

# Pregnancy-associated osteoporosis: an underestimated and underdiagnosed severe disease.

## A review of two cases in short- and long-term follow-up

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### Abstract

Pregnancy-associated osteoporosis is an uncommon condition characterized by the occurrence of painful fractures during late pregnancy or lactation. To date the pathophysiology of this entity of bone disorder is still uncertain, and its therapeutical management is poorly defined.

We report two clinical cases: a 10-years follow-up with pain medication and intermittent antiresorptive therapy courses, subsequent traumatic vertebral fracture and actually fracture of scaphoid after inadequate trauma. Beside this long-term course a young female patient with pregnancy-associated osteoporosis and painful lumbar and also thoracic vertebral fractures is described. She was treated with an osteoanabolic therapy, at the timepoint of first follow-up at 6 months of treatment a solid increase of bone mineral density and sustained pain reduction was observed.

**Key words:** osteoporosis, pregnancy, vertebral fractures, osteoanabolic therapy.

### Introduction

During pregnancy and lactation different significant alterations in the maternal environment proceed, particularly estrogen and prolactin, which may alter bone density. Therefore pregnancy and lactation might have significant impact on bone density and depending on the extent of loss in bone

density this might result in pregnancy-associated osteoporosis and vertebral fractures. At the moment exist no guidelines for the therapy of pregnancy-associated osteoporosis. The existing literature reveals several case reports [1,2] but evaluates the pregnancy associated osteoporosis altogether as rare disorder with unknown pathophysiology. With consideration of severity of the clinical findings an individual therapy concept should be initiated by specialised therapycentres. Furthermore a referencenter for pregnancy-associated osteoporosis was initiated in Germany to collect and analyze cases to be able to develop a risk profile. Although rare, diagnosis of pregnancy-associated osteoporosis should be suspected when lumbar or thoracic spine pain occur during pregnancy or in the post-partum period as it can lead to multiple vertebral fractures.

### Case report of complex course

We report a case of a 32-years old female patient, sectio half a year ago, who was treated in a hospital nearby because of severe and therapy-resistant back pain. With the suspicion of a pregnancy-associated osteoporosis the patient was transferred for further diagnosis and therapy.

We started with a bone mineral density (by DXA: dual x-ray-absorption) measurement. We diagnosed an osteoporosis with a T-score of the lumbar spine: L1-L4: -2.12, L4: -2.71, the T-score of the left femur was: -1.81. X-rays of thoracic and lumbar spine (*Fig. 1*) as the MRI of the whole spine (*Fig. 2*) showed changes of the vertebrae (wedge gibs) of the thoracic vertebra 5 and 7; fracture of thoracic vertebra 12 and changes of the cover plates of thoracic vertebrae 8, 10, and lumbar spine 2 and 3.

Due to a history of pulmonary embolism six months ago, the patient was treated with low-molecular-weight heparine (Clexane 40 sc twice daily), actually a therapy with an oral anticoagulans (Phenprocoumon) was initiated.

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**Figure 1.** Initial x-rays of thoracic and lumbar spine**Figure 3.** Control x-ray (6 weeks after fracture) of thoracic and lumbar spine

In the clinical chemistry as in 24 hours-urine assessment no pathologic values were observed.

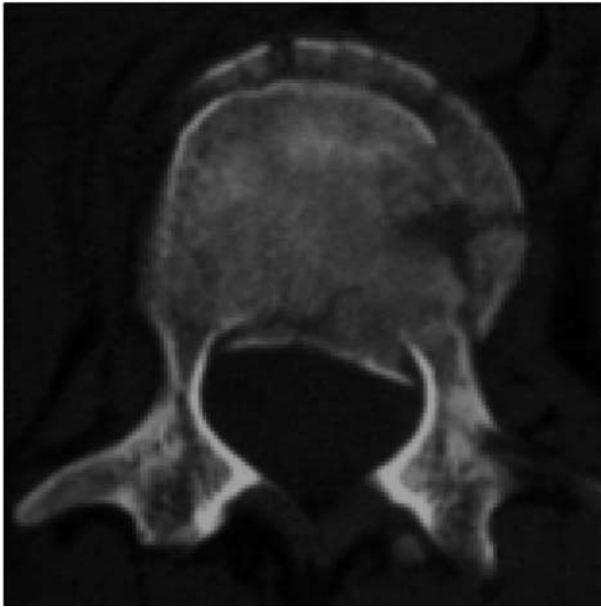
## Therapy

In accordance with the reference center for pregnancy-associated osteoporosis of the university of Marburg we initiated an osteoanabolic therapy with teriparatide (1,34 rhPTH 1-34). In the recent literature of reporting cases of pregnancy-associated osteoporosis an antiresorptive therapy with bisphosphonates was chosen as first-line therapy [1,3]. Altogether the authors

**Figure 2.** MRI of thoracic and lumbar spine before therapy: changes of the vertebrae (wedge gibs) in thoracic vertebra 5 and 7; fracture of thoracic vertebra 12 and changes of the cover plates of thoracic vertebrae 8, 10, and lumbar spine 2 and 3

reported bisphosphonates as well tolerated and effective in the long follow-up, despite to date unknown potentially long-term side-effects of bisphosphonate treatment in premenopausal women. In our patient several risk factors were condensed, so a potent and fast treatment was necessary. Because of the already progressive course of disease, the existence of multiple vertebral fractures, the high risk for secondary osteoporosis due to ongoing anticoagulant therapy and the fertile premenopausal status of the patient we decided to use a substance with specific action on bone formation not being incorporated into the bone matrix [4,5]. After full and adequate explanation to the patient and her family written informed consent was obtained from the patient in view of off-label therapy. We started therapy with teriparatide (rhPTH 1-34), accompanied with supplementation of 1000 mg calcium and 800 iE 25OH-Vit D3 per day [6]. Due to persisting back pain performed x-ray-controls after 6 weeks of treatment showed no further progress of vertebral fractures (Fig. 3) compared with the x-rays at the beginning of our therapy. And we could not measure progressive changes in the already existing vertebral fractures.

