CASE REPORT

Multiple vertebral fractures in an elderly male with macroprolactinoma

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Abstract

Hyperprolactinemia is associated with increased bone loss both in men and women. We report a case of an elderly patient with multiple osteoporotic vertebral fractures due to long-lasting hypogonadism caused by prolactinoma. The patient was treated with transphenoidal surgery, small doses of dopamine agonists, teriparatide, calcium and vitamin D supplements. Treatment led to increase in bone mineral density and decrease in lumbar pain intensity. This case highlights that clinicians should bear in mind the fact that osteoporotic vertebral fractures in men may be linked with hypogonadism and hyperprolactinemia. These conditions can be effectively treated. Therefore, detailed medical history and appropriate endocrinological evaluation should be performed in all male patients with osteoporotic fractures.

Keywords: macroprolactinoma, hypogonadism, osteoporotic fractures, pituitary surgery, remission

1. Introduction

Prolactinomas represent are the most common functional pituitary adenomas [1]. The majority of patients with prolactinomas have hypogonadism due to prolactin's inhibitory effect on pulsatile gonadotropin secretion. Patients with larger tumors often have some degree of hypopituitarism due to the compression of the pituitary stalk or destruction of normal pituitary tissue. Both hypogonadism and growth hormone deficiency have numerous metabolic effects. For instance, they are associated with higher prevalence of metabolic syndrome, but also with the decrease in bone mineral density [2,3]. There are no guidelines on screening and treatment of osteoporosis in patients with prolactinomas. In this case study, the authors aim to present an elderly patient with multiple osteoporotic vertebral fractures due to long-lasting hypogonadism caused by prolactinoma.

2. Case presentation

A 71-year old patient presented with substantial worsening of lower back pain. The pain was exacerbated by physical activity and alleviated by analgesics and resting. Besides the chronic back pain over the 10-year period, his medical history was unremarkable. Physical examination disclosed severe thoraco-lumbar scoliosis with trunk rotation. The lumbar spine segment was distinctly painful on palpation, along with tense musculature. His body height was 160 cm and his body weight 69 kg. Plain radiogram confirmed thoraco-lumbar scoliosis, caused by multiple grade 3 vertebral fractures of the lumbar spine. Dual-energy X-ray absorbiometry (DXA) revealed severe osteoporosis of the lumbar spine and osteopenia of the hip (Table 1).

He was prescribed with thoraco-lumbar orthosis and referred to an endocrinologist, who had taken a

Table 1. Dual-energy X-ray absorbiometry showing osteopenia of the hip and severe osteoporosis of the lumbar spine.

Region	Area	BMC(g)	BMD (g/cm2)	Tscore	PR(%)	Zscore	AM(%)
Hip							
Neck	6,17	2,86	0,464	-3,4	50	-2,2	60
Troch	11,88	5,15	0,434	-2,7	56	-2,3	60
Inter	21,80	20,00	0,918	-1,5	77	-0,9	84
Total	39,84	28,02	0,703	-2,2	68	-1,5	75
Wards	1,13	0,23	0,204	-4,1	26	-2,2	40
Lumbar spine							
L1	25,04	7,86	0,314	-6,3	31	-5,5	34
L2	19,95	8,83	0,443	-5,9	40	-5,0	45
L3	16,81	8,85	0,508	-5,4	46	-4,5	51
L4	14,45	6,96	0,472	-6,1	41	-5,2	45
Total	76,55	32,19	0,421	-6,1	39	-5,2	42

more detailed medical history. The patient reported impotence and low libido back from his late forties. Laboratory examination showed normal serum and urinary calcium and phosphorus, normal total protein, serum creatinine, liver enzymes and alkaline phosphatase. Vitamin D and osteocalcin levels were decreased, while beta-cross laps were normal (0,12 ug/L). Thyroid hormone tests were normal as well as PTH (14.9 pg/ml, normal range 15-65). Morning cortisol, ACTH, DHEAS and urinary-free cortisol were all within normal limits. His IGF-I level was slightly decreased (101 ng/ml, normal range 115-420). Testosterone level of 5.6 nmol/L (normal range 6.7-25.7) and normal gonadotropin levels confirmed central hypogonadism. Additionaly, marked hyperprolactinemia was noted (701 μg/L, normal range 2-20), which was the cause of central hypogonadism. Magnetic resonance confirmed a 21x18x16 mm large tumor mass of the sellar region. The diagnosis of prolactinoma has been made and purely endoscopic transsphenoidal pituitary surgery was performed.

