Rehabilitation in a case of severe osteoporosis with prevalent fractures in a patient known with multiple sclerosis and prolonged glucocorticoid therapy

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Abstract

Introduction. Osteoporosis has a major influence on the quality of life because of its impact on bone strength. Osteoporosis and fractures are frequent in patients with multiple sclerosis, decreased mobility being an important risk factor in these patients.

Objectives. This paper presents a case of severe osteoporosis in a patient with multiple sclerosis, to emphasize a correlation between these two pathologies.

Material and Methods. We present the case of a female Caucasian patient, aged 65 years, known with progressive multiple sclerosis, on long-term use of glucocorticoids, and severe osteoporosis, who is investigated for mechanical pain and functional deficiency in the lumbar spine and the right hip, motor deficit, predominantly on right limbs and walking disorders. The patient was diagnosed with severe osteoporosis treated with raloxifene and bisphosphonates, with multiple vertebral fractures and vitamin D deficiency. During hospitalization the patient followed myorelaxant therapy and an individualized rehabilitation program.

Results and discussion. During follow-up, there was a significant increase followed by a recent decrease in bone mass density in the lumbar spine and hip. The patient was recommended a loading dose of cholecalciferol for three months and initiation of teriparatide therapy after restoring 25-hydroxy vitamin D levels.

Conclusion. In patients with multiple sclerosis, screening and early management of osteoporosis and osteopenia are essential.

Keywords: multiple sclerosis, glucocorticoid therapy, osteoporosis,

INTRODUCTION

The current definition for osteoporosis was developed by an international Consensus Development Committee in 1993 as “a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk” (1).

Recent studies evaluate the incidence and prevalence of reduced bone mass in patients with multiple sclerosis. Bone mass density screening in patients with multiple sclerosis is relatively low, suggesting that an important proportion of patients with secondary osteoporosis may be missed (2,3).

Material and Methods

We report the case of a Caucasian female patient, aged 65 years, admitted in Academic Emergency Hospital of Sibiu for motor deficit, predominantly on right side, impossibility to maintain orthostatism and difficulties in walking, verbal and visual impairment, mechanical pain and functional deficiency in the lumbar spine and the right hip.

From the patient’s personal history we mention two natural births, an extrauterine pregnancy and menopause onset at 48 years. The patient is known with progressive multiple sclerosis, diagnosed shortly after menopause, on prolonged glucocorticoid therapy, osteoporosis diagnosed 8 years ago, chronic kidney disease stage III, chronic litiacic nefropathy, ischemic heart disease, left ventricular disfunction, left paramedian ischemic mesencephalic stroke, tetraparesis with predominance of right hemiplegia and dyslipidemia.

The neurological exam and the paraclinical examinations, including spinal and cerebral magnetic resonance imaging, established the diagnosis of multiple sclerosis at the age of 48 years. Since the patient refused biological therapy, corticosteroids were administered from the time of diagnosis until present, with methylprednisolone administered intermittently, in a maximum dose of 50 mg per day or in the form of pulse therapy.
From the moment when the diagnosis of multiple sclerosis was established, the patient was periodically tested on osteodensitometry, with T-score values being in osteopenia area. At 57 years old, the patient was investigated for vertebral fractures secondary to a fall from the same level which were treated conservatively. At that moment, the patient was diagnosed with severe diffuse osteoporosis with multiple vertebral fractures and vitamin D deficiency. T-score on osteodensitometry testing in the lumbar spine revealed -3.5 standard deviations (SD) at the time of diagnosis. The patient was treated with 2 grams of oral strontium ranelate and 1000 units of oral cholecalciferol, both administered daily for two years (2011-2012), then switched to oral ibandronic acid administered monthly in a dose of 150 miligrams, together with 0.5 micrograms of oral alfalcacidol administered daily and 1 gram of calcium supplements administered two weeks per month, all these for six years (2013-2019), with significant increase in bone mass in the lumbar spine, from -3.5 SD to -2.3 SD and then a slightly decrease up to -2.8 SD. The patient was recent diagnosed with left scapulohumeral dislocation with fracture of the greater tubercle of the humerus treated orthopedically with Dessault’s bandage.

