

Male Osteoporosis Associated with Longterm Cyproterone Treatment

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ABSTRACT. A 58-year-old man with previous dorsal vertebral fractures was referred for continuing management of osteoporosis. He was treated in the past with cyproterone acetate for hypersexuality. There were no other risk factors for osteoporosis. A dual energy radiographic absorptiometry scan confirmed osteoporosis. Treatment with alendronate 10 mg/day improved bone density and back pain. Patients receiving longterm treatment with cyproterone might be at risk for developing osteoporosis and would benefit from regular bone density monitoring. (J Rheumatol 2001;28:1702-3)

Key Indexing Terms:
CYPROTERONE
ALENDRONATE

MALE OSTEOPOROSIS
HYPERSEXUALITY

Osteoporosis is a well documented and recognized problem in women, and is receiving more attention in men. More than a quarter of reported hip fractures occur in men¹, and population based studies have shown that at least a similar proportion of clinically diagnosed vertebral fractures occur in men². We report a male patient with an unusual secondary cause for osteoporosis who was treated at our hospital.

CASE REPORT

A 58-year-old male prisoner was referred in June 1996 for continuing management of osteoporosis. He had been a sex offender in the past and had a history of longterm therapy for hypersexuality to which he submitted voluntarily. He was treated unsuccessfully with the antipsychotic benperidol between 1971 and 1974. He was then treated with cyproterone acetate (Androcur) between 1976 and 1979, initially at 100 mg/day and later, 200 mg/day. He was later investigated for back pain and was found to have osteoporotic wedge fractures of dorsal vertebrae in December 1987. He was given calcium 500 mg bid. A dual energy radiographic absorptiometry (DXA) scan in 1992 confirmed significant reduction in bone mineral density (BMD) at the spine (L1-L4 BMD 0.925 g/cm²; T score: -2.46; Z score: -1.96) and at the femoral neck (neck BMD 0.732 g/cm²; T score: -2.81; Z score: -1.90). A repeat DXA scan done in 1994 showed no significant change.

The patient had no other significant risk factors for osteoporosis such as thyroid dysfunction, liver disease, rheumatoid arthritis, myelomatosis, or history of longterm steroid therapy, smoking or alcohol abuse. A general assessment at his first visit in August 1996 was unremarkable except for dorsal kyphosis and a 7 cm deficit in upper versus lower segment height. Repeat radiographs showed dorsal vertebral wedge fractures at D5, D10,

and D11. A DXA scan confirmed significant bone loss at the lumbar spine and hip (Table 1 and Figure 1). A serum 25-OH-cholecalciferol level was 24 nmol/l (10-75 nmol/l) and serum testosterone was 11 nmol/l (10-35 nmol/l). A urinary hydroxyproline assay on gelatine-free diet was 0.24 mmol/24 h (normal up to 0.23 mmol/24 h).

The patient was started on alendronate 10 mg/day and calcium supplements were continued. A repeat hydroxyproline measurement in February 1997 showed a reduced excretion rate of 0.08 mmol/24 h consistent with effective treatment with alendronate. A repeat DXA scan in September

Table 1. DXA scan results showing T scores (compared to young adult male) and Z scores (age matched) at the lumbar spine (L1-4) and total hip (T.Hip) before starting alendronate (1996) and after therapy (1997 and 1999).

Year	L1-4 T score	L1-4 Z score	T. Hip T score	T. Hip Z score
1996	-2.79	-2.23	-2.02	-1.19
1997	-2.05	-1.46	-1.71	-0.85
1999	-2.20	-1.54	-1.87	-0.91

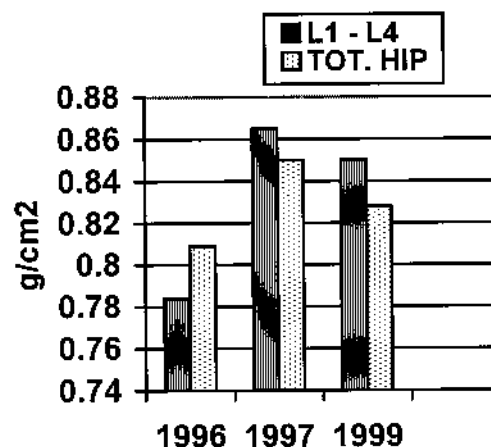


Figure 1. Lumbar spine (L1-L4) and total hip (tot. hip) bone mineral density (g/cm²) by DXA scan before starting therapy with alendronate (1996) and following treatment (1997 and 1999).

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1997 showed a clinically relevant improvement in bone density (Table 1 and Figure 1).

He remained symptomatically stable over the next 2 years with improvement in back pain. Serial radiographs of the spine did not show any new vertebral fractures. The latest DXA scan done in November 1999 showed reasonably stable bone mass (Table 1 and Figure 1). At an outpatient review a few weeks later, after release from prison, he remained symptomatically stable with very little back pain.

DISCUSSION

Various etiologies for male osteoporosis have been identified in recent years. Many male patients have a secondary cause for their osteoporosis, and some studies have found one in more than half of their male patients^{3,4}. The UK consensus group report on male osteoporosis reviewed and summarized the pathogenesis and causes of primary and secondary osteoporosis in men, and recommended bisphosphonates as a treatment of choice⁵.

This is an unusual case of male osteoporosis secondary to longterm antiandrogen therapy with cyproterone acetate, which has been used in dosages between 50 mg to 200 g/day for control of libido in hypersexuality or sexual deviation in the adult male⁶. It has also been used in treatment of the transsexual male as part of the gender reassignment therapy. Though the drug datasheet mentions rare cases of osteoporosis reported with its usage, a literature search of Medline, EMBASE and CINAHL revealed only one case report of osteoporosis in a transsexual man following treatment with cyproterone 100 mg daily⁷. The patient's bone density improved later with additional estrogen therapy.

Sequential combinations of estrogens with small doses of cyproterone (1-2 mg) have been found to maintain or improve BMD in women^{8,9}. Even with much higher doses of cyproterone, concomitant administration of estrogen was shown to maintain BMD in transsexual men¹⁰. Also, in normal men, serum estradiol has been found to be more related to BMD than free testosterone¹¹. These findings are consistent with our current understanding of sex hormone influences on bone density. Androgen precursors are converted to estrogen by the enzyme aromatase. Estrogens improve BMD through their action on estrogen-receptor alpha.

For our patient, treatment with estrogen was not an option. Treatment with cyclical etidronate has been found to

improve BMD in men with osteoporosis¹². We found that therapy with another bisphosphonate, alendronate, improved BMD initially, and later stabilized bone loss in our patient. We conclude that patients on longterm treatment with high dose cyproterone without concomitant estrogen might be at risk for developing osteoporosis and would benefit from regular bone density monitoring.

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