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Multifocal, metaphyseal osteonecrosis of knee due to pulse steroid treatment after cessation of fingolimod treatment in a 19-week-pregnant patient

Multifokální metafyzární osteonekróza kolene v důsledku pulzní léčby steroidy po ukončení léčby fingolimodem u pacientky v 19. týdnu těhotenství

Dear editor,

In MS, discontinuation of some therapies may result in increased disease activity. Fingolimod is one such agent, and severe attacks that may advance the Expanded Disability Status Scale (EDSS) may occur after the cessation of fingolimod [1]. Even though pregnancy is classically associated with a significant reduction of clinical recurrence rate, there are several reports of dramatic worsening of the disease during pregnancy following discontinuation of fingolimod [2]. Therefore, many women may face an increased risk of relapse during the period between disease modifying treatment (DMT) discontinuation and potentially protective effects of pregnancy (in MS). For pregnant women with severe or highly active MS, the treatment can be continued with glatiramer acetate before and in the course of pregnancy; however, some therapies commonly used in MS are relatively contraindicated during pregnancy [3]. These therapies include fingolimod, dimethyl fumarate and teriflunomide, which are small molecules that may cross the placenta and potentially cause birth defects [4]. The use of DMTs during pregnancy is ultimately guided by patient decisions. It is acceptable to use glatiramer acetate during pregnancy [5]. Once a woman with MS is pregnant, the prevention of relapses can be planned either with the use of monthly intravenous immunoglobulin (IVIG) treatment or monthly steroids after the first trimester; however, the safety data are limited [6]. It is well-established that corticosteroid use should be limited during pregnancy. Even so, the safe use of corticosteroids is possible during pregnancy and the administration approach depends on the type of the steroid and its dose, and on the treatment duration and gestational age [5]. At relapse, intravenous methylprednisolone (MP) treatment (1 g/day for 3–5 days) is recommended [7]. The literature on this topic demonstrates the use of high-dose corticosteroids after ceasing the fingolimod therapy due to pregnancy; nonetheless, patients who are resistant to these treatments have also been reported. The authors suggested that rebound demyelinization had been triggered by the termination of fingolimod treatment, and these attacks were resistant to high-dose steroids [8]. High-dose pulse steroid treatments may cause osteonecrosis. MS is not an independent risk factor for avascular bone necrosis, and, although the risk of osteonecrosis is known to be increased with long-term high-dose steroid treatment, this risk may also increase with short-term high-dose steroid therapies [9], as demonstrated by our case.

We present a case of multifocal, metaphyseal osteonecrosis of the knee due to pulse steroid treatment after cessation of fingolimod treatment, which developed in a 32-year-old woman patient who was pregnant for 19 weeks. She had been diagnosed with relapsing-remitting MS in 2017, and was receiving fingolimod therapy since the attack that had occurred a year prior to the admission directly related with this study. The patient was attending our clinic for a follow-up with an EDSS score of 2.5. The fingolimod treatment was discontinued on the 5th week of pregnancy. Glatiramer acetate was recommended. However, the patient refused this treatment. After approximately 14 weeks of well-being, she developed weakness in the right side extremities (when compared to the left side) and difficulty in maintaining balance (at the 19th gestational week). The eurological examination findings were as follows: motor (muscle) strength was 4–/5 in the right upper extremity, 4+/5 in the right