Osteodensitometry testing: T-score in the lumbar spine (Standard Deviations)

<table>
<thead>
<tr>
<th>Year</th>
<th>T-score</th>
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<tbody>
<tr>
<td>2011</td>
<td>-3.5</td>
</tr>
<tr>
<td>2012</td>
<td>-3.4</td>
</tr>
<tr>
<td>2013</td>
<td>-2.3</td>
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<tr>
<td>2015</td>
<td>-2.4</td>
</tr>
<tr>
<td>2017</td>
<td>-2.8</td>
</tr>
</tbody>
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Figure 1. Bone density testing in the lumbar spine

Clinically, at the time of the admission, the patient was conscious and cooperative, with mild dysarthria and intact comprehension, with a heart rate of 70 beats per minute and blood pressure of 135/95 mmHg, with a slight right facial asymmetry, left palpebral ptosis, right limbs with motor deficit evaluated on Medical Research Council (MRC) scale for muscle strength, obtaining a score for the upper limbs of 3/5 MRC proximal, of 4/5 MRC intermediate and distal and for the inferior limbs of 3/5 MRC, with prolonged physical inactivity. Spasticity was evaluated on Ashworth scale for the upper limbs obtaining a score of 1 and for the lower limbs a score of 3, deep tendon reflexes were present, Babinski sign was present bilaterally. The sitting at the edge of the bed without support was possible, orthostatism and walking test also possible but difficult, with spastic walking gait. The patient received bilateral and tetrapied support.

It was noticed:thoracic kyphosis, moderate lumbar vertebral syndrome with lumbar rectitude, dorso-lumbar scoliosis levoconvex in the lumbar region and dextroconvex in the dorsal region, a value of 10/11 centimeters at Schober test. It was observed in the right hip reduced mobility for flexion, of 90 degrees, abduction and external rotation of 25 degrees, right shoulder with stiffness and pain when mobilizing, reduced mobility for active flexion and abduction of 90 degrees, right leg with retraction of the tendon of the extensor hallucus.

A score of ten points was obtained in Barthel scale, three points in "Assesing Activities of daily living score" and two points in "Functional Ambulation Category" score. The X-ray examination at the time of diagnosis of osteoporosis revealed vertebral fracture of L3 and MRI scan revealed multiple vertebral fractures of T12-L3 and one year later also of L5. After 5 years, spine X-ray revealed marked diffuse osteoporosis, multiple thoracic vertebral fractures, especially T7-T8-T9 and significant narrowing of the disc spaces.

The X-ray examination of the thoracic and lumbar spine (anterior and profile) realized six months before the current admission revealed marked diffuse bone demineralization, lumbar levoconvex scoliosis and thoracic dextroconvex scoliosis, multiple thoracic and lumbar vertebral body fractures and lateral osteophytes.

Figure 2. Bone density testing inthe lumbar spine (diagram)

Figure 3. X-ray examination of the thoracic and lumbar spine (anterior and profile) revealing marked diffuse bone demineralization, lumbar levoconvex scoliosis and thoracic dextroconvex scoliosis, multiple thoracic and lumbar vertebral body fractures and lateral osteophytes.
At this moment, the X-ray examination of pelvis showed marked diffuse bone demineralization, narrowing of the right inferior polar joint space and calcification of lesser right trochanter with a tendency to make contact with the ischium.

During hospitalization the patient followed myorelaxant medication and an individualized rehabilitation program, the evolution being slightly favorable.

The following were recommended for discharge: a diet rich in vitamins and minerals, the continuation of specific kinetic exercises, a loading dose of cholecalciferol of 2000 units three times a day for 3 months, with monitoring of 25-hydroxy vitamin D levels and initiation of teriparatide therapy after restoring 25-hydroxy vitamin D levels.

Teriparatide is recommended considering the decreasing T-score on osteodensitometry.

Chronic medication such as baclofen 37.5 miligrams per day in three divided doses and periodic neurological monitoring were also indicated.

Results and discussion
Recent studies have evaluated the incidence of reduced bone mineral density in patients with multiple sclerosis. Multiple sclerosis is a potentially disabling disease, a chronic inflammatory demyelinating disease of the nervous system (3).

Physical inactivity is considered the most significant risk factor for osteoporosis in patients with multiple sclerosis. Other possible risk factors are low vitamin D levels, frequently present in patients with multiple sclerosis, and use of glucocorticoids and anticonvulsants as prolonged therapy (3). The first three risk factors mentioned are also present in the case presented.

Bone mass density screening in patients with multiple sclerosis is relatively low, suggesting that an important number of patients with secondary osteoporosis are underdiagnosed (4). In the case we presented, the patient was periodically tested on osteodensitometry from the moment when the diagnosis of multiple sclerosis was established, with close follow-up performed by the physiotherapist and endocrinologist.

A study presented in 2017 at Consortium of Multiple Sclerosis Centers Annual Meeting, in New Orleans have demonstrated that patients with multiple sclerosis have lower bone mineral density and increased risk of osteoporosis, suggesting that multiple sclerosis may be a cause of secondary osteoporosis. The study included 783 patients diagnosed with multiple sclerosis who had a bone mineral density screening. Each case was matched with 5 non-multiple sclerosis controls and the two groups were compared for femoral neck bone mineral density and likelihood of osteoporosis assessed by T-score ≤ -2.5 standard deviations on dual-energy X-ray absorptiometry. Results showed that patients with multiple sclerosis had an independent association with low femoral neck bone mineral density, with the average T-score at the femoral neck in patients with multiple sclerosis at -1.48 ± 1.08 versus -1.12 ± 0.98 in control group. The patient in the case we presented also had low bone mineral density in
the femoral neck, which increased during therapy, then decreased in the last year, probably worsened by long-term exposure to glucocorticoids.

