CASE REPORT

Bony non-union in a patient receiving androgen deprivation therapy for prostate cancer

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Accepted 21 May 2015

SUMMARY

We present a case of a 76-year-old man who underwent a corrective femoral osteotomy for a varus deformity and stress fractures. The patient was on androgen deprivation therapy (ADT) for prostate cancer and the osteotomy failed to heal. At 13 months, the ADT was stopped and bony union was achieved in 3 months. Orthopaedic surgeons treating fractures in this patient population need to aware of the problems associated with ADT and closely liaise with oncologists and urologists to stop ADT or start alternative treatment until bony union has been achieved.

BACKGROUND

In the UK, one in eight men will suffer from prostate cancer in their lifetime;¹ over 40 000 men are diagnosed with prostate cancer every year. Hormonal therapy is used in the treatment of prostate cancer depending on the stage and grade of the disease. The aim is to reduce testosterone levels and hence the size of the tumour. Hormonal therapy has been shown to improve survival times when given in combination with radiotherapy in men with localised prostate cancer and when given after radical prostatectomy in node-positive disease.^{2–7} As these medications result in a reduction of testosterone, it is important for clinicians to be able to understand the adverse effects and how to manage them.

Significant complications of androgen deprivation therapy (ADT) in men with prostate cancer are bone loss and fractures. These result from ADT-induced testosterone and oestrogen deficiencies.² The time

it takes for the testosterone to return to normal after treatment is longer in men with lower baseline testosterone levels, men over 65 years age and men receiving ADT for periods greater than 24–30 months. Prospective studies have shown that men with non-metastatic prostate cancer observe annual reductions in bone mineral density (BMD) of the femoral neck, lumbar spine and total hip bone of 4.6%, a rate that equals bone loss in other populations at risk of declining BMD.^{2 8–20}

CASE PRESENTATION

A 76-year-old man with bilateral total knee replacements was diagnosed with non-metastatic prostate cancer 2 years previously, with a Gleason score of 7 and a prostate specific antigen of 10.4. He lived with his wife and was a keen dancer. MRI revealed no extension of the cancer beyond the prostate capsule. After radiotherapy, he was started on zoladex (goserelin) under the care of an oncologist and urologists.

The patient presented to the emergency department with a 4-week history of bilateral pain in both thighs after jumping to avoid a puddle. X-rays revealed bilateral cortical stress fractures, for which he was referred to orthopaedics (figure 1A–C). On initial assessment, he had tenderness in both thighs and a varus deformity of his left knee; MRI and bone scan confirmed stress fractures with no other lesions (figure 2A–C). At an orthopaedic multidisciplinary team meeting, it was decided that the best option for this patient was conservative management. Four months after presentation to A and E,

Figure 1 (A–C) Initial X-rays taken when the patient reported of pain in thighs. The mid-shaft lateral cortical insufficiency fractures in right and left femurs.

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To cite: Ikram A, Singh J, Ali A. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-209950

Figure 2 (A–C) MRI anteroposterior view of both femurs, lateral of left femur. Bone scan.

Figure 3 (A–C) Four months after corrective femoral osteotomy. Note the lack of callous formation at this stage. The patient was still receiving androgen deprivation therapy.

Figure 4 (A), (B) Nine months later, from left to right anteroposterior and lateral views, note evidence of hypertrophic non-union despite 3 months of electromagnetic therapy.

however, due to his level of pain, it was decided to start with corrective femoral osteotomy and fixation with a dynamic locking plate (figure 3A–C).

OUTCOME AND FOLLOW-UP

After the procedure, the patient's symptoms improved, however, 4 months later there was evidence of hypertrophic non-union. At this point, it was decided to start 3 months of electromagnetic pulse stimulation, but there was still no significant improvement in the non-union (figure 4A, B). A year after the surgery, the patient's symptoms were gradually improving and he was walking with a hinge knee brace. It was noted at this time that the patient's concurrent treatment with Zoladex for prostate cancer had come to an end (figure 5A, B). Discussion with the oncologists confirmed the use of Zoladex might have been an indirect inhibitory factor in the fracture healing process and remodelling. Three months after stopping Zoladex, the bone had healed, with good callous formation and complete symptomatic relief of his pain; he could now resume his hobby of dancing (figure 6A, B). He is due to have a corrective right femoral osteotomy in the near future, and as he is

no longer on hormonal therapy, fracture healing should be a more straightforward process.

There was no union for thirteen months after corrective femoral osteotomy while on ADT. Finally, three months after stopping ADT, there was evidence of union.

DISCUSSION

Currently, there are no specific guidelines on how to manage fractures in patients on ADT; two options are, preventing fractures or planning for joint replacement. This is uncharted territory, with no existing research on the long-term effects of ADT on fracture healing. More research is needed along with collaboration in the management of these patients between the specialties of orthopaedics, oncology and endocrinology.

Hyperthyroidism, hyperparathyroidism, liver disease, calcium or vitamin D malabsorption are all recognised causes of bone loss, and should be investigated and treated prior to consideration of withdrawal of ADT therapy in men with prostate cancer. Patients receiving androgen deprivation therapy should be counselled on the increased loss of bone mineral density and risk of

Figure 5 (A), (B) Thirteen months later, from left to right anteroposterior and lateral views of the patient immediately prior to stopping androgen deprivation therapy.

Figure 6 (A), (B) Sixteen months later, evidence of union 3 months after stopping androgen deprivation therapy.

fractures, including measures to be taken to limit the risk of fractures, such as lifestyle modification and pharmaceutical therapy.

Orthopaedic surgeons planning elective and trauma surgery need to be aware of whether or not their patients are receiving ADT and take this into account when planning fixation and following up patients. They should plan and discuss these patients with the appropriate specialty, be it oncology, endocrinology or urology. If elective orthopaedic surgery is to be undertaken for patients on ADT therapy, there should be a multidisciplinary approach regarding benefits and risks of starting, withdrawing or postponing ADT therapy.

Learning points

- ▶ Reversible causes of bone loss should be investigated and treated prior to consideration of withdrawal of androgen deprivation therapy.
- ▶ Patients receiving androgen deprivation therapy should be counselled on the risk of loss of bone mineral density and risk of fractures.
- ▶ Patients receiving androgen deprivation therapy should be identified in preoperative assessment prior to elective orthopaedic procedures, and discussed with the relevant specialties to optimise the success of surgery.
- ▶ Patients receiving androgen deprivation therapy, who have a metal prosthesis, should be assessed for cortical defects or loosening of the prosthesis.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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