Remarkable Bone Mineral Density Increases in Patients with Glucocorticoid-Induced Osteoporosis and Crohn's Disease Treated with Teriparatide

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ABSTRACT

Crohn's disease (CD) often results in abnormalities in bone strength, and ultimately increases the risk of fragility fractures. Up to 55% of patients with CD have bone mineral density (BMD) in the osteopenia range and up to 58% have osteoporosis by BMD.

Glucocorticoids are frequently used in the treatment of CD and are associated with osteoporosis and increased fracture risk. It has been reported that the incidence of osteoporotic fractures in patients with CD are 40% more likely as compared to the general population. Malabsorption, vitamin D insufficiency, amenorrhea/hypogonadism, glucocorticoid use, and chronic inflammation have all been linked to bone loss in CD. Indicated therapies include bisphosphonates and teriparatide.

We report on the novel use of teriparatide in two CD patients with severe osteoporosis and spine fractures. Both experienced remission from CD at the same time as initiating teriparatide therapy and calcium and vitamin D supplementation. Following 24 months of teriparatide treatment, annual infusion of zoledronic acid would be initiated. Cumulative increase in lumbar spine BMD over the course of this therapy were 48% over five years in one patient and 72% over three years in the other patient. Similar, but smaller in magnitude, increases in BMD were seen at hip sites over the same timeframe.

To our knowledge, this represents the greatest reported increase in spine bone mineralization seen in clinical patients on osteoporosis therapy. We attribute these remarkable improvements in bone mineralization to the young age of the patients, the stabilization of their underlying CD, discontinuation of glucocorticoid therapy, improved nutrition, calcium and vitamin D supplementation, and the initiation of bone anabolic therapy followed by anti-resorptive treatment. This experience may indicate a role for bone anabolic therapy in such patients.

INTRODUCTION

- It has been reported that up to 55% of CD patients have osteopenia and up to 58% have osteoporosis (OP) by DXA BMD [1]
- Glucocorticoids (GC) are frequently used in the treatment of CD and are associated with osteoporosis and increased fracture risk [2]
- Malabsorption, vitamin D insufficiency, amenorrhea/hypogonadism, and chronic inflammation may all contribute to bone loss in CD [3]
- Current treatment recommendations for glucocorticoid-induced osteoporosis (GIO) include calcium, vitamin D, exercise, and pharmacotherapy
- Indicated therapies in Canada are etidronate, alendronate, risedronate, zoledronic acid, and teriparatide [4].
- To date, there have been no studies on teriparatide specifically in CD patients.
- We report two patients with CD and vertebral fractures who, to our knowledge, showed the greatest reported BMD increases, after initiating teriparatide.

CASE 1 – 33 Year Old Caucasian Male

- Diagnosed with CD at age 16 and initially managed with intermittent high-dose prednisone (15-30 mg daily)
- Not adherent to calcium and vitamin D supplementation
- At age 27, active CD managed with partial colectomy and ileostomy
- Post-operative remission of CD, discharged on prednisone15 mg/day
- Evaluation for OP at age 33 (6 years later)
- Back pain inadequately managed with narcotics and requiring walker to ambulate
- Radiograph revealed mild L4 and L1 compression fractures
- MRI and bone scan revealed additional acute T11 and T12 compression fractures
- On teriparatide, back pain resolved; no further fractures

Time (months, post-baseline BMD)	OP Treatment	CD Treatment	Lumbar Spine Z-Score *	Increase from Baseline (%)	Weight (kg) **
0	Teriparatide initiated	Prednisone 5mg daily	- 4.2	-	63.2
11	Teriparatide	Azathioprine	- 2.9	23.4	69.2
28	Teriparatide completed at month 24; Zoledronic acid initiated at month 33	Azathioprine and Adalimumab	- 1.8	42.9	58.8
45	Zoledronic acid 2nd infusion at month 45	Adalimumab	- 1.6	45.9	57.2
57	Zoledronic acid 3rd infusion at month 57	Adalimumab	- 1.5	48.2	66