In the last study mentioned above, multiple sclerosis was an independent risk factor for osteoporosis. The prevalence of osteoporosis in patients diagnosed with multiple sclerosis was of 17% versus 6.5% in control group. The study showed also that prevalent fractures were significantly associated with osteoporosis in patients with multiple sclerosis compared to the control group, as demonstrated in the case we presented (2).

Another recent study conducted in 2016 revealed a total of 74.7% of the patients from all 91 patients with multiple sclerosis included in the study to have osteopenia or osteoporosis (5).

A study using North American Research Committee on Multiple Sclerosis Registry data found that more than 25% of participants had decreased bone mass density and 15% of them had a history of fracture (multiple fractures, wrist, vertebral and hip fracture). More than half of the patients with fragility fractures were taking calcium and vitamin D supplements and more than 20% were taking a bisphosphonate (6). Our patient was on bisphosphonates therapy for six years, showing an increased bone mass density in the lumbar spine, and took calcium and vitamin D supplements continuously.

Another study using also North American Research Committee on Multiple Sclerosis Registry reported a higher risk of developing osteoporosis in women than in men with multiple sclerosis, related with increasing age and higher levels of disability (7).

Glucocorticoid-induced osteoporosis is currently the most common cause of secondary osteoporosis. In early stages, after the initiation of glucocorticoid therapy, appears bone mineral density loss, affecting significantly more the trabecular bone compared to the cortical bone, and fragility fractures (8). According to a meta-analysis of 56 cross-sectional studies and 10 longitudinal studies, bone mineral density loss can be up to 15% during the first year of glucocorticoid therapy (9). Dosage, duration of therapy and the cumulative dose are fundamental factors in developing osteoporosis. In all patients who receive glucocorticoid therapy, prevention or management of osteoporosis, which still remains under-estimated, should be considered, the medication of first choice remaining bisphosphonates and teriparatide (8,10). Because our patient refused biological therapy for treating multiple sclerosis, she received glucocorticoid therapy from the time of diagnosis until present, administered intermittently. After six years on bisphosphonates, we consider now the initiation of teriparatide therapy as a promising choice of treatment. The use of glucocorticoid therapy has a prevalence up to 0.9% in general population and up to 2.7% in women aged over 50 years. In the Global Longitudinal Study of Osteoporosis in Women (GLOW), conducted in 10 countries, 4.6% of over 60000 women in menopause included in the study were receiving glucocorticoids at baseline visit (8,11-15). In the case we presented, the decrease in T-score values in hip and lumbar spine and the multiple fragility fractures could be also associated with the prolonged use of glucocorticoid therapy.

Since immobilization in multiple sclerosis patients leads to osteocyte apoptosis and decreased bone formation, anabolic therapy with teriparatide may be more effective than bisphosphonates (16). In the case presented, teriparatide therapy is now considered to be initiated after the correction of the severe vitamin D deficiency. Recent guidelines on the management of secondary osteoporosis are available, but there is few data on multiple sclerosis related osteoporosis and the assessment of fracture risk in these patients (17,18). Literature database provides convincing evidence that bone mass is significantly reduced in patients with multiple sclerosis. The major risk factors appears to be the chronic disease process of multiple sclerosis itself and not from glucocorticoid use. We propose to evaluate the bone mineral density on osteodensitometry in all patients diagnosed with multiple sclerosis for an early diagnosis and proper management of osteoporosis.

Conclusions
The case we presented demonstrated that there is a correlation between a low bone mineral density and multiple sclerosis. Prolonged use of glucocorticoids represent an additional risk factor, being known as a major risk factor for secondary osteoporosis. The particularity of the case presented consists in the presence of severe osteoporosis with fragility fractures in a patient known with multiple sclerosis, associated with long-term exposure to glucocorticoid therapy. We emphasize the importance of monitoring these cases by a mixed team formed by a physiotherapist, an endocrinologist and a neurologist. There are currently no guidelines on the management of osteoporosis in patients with multiple sclerosis despite its increased prevalence. We propose screening and early management of osteoporosis and osteopenia in multiple sclerosis patients.

Conflict of interest
There is no conflict of interest for any of the authors regarding this article.

Informed consent
In this article was included an informed consent that was obtained from the patient.

#All authors has equal contribution in this publication.
References