CASE REPORT

# Neurofibromatosis Type 1 (Nf1) and Pregnancy - Case With Positive Outcomes

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**Abstract:**

A pregnancy is categorized as with high-risk when the life of the mother or the fetus becomes fragile due to various diseases. Many health problems can be manifested in women before pregnancy, during and after pregnancy. Some health problems can also begin in early adolescence with very light clinical signs, but during pregnancy because of the hormonal changes that may occur, lead to intensification of the disease. We report the management of a 26-year-old woman patient diagnosed with neurofibromatosis 1 (NF1), without any complications during pregnancy and childbirth.

**Keywords:** Pregnancy, Neurofibromatosis, Genetic Disorder, Outcome of Pregnancy

## Introduction:

Neurofibromatosis is an autosomal dominant disorder that causes tumors to form on nerve tissue, including; brains, spinal cord and nerves. The tumors are usually benign, but sometimes can become malignant. The incidence of neurofibromatosis type 1 is approximately 1 in 3000 live births [1]. There are three types of neurofibromatosis; Neurofibromatosis 1 (NF1), Neurofibromatosis 2 (NF2), schwannomatosis. Signs and symptoms of neurofibromatosis are different and depending type. They can often mild. However, complications of neurofibromatosis can include hearing loss, learning impairment, cardiovascular problems, loss of vision, and severe pain. Neurofibromatosis usually appears during the first years of life. Are often benign tumors and with slow growing. Signs and symptoms are often mild up to moderate. Signs and symptoms include; neurofibromas or soft bumps on or under the skin, flat, light brown spots on the skin (cafe au lait spots), freckling which is usually localized in the armpits or groin area and in skin folds, tiny bumps on the iris of the eye (lisch nodules), bone deformities, optic glioma, learning disabilities, attention deficit/hyperactivity disorder, gradual hearing loss, ringing in the ears, poor balance, headaches etc.

Neurofibromatosis is caused by genetic defects (mutations) that are either passed on by a parent or occur spontaneously at conception. The NF1 gene is located on chromosome 17. This gene normally produces a protein called neurofibromin that helps regulate cell growth. The mutated gene causes a loss of neurofibromin, which allows cells to grow uncontrolled, while the NF2 gene is located on chromosome 22, and produces a protein called merlin. The mutated gene causes a loss of merlin, leading to uncontrolled cell growth.

Approximately half of people with NF1 and NF2 inherit the disease. Hormonal changes associated with pregnancy (or with other conditions as well, puberty and menopause), might cause an increase in neurofibromas. An increase in the size of existing neurofibromas and the appearance of new neurofibromas during pregnancy is a frequent observation in women with neurofibromatosis 1 [2]. Most women with NF1 have healthy

pregnancies, but need careful monitoring. Early diagnosis and treatment are the most important factors resulting in good outcome. A physical examination, family history and genetic testing may help establish the diagnosis. Other help methods are; X-rays, CT scans or MRIs. Neurofibromatosis can't be cured, but treatments are available for signs and symptoms. We report on a pregnant woman who had multiple neurofibromas beginning after the third month of her first pregnancy leading to a diagnosis of neurofibromatosis type 1 and who had an increase in the size of existing neurofibromas and the appearance of new neurofibromas during other pregnancies.

**Case Report:**

A 26-year-old G3P2 women at 38 weeks gestation, with regular prenatal care, presents to the Obstetrics Clinic for labor. She has a past medical history significant for neurofibromatosis 1 (NF1), but she denied a family history of NF1. The patient claims to have been diagnosed with neuro-fibromatosis 1 (NF1) in the first trimester of her first pregnancy. The patient declares for dozens of new papules and nodules that beginning after the third month of her first pregnancy leading to a diagnosis of neurofibromatosis type 1 and who had an increase in the size of existing neurofibromas and the appearance of new neurofibromas during other pregnancies. Her other pregnancies were uncomplicated. Even during this pregnancy, she had no complications during pregnancy and childbirth and had regular follow-up with her obstetrician throughout pregnancy. During a general multi-system examination, she had no headache, visual changes, hearing loss, poor balance, hypertension, attention deficit/hyperactivity disorder, but a mild scoliosis was found. All results of laboratory tests done during her pregnancy were within normal limits. On physical examination, the patient had soft bumps on the skin, which clinically responded to neurofibromas and light brown spots on the skin (cafe au lait spots), with size around 2- to 11-mm, located primarily on the abdomen, neck and chest (Fig. 1). Also in her neck were noticed a dark brown hyperpigmented plaque, with dimensions around 0.5x1cm, which clinically consistent with a plexiform neurofibroma (Fig. 2). Also in the abdomen, neck, chest, face, and axillae, she had many hyperpigmented freckles, with dimensions around 2 mm, present since adolescence (Fig. 3). The diagnosis of neurofibromatosis type 1 was made based on the clinical manifestations, family history and genetic testing.

At 38 weeks of gestation, she gave birth to a 3.7 kg girl by spontaneous vaginal delivery without complication 4 hours after the presentation, with APGAR score 8 and normal phenotypic features. The placenta was macroscopically normal. She had a postpartum period completely normal. She was released from the clinic two days after birth, with adequate advice and recommendations.

