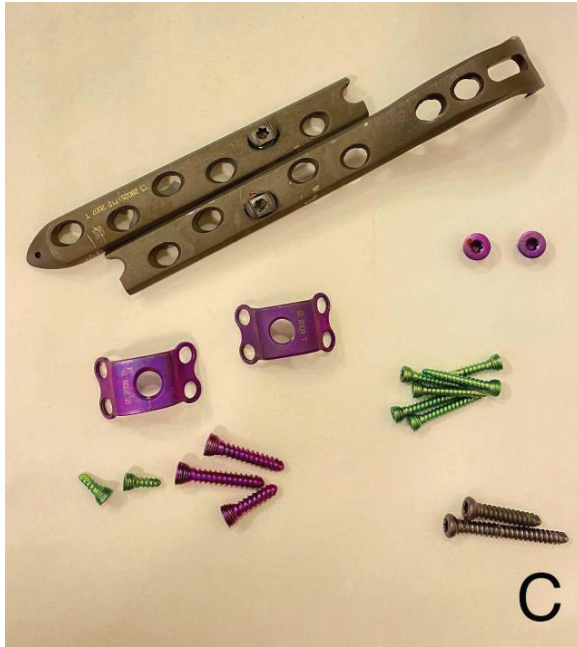
**Figure 2 (C, D)**

*Postoperative X ray after one day of surgical intervention. The periprosthetic fracture was corrected with a LCP PFHP with a bone autograft and angular stability screws with attachments*



**Figure 3**

*(A-B) Preoperative X rays of left side periprosthetic femoral shaft fracture on 2020.06.25.*



**Figure 3 (C)**

*Implants that were removed due to the break in the LCP femoral hook plate*



**Figure 4 (A, B)**

*Postoperative X ray after cadaver bone allograft implantation and a new hook plate application*



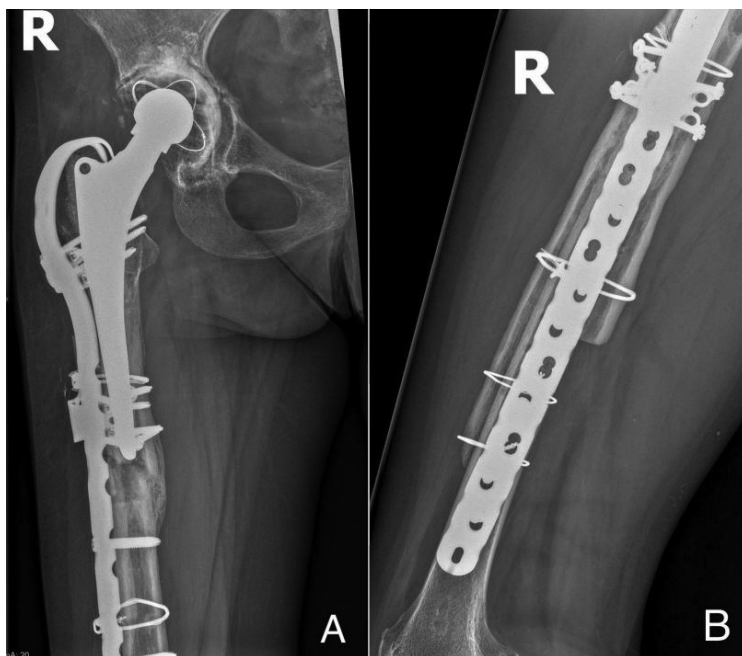
**Figure 5 (A, B)**

*Subluxation of the left radiocarpal joint taken on 2020.10.13. Conservative therapy was recommended*



**Figure 6 (A, B)**

*Postoperative X ray after left side radiocarpal arthrodesis and extensor tendon reconstruction*



**Figure 7 (A, B)**

*Right side FHP osteosynthesis after 15 months postoperative. X rays were taken in September 2021.*



**Figure 7 (C, D)**

*X ray of the left side radiocarpal arthrodesis after 10 months*



## DISCUSSION

While immunosuppressive therapy provides benefits in the treatment of autoimmune diseases, the well-known side effects can lead to serious consequences, especially osteoporosis (2). While complications of immunosuppressive therapy have been well understood and managed in older patients, the complications and its treatment of juvenile rheumatoid arthritis seems to be vague and unsettling, especially when the patients have had the disease for a longer period of time (3). Not only do the young patients have to struggle with complications from taking immunosuppressants in itself, pregnancy while under immunosuppression also exacerbates the patient's condition; the alteration of the patients osteobiology, osteoporosis (1).

In our case report, the patient had had a history of 30 years of immunosuppression at the age of 38, and received multiple surgeries over the course of more than ten years. Because of her advanced RA, she received three large total joint arthroplasties in her 20s. Also the fact that she gave birth accelerated her change in osteobiology, leaving her with brittle bone structure similar to an elderly patient. This led to a cascade of periprosthetic fractures, leading to multiple challenging surgical interventions. The challenges here that must be dealt with are numerous strategies.

