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Case Report

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Neurofibromatosis type 1 case with cerebral involvement complicating pregnancy

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Abstract

Objective: Neurofibromatosis-1 is a disease with an autosomal dominant inheritance pattern and heterogenous clinical presentation. Although it is not rare, its diagnosis may be overlooked except the cases evaluated by the specialists from related disciplines. In this report, we aimed to discuss the progress and complications of the disease during pregnancy over a case diagnosed with neurofibromatosis-1 during pregnancy.

Case: Twenty-eight-year-old case who was pregnant for 30 weeks admitted with hypertension, proteinuria and convulsions. The patient delivered with the diagnosis of preeclampsia/eclampsia was established the diagnosis of neurofibromatosis-1 during postoperative period.

Conclusion: Neurofibromatosis-1 during pregnancy may cause serious problems with the rapid growth of neurofibromas, changing characteristics or the addition of new ones. To predict possible complications that may develop and to minimize them, neurofibromatosis-1 cases should be managed with an experienced and multidisciplinary team approach.

Keywords: Neurofibromatozis, pregnancy, preeclampsia.

Özet: Gebeliği komplike eden serebral tutulumlu nörofibromatozis tip 1 olgusu

Amaç: Nörofibromatozis-1, klinik sunumu heterojen olan otozomal dominant geçişli bir hastalıktır. Çok ender rastlanmadığı halde ilgili branş uzmanlarınca değerlendirilmiş olgular dışında tanısı gözden kaçabilmektedir. Burada, gebeliği sırasında nörofibromatozis-1 tanısı alan bir olgu üzerinden hastalığın gebelikteki seyri ve komplikasyonlarını tartışmayı amaçladık.

Olgu: Yirmi sekiz yaşında ve 30 haftalık gebe olgu, hipertansiyon, proteinüri ve konvülziyonlarla başvurdu. Preeklampsi/eklampsi tanısıyla doğumu gerçekleştirilen hastada postoperatif dönemde nörofibromatozis-1 tanısı kondu.

Sonuç: Gebelikte nörofibromatozis-1, nörofibromaların hızla büyümesi, karakter değiştirmesi veya yenilerinin eklenmesi ile ciddi problemlere yol açabilir. Gelişebilecek olası komplikasyonların öngörülebilmesi ve en aza indirgenebilmesi için gebe nörofibromatozis-1 olguları deneyimli ve multidisipliner bir ekip yaklaşımı içerisinde yönetilmelidir.

Anahtar sözcükler: Gebelik, nörofibromatozis, preeklampsi.

Introduction

Neurofibromatosis-1 (NF-1) is an autosomal dominant disease presenting with cafe-au-lait spots, iris hamartomas and neurofibromas.[1] Diagnosis is established usually during adulthood. It is known that the prevalence, which is about 1:3000, does not change in pregnant population.[2]

It was claimed that some of the various complications, which are sometimes severe, seen in the pregnancies of women diagnosed with NF-1 were more frequent compared to the normal population.[3–6] In this report, we aim to review the progress and possible complications of NF-1 through our case.

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Case Report

Our case who was twenty-eight years old and had the history of cesarean delivery was referred to our clinic due to convulsions and the loss of consciousness at 30 weeks of gestation. In the first examination, confusion, hypertension (160/80 mmHg) and tachycardia (155 beat/min) were noted. In the laboratory findings by hepatic function tests of the patient who was afebrile, it was found that thrombocyte count (170,000/dl) was normal, urea and creatinine values were within normal range but they were above the lower levels expected for pregnant women (38.7 mg/dl and 0.79 mg/dl, respectively). Also, +1 proteinuria and hemoconcentration (hemoglobin value, 14 g/dl) were noted. With preeclampsia-eclampsia pre-diagnosis, intravenous magnesium sulfate neuroprophylaxis protocol was applied to the patient with lethargy, hypertension and proteinuria. The patient found to have normal fetal heartbeat was taken to urgent cesarean delivery with previous cesarean indication. The female newborn whose birth weight was 2345 g, first-minute APGAR score was 5, five-minute score 8 was taken to intense care service for monitoring. During the cesarean delivery, common cafe-au-lait spots and lesions consistent with cutaneous neurofibromas were noted on the skin of patients. The consistency of findings with the diagnosis of neurofibromatosis-1 was confirmed by neurology specialist.