Pathohistological analysis confirmed the diagnosis of prolactinoma. Prolactin decreased to 15 μg/L on seventh postoperative day, but finally increased to 88 μg/L three months after the surgery. Therefore, 2.5 mg of bromocriptin was initiated; prolactin levels have finally normalized and testosterone increased to 13 nmol/L. Daily teriparatide, vitamin D and calcium supplementation therapy were also initiated. His back pain diminished six months later. The patient was well and had no complaints during the follow up. Teriparatide and bromocriptine were discontinued two years later and MRI of the sellar region showed no signs of residual prolactinoma. DXA showed an increase in BMD; total

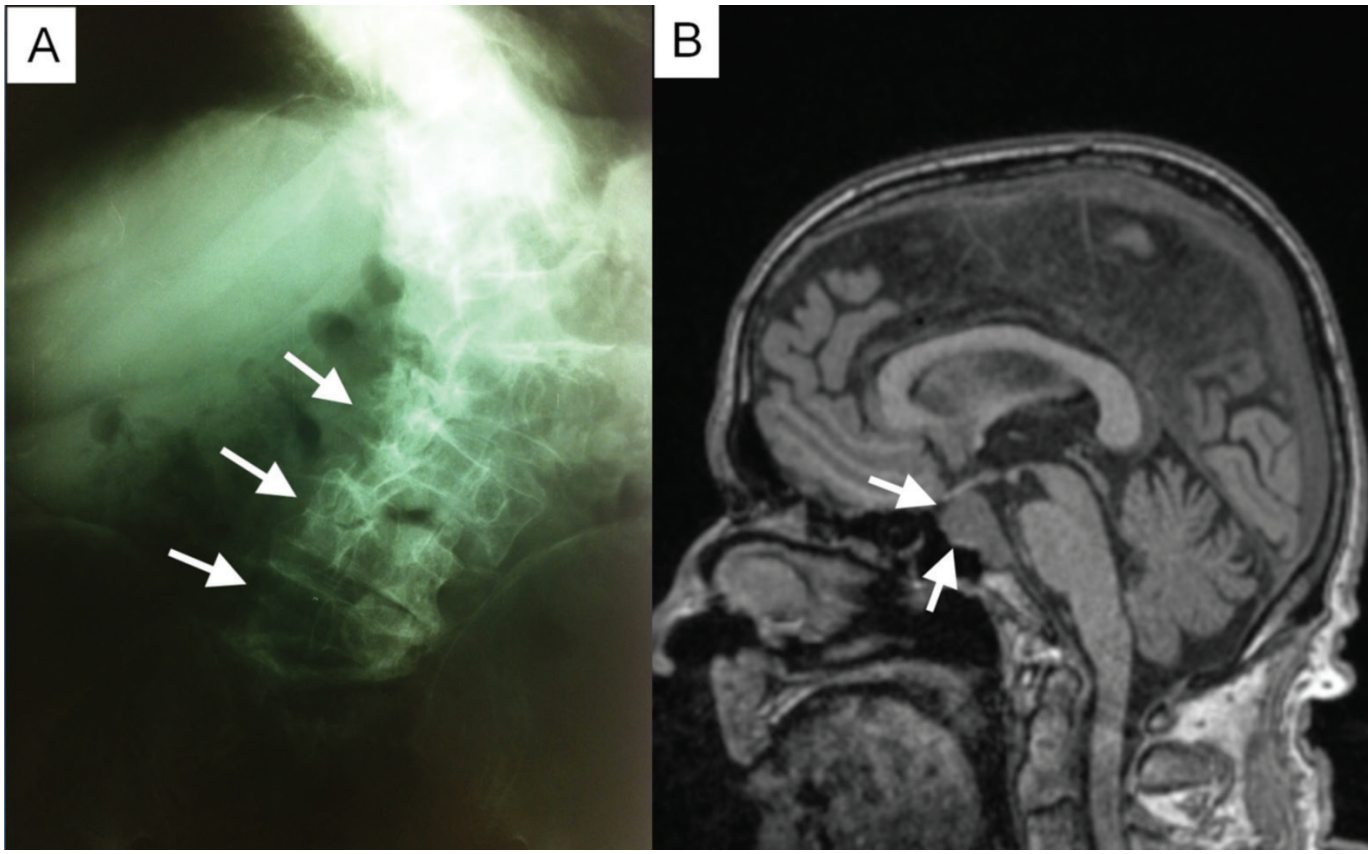

Figure 1. Plain radiogram showing thoraco-lumbar scoliosis, caused by multiple grade 3 vertebral fractures of the lumbar spine (A). Magnetic resonance sagittal native T1-sequence showing 21x18x16 mm large pituitary adenoma with suprasellar extension and impingement of the suprasellar cistern (B).

hip T score increased from -2.2 to -1.5 and total lumbar spine T score increased from -6.1 to -3.9. Calcium and vitamin D supplementation were continued and risedronate 150 mg monthly was initiated. Two and a half years after the pituitary surgery, patient experienced out-of-hospital cardiac arrest. Cardiopulmonary resuscitation was successful and elective coronarography was consistent with three vessel coronary artery disease. The patient is scheduled for coronary artery bypass grafting surgery.

3. Discussion

Acquired secondary hypogonadism may be a consequence of obesity, insulin resistance, type 2 diabetes, obstructive "sleep apnea" syndrome, aging, hyperprolactinemia, hemochromatosis, abuse of anabolic steroids, primary hypothyroidism, alcoholism and other acute diseases [4]. Hyperprolactinemia causes hypogonadotrophic hypogonadism, which inhibits pulsatile gonadotrophin releasing hormone (GRH), consequently reducing the levels of FSH, LH and testosterone. Hyperprolactinemia in men is mostly caused by macroprolactinomas (>10 mm in diameter), which can be found in approximately 16% of patients with erectile dysfunction and 11% of patients with oligospermia [1,5]. Moreover, hypogonadism is associated with osteoporosis both in men and women, regardless of its cause. Increasing evidence exists that hypogonadism is an important cause of male osteoporosis, which is present in 20% of men with vertebral fractures and in 50% of men with hip fracture [6]. Increased prevalence of radiological vertebral osteoporotic fractures was observed