Because of the advanced osteoporosis, she was put on an early treatment regime. *Sunyecz* reviewed that in compliant patients the use of calcium and vitamin D therapy decreases the risk of osteoporotic fractures (13). The patient also took alendronate, which the American College of Rheumatology recommends against glucocorticoid induced osteoporosis. Because of the patients' multiple re-surgeries, Teriparatide was also introduced in November 2019. Although the effectiveness of teriparatide is moderate with a 7% increase in premenopausal women with glucocorticoid use when compared to alendronate, its adverse effect cannot be ignored (8). While literature reviews that teriparatide increases the risk of osteosarcoma in rodents, it has not been shown to increase the risk in humans (15). In humans, hypercalcemia after subcutaneous administration and urinary calcium excretion

seems to be the most common complications, in our case the patient presented with palpitations and tachycardia, which could have been caused by ionic disturbances caused by multiple drug interactions. After discontinuation, the side effects resided, and to our surprise the patient later did not suffer from further periprosthetic fracture complications. According to *Lane et al.*, even in glucocorticoid-induced osteoporosis, the effects of teriparatide continue up to 6 to 12 months, which may have been the cause of successful postoperative course in our patient as well (5).

In the initial periprosthetic fracture treatment in October 2019, the application of the FHP resulted in a periprosthetic fracture and the destruction of the titanium plate. In our initial treatment, an autograft collected from the patient's own pelvis was applied, which unfortunately resulted in the previously mentioned complication. Perhaps in an advanced osteoporotic patient with glucocorticoid use, the autograft was also osteoporotic in nature, which did not accelerate the ossification process, as expected (14). Literatures mostly focus only on the decrease in bone mass in the hip and spine, and not on the pelvis, it difficult to project the effectiveness of autograft application in patients with glucocorticoid, let alone premenopausal women. Allograft implantations can be indicated in case of Type B3 Vancouver periprosthetic fractures, especially in young and active patients (10). While *Hui et al.* suggests that in Vancouver type B1 or C fractures, the union rates are similar with or without strut allografting, our case report indicates otherwise (6). As unfortunate as it is, this specific case provides a rare perspective on the effectiveness of multiple osteoporotic medications and surgical techniques.

During the follow ups, we restricted the weight bearing of the patient's operated limb (15 kg during the first week, plus 5 kg per week), and introduced partial weight bearing as part of the patients rehabilitation program. As a general rule, most literature provides positive insight on immediate weight bearing during postoperative rehabilitation. They mostly analyzed cases in elderly patients

without long term glucocorticoid use (11, 12). One other important factor that should be taken into consideration is also the weight of the patient. According to Keenan *et al.*, immediate weight bearing had no noticeable effect on reoperation risks in patients with lateral locked plate fixation of periprosthetic distal femoral fractures, although these apply to those older patients and not patients with histories of long term glucocorticoid use (4). No differences in functional outcomes were noted in a randomized control study by Paulsson *et al.* (9). In cases of those with obesity, postoperative complications of THP are noticeably increased, which should be a consideration factor when introducing weight bearing exercises in rehabilitation (7). While we proceeded with caution, the first FHP did in fact break not right after the surgery, but gradually. We might be able to suspect that the outcome would have been similar even if we started immediate weight bearing. However, considering the fact that our patient had a rare history of long term glucocorticoid use, alendronate and teriparatide application, the osteobiological changes cannot be simply applied in the general rule of periprosthetic fracture treatment in the elderly. In our latest attempt, we reconsidered the biological changes of the patient by utilizing an allograft to stabilize the periprosthetic fracture both mechanically and osteogenetically, which lead to successful results.

On another note, the subluxation of the

radiocarpal joint was most likely caused by the compensatory stress caused by use of walkers while restricted weight bearing, or from an imbalance in the flexor and extensor tendons. In our intraoperative assessment, the extensor tendons were ruptured, and the latter may be a more plausible cause. Nevertheless, if the rupture of the extensor tendons were caused by the excess stress still remains a possible mechanism of injury as well. Cases have been reported that excessive and multiple steroid uses cause spontaneous ruptures of extensor tendons (16).

## CONCLUSION

Even in young patients, long term immunosuppression leads to drastic changes in osteobiology, and the surgical treatment of complicated fractures should be planned considering the altered osteobiology. The timing of administration of parathyroid hormone analogues could enhance the strength of the bone structure temporarily, but should be used with caution and medication alone may not be enough to treat periprosthetic fractures in patients with long term glucocorticoid use. In cases of treating young pre-menopausal women with a long history of immunosuppression, multidisciplinary perioperative planning is necessary to ensure a successful postoperative course.

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