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Pregnancy in a woman with secondary osteoporosis. A case report

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BACKGROUND: Glucocorticoid-induced osteoporosis is one of the most serious complications of prolonged (more than three months) systemic glucocorticoid therapy. Rapid bone loss occurs in the first months of treatment, which is a significant risk factor, especially during pregnancy and lactation. When taking systemic glucocorticoid therapy in a daily dose of 5 mg or more (in prednisone equivalent), the relative risk of vertebral fractures increases by 2.9 times.

RESULTS: This article examines a clinical case of pregnancy and childbirth of 32-year-old woman diagnosed with secondary complicated osteoporosis during treatment with systemic glucocorticosteroids, who has a history of spine compression fractures during lactation after a previous pregnancy. Vitamin D deficiency was diagnosed and corrected during this pregnancy, which minimized the risk of fractures. A baby was delivered through the birth canal. Bisphosphonate therapy was started six months after birth. No new fractures were diagnosed within two years of observation.

CONCLUSIONS: The approach to the management, diagnosis and delivery of pregnant patients with secondary osteoporosis treated long-term with glucocorticosteroids should be multidisciplinary. It is imperative to prescribe vitamin D and calcium preparations throughout pregnancy and lactation.

Keywords: clinical case; secondary osteoporosis; bone diseases; glucocorticosteroids; pregnancy.

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Беременность на фоне вторичного осложненного остеопороза матери (клинический случай)

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Обоснование. Глюкокортикоид-индуцированный остеопороз — одно из осложнений длительной (более трех месяцев) системной терапии глюкокортикоидами. Быстрая потеря костной массы происходит уже в первые месяцы лечения, что является значимым фактором риска на фоне беременности и лактации. При приеме системных глюкокортикоидов в суточной дозе 5 мг и более (в преднизолоновом эквиваленте) относительный риск переломов позвонков увеличивается в 2,9 раза.

Результаты. В статье рассмотрен случай течения беременности и родов пациентки 32 лет с диагнозом «вторичный осложненный остеопороз» на фоне терапии системными глюкокортикоидами, имеющей в анамнезе компрессионные переломы позвоночника в период лактации после предыдущей беременности. Во время данной беременности был диагностирован и скорректирован дефицит витамина D, что минимизировало риск возникновения переломов. Пациентка была родоразрешена при доношенном сроке беременности через естественные родовые пути. Через 6 мес. после родов начата терапия бисфосфонатами. В течение двух лет наблюдения новых переломов не диагностировано.

Заключение. Подход к ведению, диагностике и родоразрешению беременных пациенток с вторичным остеопорозом на фоне длительного приема глюкокортикоидных препаратов должен быть мультидисциплинарным. Обязательно назначение препаратов витамина D и кальция на протяжении всей беременности и лактации.

Ключевые слова: клинический случай; вторичный остеопороз; заболевания костной системы; глюкокортикоиды; беременность.

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BACKGROUND

Osteoporosis is a metabolic disease of the skeletal system characterized by decreased bone mass, impaired microarchitectonics of bone tissues, and fractures with minimal trauma. Bone mineral density (BMD), at reproductive age, is determined by peak bone mass and degree of subsequent bone mass loss. Peak bone mass depends on genetic factors, comorbidity, physical activity, age at menarche, hormonal disorders, calcium intake, and vitamin D deficiency [1, 2].

Vitamin D deficiency and insufficiency are widespread in pregnant women [3–6]. This vitamin easily enters the breast milk, therefore its level decreases rapidly after pregnancy during lactation [7, 8]. Women with unreplenished vitamin D levels may experience significant changes in mineral metabolism and bone remodeling [9–11]. Insufficiency and deficiency of vitamin D were proven to be modifiable risk factors for fractures [12–14]. Secondary osteoporosis develops due to comorbidity or drug intake.