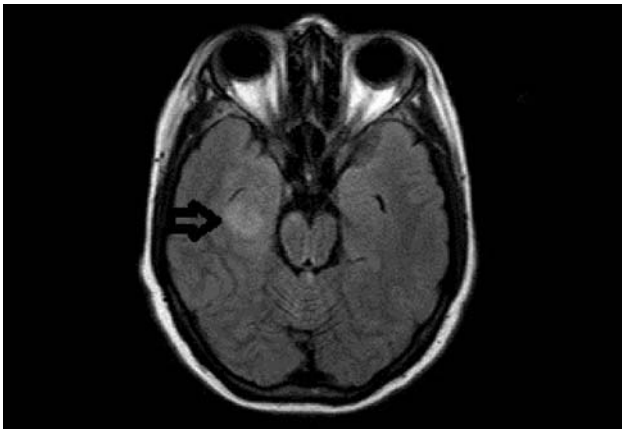

Fig. 1. Increase of right parahippocampal intensity in MR FLAIR and T2A views (arrow).

In the magnetic resonance imaging (MRI) of brain performed on the postoperative second day, 3.5×2 cm FLAIR (fluid-attenuated inversion recovery) signal increase and edema were observed on the right cerebral peduncle anterior and right temporal lobe parahip-

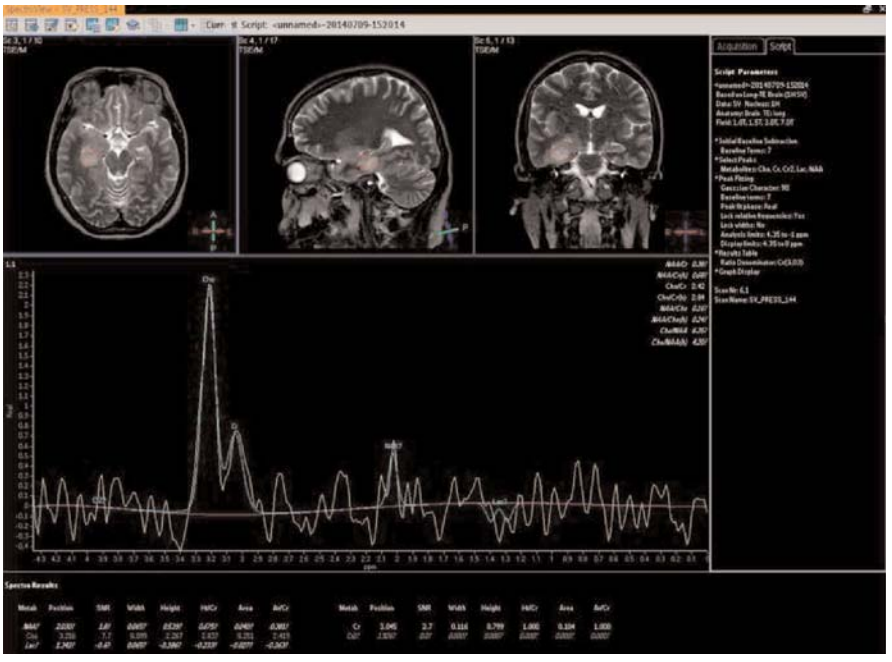

Fig. 2. Distinctive choline peak supporting neoplasia in MR spectroscopy for lesion.

pocampal levels (**Fig. 1**). When choline (Cho) peak became clear in the MR spectroscopy of this area, it was considered that the decrease in the amount of N-acetyl aspartate (NAA) supported the neoplasia (**Fig. 2**).

When the records of the case for this pregnancy were reviewed, it was seen that her routine laboratory examinations were normal except high levels of free thyroid hormone and suppressed thyroid stimulating hormone levels (TSH 0.055 mIU/ml), and initiating treatment for them. In the family history, it was found out that her father and brother also had similar common spots (cafe-au-lait). Neurological and other clinical findings of patient were recovered during the follow-up in the intense care unit, and she was discharged on the postoperative fifth day with a non-complicated progress. Similarly, the newborn which had no problem during postpartum follow-up was discharged on 12th day.

In the follow-up MRI examinations carried out one and three months later, cystic changes and dimension increase (4.5×3 cm) in the right parahippocampal lesion. The MR spectroscopy of the lesion with clear perfusion increase in the perfusion MRI supported the glial tumor possibility including malign degeneration (**Figs. 3** and **4**).

