Editorial paper

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Pregnancy- and lactation-related osteoporosis: an important topic also for rheumatologists

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Pregnancy- and lactation-related osteoporosis (PLO) is a rare problem characterized by low-energy fractures, usually of the vertebral bodies, in advanced pregnancy or early postpartum. Approximately 100 cases of the disease have been described, usually in single case reports; the largest described group included 29 women, identified retrospectively based on an insurer's database and confirmed by letter [1–10]. While most of the patients described are primiparous women, the problem also affects women who have previously given birth without any complications [9].

Autoimmune rheumatic diseases such as systemic lupus erythematosus or rheumatoid arthritis, often affect the population of women of reproductive age, and are associated with an increased risk of osteoporosis. Therefore, the problem of bone density reduction and even osteoporosis during pregnancy and breastfeeding seems to be very important also for rheumatologists.

Regardless of the rarity of the phenomenon, PLO causes significant morbidity, results in prolonged, severe back pain and decreased growth, and significantly limits the mother's ability to care for her child. The etiology of PLO remains unclear, although a major pathological role is attributed to the action of parathyroid hormone-related protein (PTH-rP) [11, 12]. Excessive secretion of PTH-rP by the mammary gland into the mother's circulation during the third trimester of pregnancy and during lactation enhances bone resorption and demineralization, accounting for a sharp decrease in bone mineral content (BMC) of 3 to 10% after 2 to 6 months of lactation.

After cessation of lactation, there is a gradual increase in bone mineral density (BMD), estimated at 0.5–2% per month, until it returns to baseline values. However, in general, the consequences of pregnancy- and lactation-related bone mass loss appear to be clinically insignificant, so it seems that other factors must play a role in the pathogenesis of PLO.

The majority of patients are found to have classic risk factors for osteoporotic fractures, especially low BMI (up to 65%), a history of osteoporotic fractures in parents (36%) and smoking [3, 13].

This raises the potential role of "traditional" risk factors in the development of PLO. Bone mineral density is significantly reduced, to a greater extent in the lumbar vertebrae, compared to the hip, generally meeting densitometric criteria for the diagnosis of osteoporosis [12–14].

In most cases, however, it cannot be ruled out that the woman had low bone mass even before pregnancy. Some pregnant women may experience excessive bone resorption, especially pregnant women with inadequate dietary calcium supply and vitamin D deficiency [15]. An outstanding increase in metabolic bone turnover is an independent risk factor for osteoporotic fractures in any type of this disease, including in PLO, so it can significantly increase the risk of fractures regardless of current bone mass.

A standard management of PLO is limited to calcium and vitamin D supplementation and cessation of feeding. Such management is associated with an increase in BMD of about 10% after two years, markedly greater in the lumbar vertebrae, but rarely with a return of BMD to normal values [1, 6, 13].

The rapid metabolic turnover of bone in PLO makes it rational to attempt treatment with antiresorptive drugs, mainly bisphosphonates. Due to the rarity of the disease, observations are sparse; however, it appears that early inclusion of bisphosphonates significantly increases the achieved increase in BMD, by an average of 23% to 35% after two years [5, 13].

The BMD increase observed in bisphosphonate-treated women with PLO is thus incomparably greater than in postmenopausal women with osteoporosis

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treated the same way. Compounding this may be the eminently enhanced bone remodeling at the time of the concept of therapy, together with the numerous changes in calcium and bone metabolism resulting from cessation of lactation. The optimal duration of treatment with PLO bisphosphonates is not known, but it seems reasonable to conduct therapy for up to 5 years, under densitometric control. There are also single case reports about the effectiveness of denosumab.

An important question in the management of PLO is the problem of the risk of recurrence in subsequent pregnancies. Analyses of available cases indicate a risk of fractures in subsequent pregnancies of up to 33%, but these observations apply to patients who have not been treated with bisphosphonates [2, 6]. There are no data on whether bisphosphonate therapy reduces this risk. Thus, in light of this information, it seems reasonable to inform women with PLO that subsequent pregnancies may carry the risk of further fractures.

The rapidity of the changes occurring in the skeleton of pregnant and lactating women is not comparable to anything, and the mechanisms responsible are not fully understood. However, it should be stated unequivocally that although individual women will experience fractures as a consequence of pregnancy or lactation, in the vast majority of women, changes in calcium and bone metabolism during pregnancy and lactation will not cause any adverse health consequences.

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