Glucocorticoid-induced osteoporosis is one of the most severe complications of long-term (>3 months) systemic glucocorticoid therapy. Rapid bone loss already occurs in the first months of treatment, which is a significant risk factor [15]. Osteoporotic fractures are recorded in 30%-50% of patients taking systemic glucocorticoids for a long time. When taking systemic glucocorticoids in a daily dose of 5 mg or more (in prednisolone equivalent), the relative risk of fractures as a whole compared with the general population increases by 1.9 times, the risk of femoral fractures increases by 2 times, and that of vertebrae increases by almost 2.9 times [16]. Patients with systemic lupus erythematosus (SLE) are at high risk of osteoporosis due to autoimmune inflammation, comorbidities, and treatment. When osteoporosis occurs in SLE, bone loss begins early and is associated with glucocorticoid administrations [17]. Pregnancy and lactation are considered risk factors for osteoporosis and an increased risk of fractures in a certain category of women [2, 11-13, 18].

CLINICAL CASE DESCRIPTION

A 32-year-old female patient, multigravida, visited the V.A. Almazov National Medical Research Center at 12 weeks of gestation for consultation, with the aim for zoledronic acid re-administration to prevent recurrent fractures and determine the management approach for pregnancy and childbirth due to complaints of back pain with minimal exertion. The anamnesis revealed that heredity for osteoporosis and diseases of the musculoskeletal system was not burdened. For a long time (>4 years), she received systemic glucocorticoid therapy for SLE. While taking systemic glucocorticoids after the first birth during lactation,

she had a compression fracture of Th_7 and Th_{12} . The complex treatment of osteoporosis with calcium and vitamin D was prescribed. Within a year she received bisphosphonates (alendronic acid at 70 mg weekly). To assess calciumphosphorus metabolism and risk of fractures, as well as correct the therapy and resolve the issue of delivery timing and method, the patient was hospitalized at the perinatal center of the V.A. Almazov National Medical Research Center.

Treatment during pregnancy included vitamin D preparations at 4000 IU and calcium preparations at 1200 mg daily and nutritional correction with increased calcium in the diet.

Results of laboratory and instrumental research. Clinical and laboratory examination data showed a parathyroid hormone level of 25 pg/ml, a serum calcium level of 2.3 mmol/l, and daily urinary calcium excretion of 5.2 mmol/day. At 11/12 weeks of gestation, the level of 25-hydroxycalciferol (25[OH]D3) was 15.65 ng/ml (vitamin D deficiency), thus a vitamin D preparation was prescribed at 4000 IU daily. After 6 weeks, the 25(OH)D3 level was 29.3 ng/ml (vitamin D insufficiency). The therapy with vitamin D at 4000 IU daily was continued. At 21/22 and 39/40 weeks of gestation, the level of 25(OH)D3 reached 53.4 and 62.05 ng/ml, respectively (normal). All this time, the patient was taking a vitamin D preparation at 4000 IU daily. The rest of the clinical and biochemical parameters were within the reference values.

Fetal ultrasound readings corresponded to 38 weeks of gestation. Congenital malformations of the fetus were not determined and indicators of fetal-placental and uteroplacental blood flow were normal. Given the gestational age of more than 30 weeks, the medical council decided to perform dual-energy X-ray absorptiometry (DXA) of the lumbar spine and proximal femur to determine BMD and assess the risk of fractures during childbirth and develop an approach to managing the patient, as well as the term and method of delivery. The lumbar spine DXA results revealed a pronounced decreased BMD. T-test showed the L₁ of 3.1 SD, L_1 – L_4 of 1.9 SD, and L_4 revealed local decrease to -2.7 SD. Z-criterion showed L₁ of 2.5 SD, L₁-L₄ of 1.5 SD, and L_{ℓ} of 1.9 SD, which is below the expected age indicators. The risk of fracture was high. The proximal femur DXA revealed no decreased BMD. T-score was -0.3 SD (femoral neck) and +0.1 SD (total). Z-score was +0.3 SD (femoral neck) and +0.7 SD (total), which is within the age range.

According to the interdisciplinary consultation results, taking into account the anamnesis data (uncomplicated heredity and gynecological history, repeated pregnancy, thoracic spine fractures during the previous lactation, long-term therapy with systemic glucocorticoids, no complaints, good nutrition, complex therapy before pregnancy, replenished vitamin D levels during the current pregnancy, normal bone metabolism, ultrasound and DXA data, and

absence of obstetric indications for surgical delivery), the delivery was decided to be through the vaginal birth canal when regular labor occurs.