Discussion

Neurofibromatosis (NF-1) is an autosomal dominant disease developing with the mutation of NF1 gene which codes neurofibromin protein and standing out with cafe-au-lait spots, iris hamartomas and neurofibromas in clinical conditions.[1] Although it displays full penetrance, its clinical condition varies significantly among patients even among the family members. While it may progress with some cafe-au-lait spots in some individuals, it may have severe orthopedic and vascular findings in others. There is no evidence showing any impact on fertility, and it was reported that its incidence does not change during pregnancy.[2,4]

Our knowledge about the problems specific to the pregnancies of patients with NF-1 is based on some case series, a wide retrospective cohort study and other case reports reporting its rare complications.[7–11] Complications such as oligohydramnios, polyhydramnios, fetal growth retardation, intrauterine fetal death, gestational hypertension, preeclampsia, HELLP syndrome, chronic hypertension with superimposed preeclampsia, increased incidence of abortion and cesarean were reported during pregnancy, and it was claimed that some of them had higher rates compared to

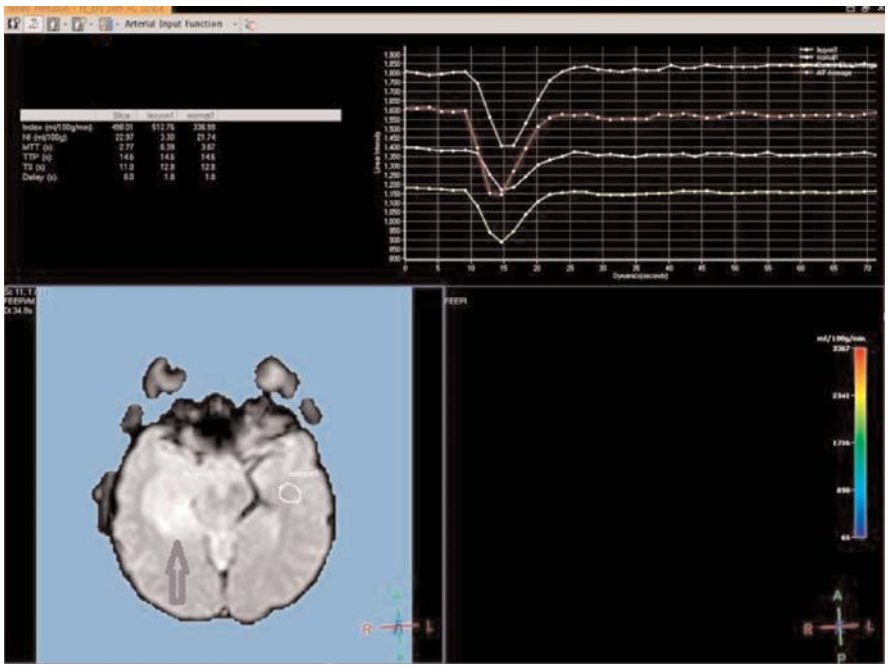

Fig. 3. Distinctive perfusion increase indicating neoplasia in lesion region compared to normal side in perfusion MR examination (**arrow**).

pregnant population without NF-1 diagnosis.[3–6] However, the claim of increased obstetric complications in some series was not supported.[12]

It was reported that neurofibromas grow during pregnancy and their numbers increase, and they decrease after delivery.[7,13] At this point, the impact of progesterone is focused due to the fact that a major part of neurofibromas (75%) express progesterone receptor.[14] The presence of mediastinal and abdominal tumors causing morbidities and even maternal and fetal losses with repeating or malign changes during pregnancy was reported.[15,16] Therefore, pregnant women established NF-1 diagnosis should be evaluated carefully in terms of neurofibromas and it should be kept in mind that the tumors in localizations not seen in the inspection in particular may develop complications secondary to pressure.[15]

Lesion similar to glial tumor was found in the right temporal lobe parahippocampal region and uncus during postpartum period in our case which did not have any neurological finding before pregnancy. It is reported that the neurofibromas with spinial localization may lead to severe morbidity during pregnancy and early postpartum period.[17] It was shown in MR studies that about 40% of patients with NF-1 which are mostly asymptomatic have spinal neurofibromas.[18,19]

Vascular anomalies such as aneurysm, arteriovenous malformation and stenosis are the most common reasons of death in NF-1.[20] Among them, renal artery stenosis may cause serious complications during pregnancy.[21] It was reported that pheochromocytomas progressing with hypertensive attacks are seen more frequently in NF-1.[22] Hemodynamic balances changing in normal pregnancy physiology require to be more careful about cardiovascular pathologies.

Severe hypertensive complications may develop in some patients except renal artery stenosis or pheochromocytoma etiology. While no increase in the incidence of hypertensive disease was shown in the series of eight cases by Segal et al., an increase was observed in the complications of gestational hypertension, preeclampsia, IUGR, preterm labor, cesarean delivery and cerebrovascular complications in a retrospective cohort study where antepartum, intrapartum and postpartum complications were investigated in 1500 NF-1 cases among about 20 million pregnant women.[4,23] Also, it was highlighted by analyses performed after the factors such as chronic hypertension, diabetes and renal diseases that