Altogether a consolidation of the disease could be diagnosed. Collateral therapy with immobilisation of the spine by a corset (Spinomed®) [7] was run for 3 months. Further accom-

**Figure 4.** CT of instable fracture L1

panying therapy was pain therapy and physiotherapy. Control measurements of bone mineral density were done after 6 months of treatment.

The mean value of T-score L1-L4 was -0.9, corresponding to a gain of 42.45%. No further non-traumatic vertebral fractures occurred. In conclusion the applied therapy showed an immediate effect on biomechanical properties of bone and reduced future fracture risk.

### Case report with 10-years-follow-up

A 41-years-old, premenopausal, slim (BMI=19) woman is accompanied by pain of the whole spine and the musculoskeletal system in general since 10 years. Within her adolescence she suffered from traumatic fractures of the jaw, metatarsus and toes. She had two pregnancies 10 and 8 years ago. Since the first pregnancy a PAO was known, which impaired after the second pregnancy. A possible cause for secondary osteoporosis is the treatment for asthma bronchiale over 12 years with inhalative, intermittent oral, corticosteroids (CS) in the range between 5-16 mg/die [8]. Seven years ago, the first DXA-scan was performed and showed a T-score (L2-L4) of -2.1 (z-score: -2.0), specific antiosteoporotic therapy was initiated with etidronate, calcitonin and ongoing supplementation of calcium and vitamin D3. In the DXA-scan after 1 year of therapy, a densitometric consolidation of the PAO could be observed (T-score L2-L4: -1.7; z-score-1.6). With this medication also back pain was improved and well tolerated by the patient. 5 years ago, the patient had a horse-riding accident with an instable burst-fracture of L 1 (Fig. 4), which was stabilised by internal fixator from Th12 to L2 (Fig. 5).

In the actual DXA-scan an increase of bone mineral density up to a T-score L2-L4 of -1.3 (z-score:-1.3) was observed. In the first laboratory assessment of biochemical markers of bone

**Figure 5.** Internal fixator from Th 12 to L2

metabolism an overall low turnover of bone was observed, due to corticosteroid therapy without accelerated bone resorption, PTH and vitamin D3 in normal range. Furthermore, a low estradiol (24 pg/ml range: 0.0-270.00 female) despite regular menstrual cycle was noticed.

### Therapy

We continued with a combined antiosteoporotic (ibandronate 3 mg iv./12 weeks) and pain treatment (level I WHO) with supplementation of 1000 mg calcium and 800 IU vitamin 25OH-Vit.D3 per day.

### Discussion of differential therapy

Effective treatment of pregnancy-associated osteoporosis is discussed controversial due to few reported cases in the literature and widespread underestimation of this distinct entity of bone metabolism disturbance. The lack of controlled studies and the severity of disease courses deserve effective therapy regimen. Recent case histories report usefulness and rapid improvement under antiresorptive treatment with bisphosphonates even in a younger patient [9].

Balancing existing risk factors and the progressive course of the disease against possible risk factors and the off-label-use of teriparatide [6,10] we decided interdisciplinary for this new therapeutic option: to use teriparatide in the treatment of severe pregnancy-associated osteoporosis. The decision to use teriparatide was supported by the fact of incompleting family planning. Accepting

the possibility of further pregnancies we did not use bisphosphonates in this case. There is no prediction of long-term follow-up adverse events concerning prenatal impairments. To enable further healthy pregnancies we decided to use teriparatide, which is not stored in bone matrix for years like the bisphosphonates.

We observed the beneficial effects of anabolic treatment with rhPTH 1-34 (teriparatide), especially in gain of bone mineral density and the prevention of further vertebral fractures. Up to now the treatment is well tolerated and showed the expected positive gain in bone mineral density and fracture-protective effect: no further deterioration or new fractures occurred. Also she reported substantial pain relief as an additional benefit from the osteoanabolic treatment.

In the long-term follow-up of the other patient sequentially bisphosphonates and calcitonin were used as antiresorptive treatment options. The premenopausal patient underwent bisphosphonate therapy as an off-label-therapy as well. Due to the age of 41 of this female patient and completed personal family planning we decided to use ibandronate. The iv.-medication was very well tolerated by the patient and after 4 weeks of therapy a substantial reduction of back pain was achieved.

## Conclusion

As we can see in this long-term follow-up the PAO accompanies the patient their whole life and should not be underestimated. We conclude that it is necessary to avoid a long course of pain and fractures in these young women in order to treat the PAO initially adequate with antiresorptive or even osteoanabolic medication to obtain a fast consolidation of BMD and to substantially reduce the risk of further fractures and chronification of pain.

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