At 40 4/7 weeks of gestation, the patient complained of nagging pain in the lower abdomen. Labor induction was performed due to the conditions for amniotomy in a pregnant woman with a preliminary period. The birth took place at a moderate pace. A live, full-term, female neonate, weighing 3,510 g, with a length of 52 cm, was born in a satisfactory condition. Apgar's score was 8/9 points. The postpartum period was uneventful. The patient with the child was discharged on day 5 after childbirth, with a recommendation to continue the intake of calcium and vitamin D supplements, have repeated DXA after 6 months, and, according to study results, prescribed with bisphosphonates under the supervision of a rheumatologist. Bisphosphonates (alendronic acid at 70 mg weekly) was started 6 months after childbirth. Musculoskeletal system fractures were not encountered in the postpartum period and for 2 years after childbirth.

DISCUSSION

This clinical case presents the need for an integrated approach to assess the calcium-phosphorus metabolism of pregnant women, severity of osteoporosis during pregnancy, choice of examination methods, pregnancy management approach, and delivery method. Due to the high risk of fractures, interdisciplinary management is required in a third-level perinatal center.

During the follow-up period, the most complete clinical and laboratory examination was performed, the biochemical parameters of bone metabolism were determined, and timely correction of revealed disorders was performed; therefore, the pregnant woman had no clinical manifestations of osteoporosis in the form of fractures. During the pregnancy planning, a comprehensive examination was performed, and according to its results, bisphosphonate therapy was prescribed, which the patient received 12 months before pregnancy, affecting the state of bone metabolism.

In this clinical case, the doctor who referred the pregnant woman to resolve the issue of bisphosphonate administration in the presence of pain was concerned about the recurrence of fractures. Bisphosphonates accumulate in the bone tissue and the final half-life of some reaches 10 years [19, 20]. The Russian Federation contraindicated the use of

bisphosphonates during pregnancy since they can penetrate through the placenta and enter the fetus. The published data indicate that bisphosphonates do not have a serious direct teratogenic effect on the fetus [21–23]. However, the amount of such data is limited; therefore, before using this group of drugs, accurately weighing the benefits for the woman and the risk for the pregnancy outcome is required [19, 20, 24, 25].

This clinical case assessed the level of vitamin D, which was an important participant in the regulation of calcium-phosphorus metabolism. At weeks 11/12 of gestation, the patient was diagnosed with vitamin D deficiency. This condition was corrected by prescribing a therapeutic dose of vitamin D preparations of 4000 IU daily, for a long time. By the end of pregnancy, the blood concentration of 25(OH)D was 62.05 ng/ml, which, according to the World Health Organization recommendations, is an adequate level of vitamin D and reduces the risk of fractures by 20% [26].

CONCLUSION

The management, diagnostics, and delivery approach in pregnant women with secondary osteoporosis with long-term glucocorticoid intake for SLE treatment should be multidisciplinary, determining a timely approach of management, as well as the delivery timing and method, taking into account the gestational age, risk of fractures (determination of BMD), and minimization of risks to the mother and the fetus. The presence of complaints, symptoms, and additional study results in bone metabolism is an indication for specific therapy of osteoporosis beyond pregnancy and the basis for the prescription of antiresorptive therapy and vitamin D and calcium preparations throughout the entire pregnancy and lactation period.

ADDITIONAL INFORMATION

Patient consent. The patient voluntarily signed informed consent for the publication of personal medical information in an anonymized form.

Conflict of interest. The authors declare no conflict of interest. **Acknowledgments.** We express gratitude to T.S. Alkhova, the Head of the Department of Physiology of Newborns of the Perinatal Center of the V.A. Almazov National Medical Research Center, and E.S. Shelepova, an obstetrician-gynecologist of the Department of Pathology of Pregnancy of the Perinatal Center of the V.A. Almazov National Medical Research Center.

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