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LETTER

Efficacy of denosumab against osteoporosis determined using quantitative computed tomography in treatment-naïve male patients with ankylosing spondylitis: case series of six patients

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Ankylosing spondylitis (AS), which develops early in life, is a risk factor for osteoporosis in earlier ages (1). Despite the high risk of osteoporotic fractures in patients with AS, men undergo treatment less frequently than women. No guidelines for managing osteoporosis specifically address the screening time or measurement tools for low bone marrow density (BMD) in patients with AS.

Among anti-osteoporotic agents, denosumab is the most effective for preventing osteoporotic vertebral fractures in men. However, little is known about denosumab use in patients with AS, in whom excessive bone formations such as syndesmophytes and ligament ossifications obscure accurate BMD measurements, which is overestimated compared to its value determined via dual-energy X-ray absorptiometry (DXA). Quantitative computed tomography (qCT) is a useful alternative to DXA because it measures volumetric trabecular bone density while avoiding surrounding structures (2). Herein, we report a case series of six male patients treated with denosumab who were naïve to other osteoporosis (detected by qCT) pharmacotherapeutics.

This was a single-centre retrospective study performed at Kyung Hee University Hospital at Gangdong, South Korea. We included male patients with AS fulfilling the modified New York criteria for AS (3) who had not been diagnosed with osteoporosis and had not previously received anti-osteoporotic agents. Patients with a history of previous vertebral fracture were excluded. The patients' median age was 46 (range 44–50) years. Table 1 describes their clinical demographics. One patient had received conventional synthetic disease-modifying anti-rheumatic drugs (DMARDs) and three had received biological DMARDs (all tumour necrosis factor inhibitors). The average L1–L4-level spine BMD in the anteroposterior projection was measured using DXA (GE Healthcare Lunar, Madison, WI, USA), and BMD results were calculated as the standard deviations for young Korean adults (T-score) and an age-matched Korean population (Z-score) provided by the manufacturer. On DXA, $-2.5 <$ T-score < -1.0 and T-score ≤ -2.5 indicate osteopenia and osteoporosis, respectively (defined by the World Health Organization) (4). qCT was performed using a Brilliance 64-slice CT scanner (Philips, Israel) with a solid Mindways qCT calibration phantom containing bone-equivalent inserts (Mindways Software, Austin, TX, USA), T11–L5, in the supine position. The L1–L4-level BMD was used to balance the DXA. The average L1–L4 BMD was calculated (mg/cm^3). On qCT, BMD > 80–120 and ≤80 mg/cm^3 indicate osteopenia and osteoporosis, respectively (5). Among the five patients who underwent DXA, one had osteoporosis and four had normal BMD. Conversely, qCT identified osteoporosis in all [mean baseline qCT value 48.7 (12.48–59.93) mg/cm^3]. After confirmation of osteoporosis on qCT, denosumab 60 mg injections were administered every 6 months and qCT was conducted after every second dose (annually). After receiving two doses of denosumab (1 year), the median qCT value increased to 60.08 (16.4–85.25) mg/cm^3 [median change rate from baseline 29.9% (1.9–42.3%)]. One patient discontinued denosumab because the BMD exceeded the osteoporosis range. After four doses of denosumab (2 years), the median qCT value increased to 68.73 (17.23–68.73) mg/cm^3 [median change rate 7.9% (–0.6 to –20.0%)] compared to the 1 year follow-up. No adverse effects occurred.

This is the first case series to show that denosumab increases spinal BMD in men with AS. Denosumab is a potent anti-resorptive agent that inhibits the receptor activators of nuclear factor-kappa B ligand (RANKL), which is involved in regulating osteoclast differentiation. In a meta-analysis on AS, elevated serum RANKL levels correlated with Asian ethnicity, longer disease duration, and higher disease activity scores (6). Thus,

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Table 1. Baseline demographics and follow-up bone marrow density (BMD) measured by quantitative computed tomography (qCT).

				Drugs							Baseline DXA			qCT				
Patient no.	Age (years)/ sex	Disease duration (years)	HLA-B27	GC	Vit D	Ca	PPI	NSAIDs	csDMARDs	bDMARDs, type	BMD (g/ cm^2)	Z-score	T-score	Baseline BMD (mg/cm^3)	1 year follow-up (mg/cm^3)	Change 1st year (%)	2 year follow-up (mg/cm^3)	Change 2nd year* (%)
1	45/M	25	+	No	Yes	No	No	No	No	Yes, adalimumab 40 mg biweekly	1.06	–1.6	–1.0	59.93	85.25	+42.3	No treatment	No treatment
2	48/M	18	+	No	No	No	Yes	Yes	No	Yes, etanercept 50 mg weekly	1.15	–0.7	–0.3	49.60	63.68	+28.4	68.73	+7.9
3	45/M	22	+	No	No	No	No	No	No	Yes, adalimumab 40 mg once every 2 weeks	1.44	0.3	2.2	12.48	16.40	+31.5	17.23	+5.0
4	44/M	19	+	Yes	No	No	No	Yes	Yes	No	–	–	–	48.70	63.25	+29.9	62.90	–0.6
5	50/M	23	+	No	No	No	No	Yes	No	No	0.68	–3.1	–4.1	43.20	58.48	+35.4	68.73	+17.5
6	50/M	5	+	No	No	No	No	No	No	No	1.22	1.0	0.4	58.95	60.08	+1.9	72.10	+20.0

HLA, human leucocyte antigen; GC, glucocorticoid; Vit D, vitamin D; Ca, calcium; PPI, proton pump inhibitor; NSAID, non-steroidal anti-inflammatory drug; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; bDMARD, biological disease-modifying anti-rheumatic drug; DXA, dual-energy X-ray absorptiometry; M, male; F, female.
*BMD change from 1 year to 2 year follow-up.

RANKL may be an appropriate target for increasing the BMD in patients with AS. In our study, denosumab increased BMD by almost 30% after the first two doses, and its efficacy persisted for the next two doses.

When focusing on ankylosis as a treatment target, bone loss in AS patients is overlooked. In a multicentre study in South Korea, the prevalence of osteoporosis was 18.8%, and the rate of high risk of fracture using the fracture risk assessment tool with BMD was 12.5% in men with AS (7). The osteoporosis rate in the spine for advanced AS was much higher when qCT was used than when DXA was used (86.3% vs 32%, $p < 0.001$) (8). This was compatible with our report, in which four patients had normal BMD, although qCT revealed osteoporosis in all six. One patient who had a low BMD on DXA had only one level of syndesmophytes at the lumbar spine and no ligament ossification, while the remainder had advanced ankylosis in the spine. In patients with advanced-stage AS, qCT can significantly contribute to identifying osteoporosis.

This report highlights the utility of qCT for the assessment of BMD in men with AS, and for evaluation of the treatment effect of denosumab. Further research is needed as a basis for recommendations on screening for osteoporosis and treatment with denosumab and other agents in patients with AS and osteoporosis.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Ethics statement

The present study was approved by the Institutional Review Board of Kyung Hee University Hospital at Gangdong (KHNMC 2023-08-023). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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