in women with hyperprolactinemia, although it was unclear whether the prevalence of fractures is linked only with gonadal status. One small study that included male patients with prolactinomas showed no association between the incidence of osteoporotic fractures and serum testosterone levels, suggesting that prolactin has direct effect on bone loss [7]. On the other hand, study by Ciccarelli et al. compared BMD in female patients with hyperprolactinemia and normal menstrual cycle and amenorrhea, with normoprolactinemic control subjects. Patients with hyperprolactinemia with normal menstrual cycle had similar BMD as controls. On the other hand, patients with amenorrhea had lower BMD. The authors concluded that hyperprolactinaemia by itself is not a risk factor for the development of osteoporosis [8].

Studies regarding the interaction between bone metabolism and prolactin in animal models showed conflicting results. Clément-Lacroix et al reported that osteoblasts, but not osteoclasts, express PRL receptors and that an effect of PRL on osteoblasts could be required for normal bone formation and maintenance of bone mass [9]. However, different study reported that prolactin does have effect both on osteoblasts and osteoclasts. The authors concluded that hyperprolactinemia could act directly on bone to stimulate bone turnover, with more influence on bone resorption than formation. PRL enhanced bone resorption in part by increasing RANKL and decreasing OPG expressions by osteoblasts [10].

These data suggest that hyperprolactinemia has a negative effect on bone metabolism; however it is unclear whether prolactin directly enhances bone loss or this is mediated by hypogonadism. Interestingly, there are no studies that analyzed the role of prolactin in screening for secondary osteoporosis. In conclusion, clinicians should bear in mind the fact that osteoporotic vertebral fractures in men are often linked with hypogonadism and hyperprolactinemia. These conditions can be effectively treated. Therefore, detailed medical history and appropriate endocrinological evaluations should be performed in all male patients with osteoporotic fractures.

Author contributions

SM and ZSM gave the idea for the article, were engaged initial patient's work-up, reviewed the final version of the manuscript and gave their approval for publication. IK and MV were engaged in patients treatment and follow-up, critically revised the manuscript and gave final approval. MĆ wrote and drafted the manuscript and gave final approval.

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