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lower extremity. The deep tendon reflexes (DTR) were +++ on the right, ++ on the left. The Babinski reflexes were positive on the right and unresponsive on the left. The patient was found to have mild hemiparesis on the right. Her EDSS assessment without fingolimod therapy was 3.5 points. The observation of gait revealed that the patient was walking cautiously due to right-sided mild hemiparesis accompanied by sensorial ataxia. The patient had never smoked or consumed alcohol and had no other systemic disease history. The laboratory findings were as follows: C-reactive protein: 6.0 (mg/dL), erythrocyte sedimentation rate: 68 (mm/h), hemoglobin: 10.6 (g/dL), hematocrit: 31.3%, leukocyte count: 7,300/mm^3, lymphocyte count: 1,600/mm^3, rheumatoid factor: negative, Brucella test: negative. The thyroid function test values and vitamin B_{12} levels were within reference ranges. The development of the fetus was normal. Compared to the contrast MRI findings performed a year before, there have been cross-sectional milimetre deviations depending on the technical shooting in the non-contrast cranial and cervical MRI findings obtained during pregnancy. We planned an initial 5-day pulse steroid treatment. However, the patient was unresponsive to the therapy and on the 7th day of MP application, the patient was seen at our clinic, describing increased pain in the right knee during its movement. She was diagnosed with stage 2 osteonecrosis according to the radiographic classification of knee osteonecrosis by Aglietti et al [10]. The recommendation was to take a rest. Orthopedic surgery was not considered in the patient during the follow-up. The birth took place by cesarean section, after which the mother did not experience a relapse. Glatiramer acetate was recommended in the postpartum period. The neurological examination remained stable (EDSS: 3.5). In the baby, no congenital malformation was found, but the baby had a low birth weight (2,450 g).

Taking into account the prior literature and case reports on this topic, our case supports the suggestion that pregnant patients may be resistant to high-dose steroid treatment and active disease may progress in these patients who cease fingolimod therapy. Such data are evidently valuable for clinicians, especially with respect to the treatment planning and management of pregnant patients.

References

1. Hatcher SE, Waubant E, Nourbakhsh B et al. Rebound syndrome in patients with multiple sclerosis after cessation of fingolimod treatment. JAMA Neurol 2016; 73(7): 790–794. doi: 10.1001/jamaneurol.2016.0826.

2. Novi G, Ghezzi A, Pizzorno M et al. Dramatic rebounds of MS during pregnancy following fingolimod withdrawal. Neurol Neuroimmunol Neuroinflamm 2018; 5(3): e462. doi: 10.1212/NXI.0000000000000462.

3. Cree BA. Update on reproductive safety of current and emerging disease-modifying therapies for multiple sclerosis. Mult Scler J 2013; 19(7): 835–843. doi: 10.1177/1352458512471880.

4. Guilloton L, Pegat A, Defrance J et al. Neonatal pancytopenia in a child, born after maternal exposure to natalizumab throughout pregnancy. J Gynecol Obstat Hum Reprod 2017; 46(3): 301–302. doi: 10.1016/j.jogoh.2017.02.008.

5. Coyle PK. Multiple sclerosis and pregnancy prescriptions. Expert Opin Drug Saf 2014; 13(12): 1565–1568. doi: 10.1517/14740338.2014.973848.

6. Bove R, Alwan S, Friedman JM et al. Management of multiple sclerosis during pregnancy and the reproductive years a systematic review. Obstet Gynecol 2014; 124(6): 1157–1168. doi: 10.1097/AOG.0000000000000541.

7. Ramašauskaite D, Laužikiene D, Arlauskien A. Pregnancy and multiple sclerosis: an update on the disease modifying treatment strategy and a review of pregnancy's ımpact on disease activity. Medicina (Kaunas) 2020; 56(2): 49. doi: 10.3390/medicina56020049.

8. Dalka L, Harb A, Mikesell K et al. Medically refractory multiple sclerosis ıs successfully treated with plasmapheresis in a super morbidly obese pregnant patient case. Rep Neurol Med 2020; 2020: 4536145. doi: 10.1155/2020/4536145.

9. Weinstein RS. Glucocorticoid-induced osteoporosis and osteonecrosis. Endocrinol Metab Clin North Am 2012; 41(3): 595. doi: 10.1016/j.ecl.2012.04.004.

10. Aglietti P, Insall J, Buzzi R et al. Idiopathic osteonecrosis of the knee. Aetiology, prognosis and treatment. J Bone Joint Surg Br 1983; 65(5): 588–597. doi: 10.1302/0301-620X.65B5.6643563.

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