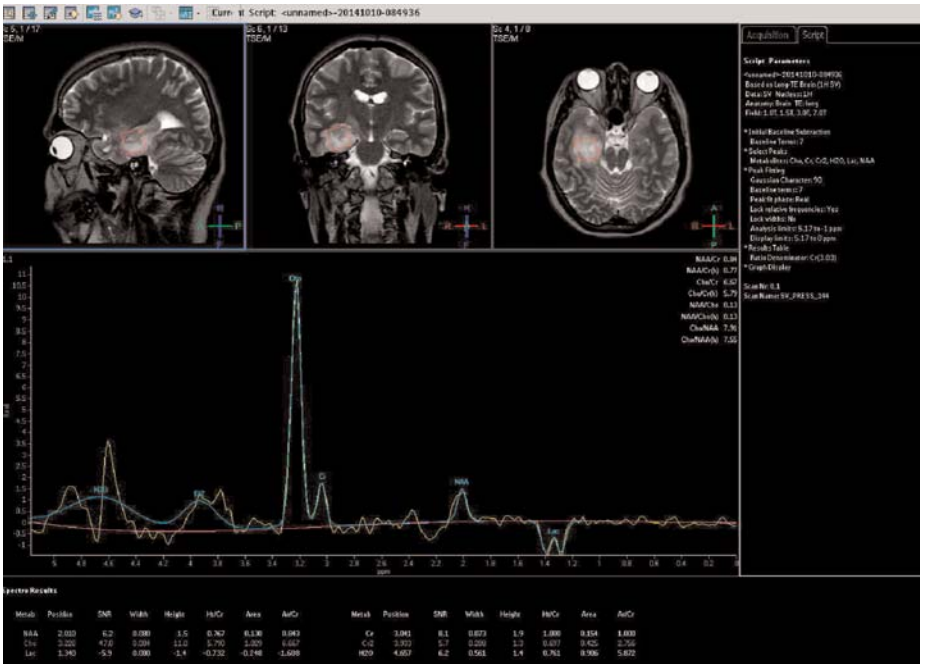

Fig. 4. Distinctive increase of choline peak in MR spectroscopy 3 months later, and increase of choline/NAA rate supporting neoplasia.

the risk continues. Although rare maternal death cases secondary to the increased morbidity were reported in pregnant women with NF-1, it was stated that the mortality rates were not significantly different than the general population.[23]

Magnesium sulfate neuroprophylaxis protocol was initiated in our case with the diagnosis of preeclampsia-eclampsia based on convulsions, hypertension and proteinuria findings. While it can be considered that the convulsions depend on the effects of right temporal lobe tumor, they cannot explain proteinuria and hypertension.

The increase of cesarean rates is also a common problem seen in pregnant women with NF-1 frequently. Kyphoscoliosis, failed labor induction, hypertensive complications, cephalopelvic disproportion and non-indicated approaches are among the possible reasons.[2,7] In our case, preterm cesarean labor was preferred due to previous cesarean delivery.

Neuroaxial anesthesia procedure commonly required in the obstetric population is characterized in pregnant women with NF-1 diagnosis. Ruling out the involvement of central nervous system is of vital importance in terms of preventing a possible bleeding. Respiratory tracts should be evaluated carefully for neurofibromas, it should be prepared in advance for any emergency or planned intubation need.

Since complications associated with hypertension and the localization of neurofibromas in pregnancy with NF-1 are more common, directing precautions towards these areas would be reasonable. Identifying neurofibromas at significant anatomic localizations before or during early weeks of gestation which can be detected with simple imaging modalities is a significant step to prevent complications. Even asymptomatic, it should be kept in mind that spinal neurofibromas may grow rapidly during pregnancy. Questioning previous neurofibromas treated with medical or surgical methods is significant in terms of predicting recurrence or malign transformation.

Even though prognostic activity studies and cost analyses have not been performed yet, it may be required to rule out renal artery stenosis and pheochromocytoma in patients with suspicious history. Renal arteriography is indicated in cases found to have hypertension. In the increases of sudden blood pressure progressing with attacks such as sweating, palpitation and headache, it is required to investigate catecholamine in urine and other related metabolites.[21] In cases without previous hypertension, being cautious for preeclampsia which may develop based on cardiovascular complication risk may help to decrease morbidity rate. In our case, the tests required to rule out pheochromocytoma diagnosis could not be performed due to the shortness of postoperative hospitalization period and some social reasons; however, the patient was called for follow-up by informing in detail on this matter.

Conclusion

Skin examinations and investigating the family history of pregnant women in terms of cafe-au-lait spots and neurofibroma are significant for the diagnosis of NF-1. Eclampsia may accompany to NF-1 cases. However, other reasons such as pheochromocytoma and brain tumor should also be investigated in these cases. Therefore, interdisciplinary approach in the diagnosis and follow-up of NF-1 during pregnancy is important.

Conflicts of Interest: No conflicts declared.

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