

Image Challenge

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Case Presentation

An 80-year-old female with osteoporosis presented to the clinic in September 2026 reporting acute, severe, and spontaneous mid-to-lower back pain. Baseline dual-energy X-ray absorptiometry (DXA) in April 2022 demonstrated a T-score of -3.0 at the femoral neck, -2.8 at the total hip, and -3.2 at the lumbar spine (L1–L4). She had no prior history of fragility fractures. She had received denosumab 60 mg subcutaneously every 6 months for 6 doses between April 2022 and April 2025 (total exposure 7 doses). She was lost to follow-up because she felt well and did not receive her scheduled dose in October 2025 or any subsequent antiresorptive therapy. Approximately 17 months after her last denosumab injection, she developed sudden, debilitating thoracic and lumbar back pain without preceding trauma. Physical examination revealed 3 centimeters of height loss since the April 2025 visit, thoracic spine tenderness, and increased kyphosis compared with prior visits. Thoracolumbar radiographs were obtained (Figures 1 and 2).



Figure 1



Figure 2

Questions

1. Please describe the imaging.
2. What is her diagnosis?
3. How should this condition be treated?

Answers

1. Imaging Description

Generalized osteopenia. Significant vertebral height loss with prominent anterior wedging and endplate depression consistent with multiple vertebral compression fractures at T7, T10, L1, and L2.

The lateral radiograph (Figure 1) shows multilevel thoracic and lumbar vertebral bodies with wedge- and biconcave-type compression deformities, with clear loss of anterior vertebral body height relative to the posterior height, resulting in accentuated thoracic kyphosis. There is no evidence of cortical or pedicle destruction and no paraspinal soft-tissue mass. The AP view (Figure 2) shows intact pedicles at all visualized levels, with no focal lytic or sclerotic lesion. The overall appearance is that of multiple vertebral compression fractures at T7, T10, L1, and L2, without features suggesting malignancy or infection.

2. Diagnosis

Rebound multiple vertebral compression fractures following denosumab discontinuation.

3. Treatment and Management Strategy

Management requires addressing both acute pain control for symptomatic back pain and the treatment of hyper-resorptive storm with a potent anti-resorptive therapy, particularly restarting denosumab.

Short review: Preventing and Managing Rebound Multiple Vertebral Compression Fractures Following Denosumab Discontinuation (RVFx)

Rebound Multiple Vertebral Compression Fractures Following Denosumab Discontinuation (RVFx) usually present with sudden, severe thoracic or lumbar back pain. Diagnosis can be established using a lateral thoracolumbar spine radiograph compared to a baseline radiograph. Spinal magnetic resonance imaging (MRI) is essential to detect acute non-collapsed fractures and differentiate acute marrow edema from chronic osteoporotic deformities or malignant infiltration.

Pathophysiology

Denosumab is a monoclonal antibody that inhibits RANKL without binding permanently to bone surfaces, unlike bisphosphonates. When its effect wanes, a rebound phenomenon occurs, characterized by an exaggerated overshoot in bone turnover; serum C-terminal telopeptide (CTX) can rise to about 70% above pretreatment baseline by 6 months after discontinuation¹. The key mechanism is accumulation of osteoclast precursors and "osteomorphs" during denosumab therapy, since the drug inhibits both osteoclast activity and precursor fusion. On withdrawal, RANKL signaling resumes rapidly, faster than osteoblast and osteoprotegerin (OPG) recovery, driving the accumulated precursor pool to differentiate and fuse into large numbers of active osteoclasts simultaneously. This produces an imbalance between bone resorption and formation; as a result, bone mineral density (BMD) gains during denosumab treatment are rapidly lost, particularly in the vertebrae, which are rich in trabecular bone and bear axial load, making them especially prone to fracture². Established risk factors for rebound fracture include longer treatment duration (>2-3 years), greater on-treatment BMD gain, a prior history of vertebral fracture, and lack of follow-on antiresorptive therapy after stopping denosumab, longer duration off-therapy, greater hip BMD loss off-therapy, and higher serum CTX off-treatment².

Treatment

1. Acute pain control

- **Analgesic Regimens:** Rebound fractures characteristically cause incapacitating pain that frequently fails non-opioid analgesics. Stepwise analgesia requires potent oral or parenteral opioids (e.g., tapentadol, oxycodone, buprenorphine), and adjunctive short-term muscle relaxants are indicated during the acute healing phase.
- **Biomechanical Support and Conservative Care**
- **Dynamic Spinal Bracing:** Thoracolumbar orthoses decrease compressive loads on the anterior column, maintain spinal alignment, and mitigate progressive kyphotic collapse. Semirigid dynamic orthoses are preferred over prolonged rigid immobilization to avoid rapid trunk muscle atrophy.
 - **Structured Physical Rehabilitation:** Strict, prolonged bed rest must be avoided to prevent disuse-related demineralization. Physical therapy should emphasize early mobilization, back-extensor and pelvic tilt strengthening, and balance training, while strictly avoiding forward spinal flexion, which elevates anterior vertebral loading.
- **Interventional Procedures:** Percutaneous vertebroplasty or balloon kyphoplasty are relatively contraindicated; however, these may be considered for refractory pain, because cement augmentation in the presence of unsuppressed rebound turnover carries an increased risk of adjacent level fractures³.

2. Long-term pharmacological therapy for osteoporosis

- **Immediate Antiresorptive Therapy:** Unlike primary severe osteoporosis, in which bone-forming agents are first-line, RVFx management prioritizes the immediate suppression of accelerated bone turnover. Initiate immediate denosumab reinstitution or intravenous potent bisphosphonates (zoledronic acid) to inhibit osteoclast activity and arrest the vertebral fracture cascade.
- **Role of anabolic agent**
 - **Teriparatide**
 - Teriparatide monotherapy is contraindicated. Recombinant human PTH analogs (teriparatide) must not be administered as monotherapy, as they exacerbate high cortical bone turnover and accelerate rapid bone loss.
 - **Romosozumab**
 - Although Romosozumab remains unproven for suppressing acute rebound osteoclast activity and has documented failure in preventing multiple RVFx in this setting⁴. However, recently there has been a report of four patients who developed vertebral fractures following denosumab withdrawal and were subsequently treated with romosozumab, which resulted in progressive improvement in BMD and microarchitecture, with suppression of bone turnover markers and no new clinical fractures during treatment and follow-up⁵.

Take-home message

Do not stop denosumab without follow-on potent bisphosphonate therapy, particularly after receiving more than 5 denosumab injections⁶. In contrast to multiple vertebral fractures in primary osteoporosis, for which anabolic agents should be initiated, restarting denosumab is the mainstay pharmacologic therapy. Percutaneous vertebroplasty or balloon kyphoplasty should be avoided since it might increase the risk of adjacent level fractures. Patients must be educated that missing an injection by more than 4 to 8 weeks can trigger rebound bone loss and spinal fractures.

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