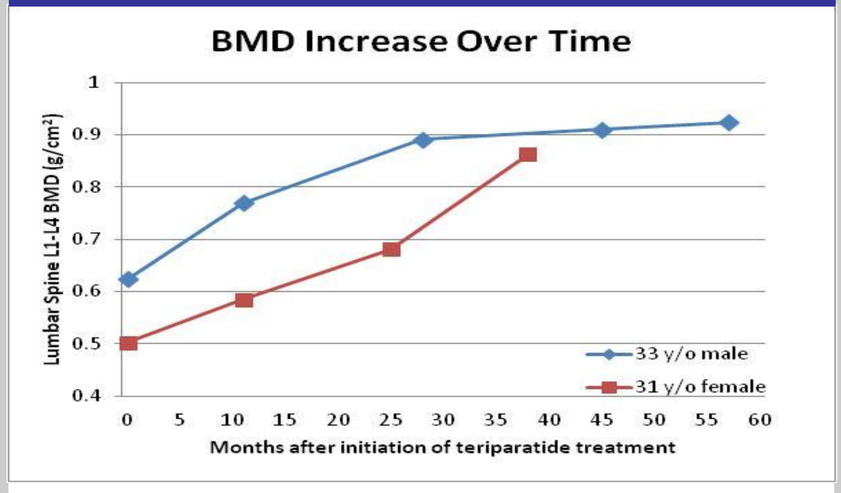
CASE 2 – 31 Year Old Chinese Female

- Diagnosed with CD age 13 and initially managed with ileal resection and right hemicolectomy
- At age 20, enterocutaneous fistula managed with second ileal resection
- CD managed with intermittent high-dose prednisone (10-30 mg daily)
- At age 24, third ileal resection for active disease
- At age 25, prolonged amenorrhea, iron deficiency, receiving iron infusions twice monthly for microcytic anemia. Chronic gastrointestinal blood loss on celecoxib and prednisone (average 15 mg/day)
- At age 27, severe back pain. Radiographs of thoracic and lumbar spine revealed L1 (mild) and L2 (mild) compression fractures
- Supplementing with 1500 mg/day elemental calcium and 1000 IU/day vitamin D
- On teriparatide, back pain resolved and no further fractures were documented

Time (months, post-baseline BMD)	OP Treatment	CD Treatment	Lumbar Spine Z-Score *	Increase from Baseline (%)	Weight (kg) **
0	Teriparatide initiated at month 3	Prednisone 5mg daily	- 5.2	0	41.4
11	Teriparatide on hold at month 11; bowel re-section	Prednisone 5mg daily	- 4.2	16.6	41.6
25	Teriparatide re-initiated at month 25	Weaned off Prednisone at month 14; Adalimumab initiated	- 3.1	35.7	48.7
38	Teriparatide	Adalimumab	- 1.4	71.9	58.4

* Hologic DXA, calibrated daily
** Weight by scales, calibrated monthly

RESULTS



- 33 year old male received teriparatide for 24 months, followed by zoledronic acid annual infusions
- 31 year old female received teriparatide treatment for 8 months, stopped for 13 months following bowel resection, then re-initiated for a further 12 months

DISCUSSION AND CONCLUSIONS

- GIO and CD are well-documented risks for fragility fracture, particularly in menopausal women and men over the age of 50
- In younger individuals with GIO, prevalent vertebral fractures, very low BMD, or declining BMD may motivate pharmacotherapy treatment
- Teriparatide is the only anabolic therapy indicated for treatment of men and women with GIO [5-6]
- Controlled clinical trials in patients with GIOP demonstrated lumbar spine DXA BMD increases from baseline of 7.2% vs 3.4% in those treated with alendronate after 18 months [7]
- Both reported patients were able to discontinue GC and maintained CD remission on azathioprine or adalimumab during teriparatide therapy. This may have contributed to the increases in BMD
- Case 1 did not have much change in weight; Case 2 gained 17kg in weight. Weight gain may artifactually increase the DXA BMD measurement
- GC use has been identified as a strong predictor of declines in BMD at most skeletal sites in patients with CD [1]. Teriparatide may have played a role in reversing this in both reported patients
- Since one of the primary actions of GC on bone is to reduce osteoblast function, the anabolic effects of teriparatide may directly target key pathogenic mechanisms associated with long-term glucocorticoid therapy [8]
- Further increases in BMD (in one case) when switched to bisphosphonate after completion of teriparatide, may in part be due to increases in mineralization with suppression of bone turnover
- Limitation to this study is the inability to extrapolate results given reporting of only 2 cases
- The observation of such remarkable increases in BMD in these younger individuals treated with teriparatide may indicate a greater anabolic potential related to their young age

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