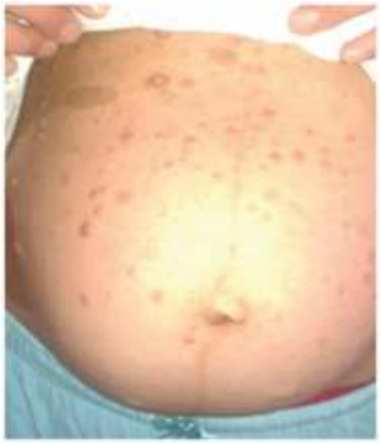

**Fig. 1: Multiple Neurofibromas and café-au-lait spots in a Pregnant Woman**

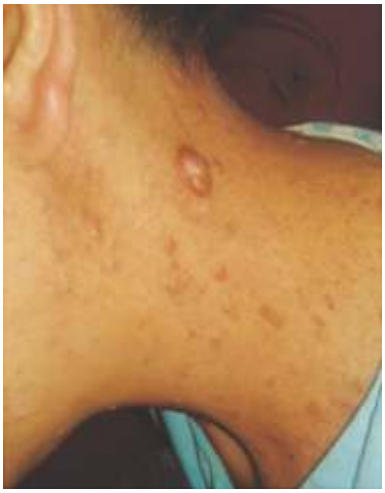

**Fig. 2: Plexiform Neurofibroma**

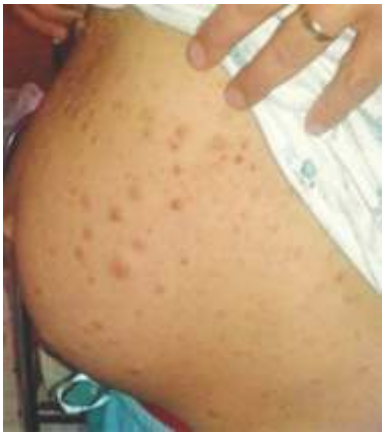

**Fig. 3: Hyperpigmented Freckles**

**Discussion**

Neurofibromatosis type 1 is an genetic disorders that have an incidence approximately 1 in 3000 live births. It is an autosomal dominant disorders that have various clinical manifestations ranging from mild cutaneous lesions like café-au-lait spots and axillary freckling up to plexiform neurofibromas, optic gliomas, bony abnormalities, learning disabilities, attention deficit/hyperactivity disorder, gradual hearing loss, ringing in the ears, poor balance, headaches, and malignancies [1-2].

Neurofibromatosis is one genetic disorder that associated with increased maternal morbidity during pregnancy, but does not impact increased maternal mortality. However, we need to know that we can have an increase of antenatal and peripartum complications among women with neurofibromatosis 1. Although most pregnancies in women with neurofibromatosis 1 are without complications, sometimes serious complications can occur [3, 4]. In the most frequent complications of pregnant women with neurofibromatosis 1 included gestational hypertension, preeclampsia, intrauterine growth restriction (IUGR), cerebrovascular disease, preterm labor, cesarean delivery etc. [4].

Our patient did not have any complications during the three pregnancies she received careful antenatal monitoring, appropriate prenatal counseling and adequate genetic counseling.

Most of the women with neurofibromatosis 1 have a rapid increase in the number and size of neurofibromas during any pregnancy. In a study, it was found that sixty-four percent of pregnant women had increase of new neurofibromas during pregnancy and fifty-five percent had enlargement of existing neurofibromas [5]. Several studies suggest that growth of neurofibromas during pregnancy occurs due to hormonal changes, which normally occur during pregnancy (such as physiological increase of estrogen and progesterone) [6].

Neurofibromatosis type 1 is one genetic disorder, so the disease can be inherited from the parents. In a study, it is reported that about two thirds of the patients who have neurofibromatosis type 1 inherit the disease from the parents and the risk for each child is estimated at about fifty percent [7]. While about fifty percent of cases with neurofibromatosis type 1 result from de novo mutations [8-10].

In this case report, we describe the case of a woman with neurofibromatosis type 1, which did not have any complications during the three her pregnancies. She received careful antenatal monitoring, appropriate prenatal counseling, and adequate genetic counseling and did birth with vaginal delivery three healthy children.

## References


1. Farrell CJ, Plotkin, SR. Genetic causes of brain tumors: neurofibromatosis, tuberous sclerosis, von Hippel-Lindau, and other syndromes. *Neurologic clinics* 2007; 25(4): 925-46.
2. Dugoff L, Sujansky E. Neurofibromatosis type 1 and pregnancy. *Am J Med Gen Part A* 1996; 66 (1):7-10.
3. Chetty SP, Shaffer, BL, Norton ME. Management of pregnancy in women with genetic disorders: Part 2: Inborn errors of metabolism, cystic fibrosis, neurofibromatosis type 1, and Turner syndrome in pregnancy. *Obstetrical & Gynecological Survey* 2011; 66(12):765-76.
4. Terry AR, Barker FG, Leffert L, Bateman BT, Souter I, Plotkin SR. Neurofibromatosis type 1 and pregnancy complications: a population-based study. *Am J Obst Gyn* 2013; 209(1): 46-e1.
5. Dugoff L, Sujansky E. Neurofibromatosis type 1 and pregnancy. *Am J Med Gen Part A* 1996; 66(1): 7-10.
6. Roth TM, Ramamurthy P, Muir D, Wallace MR, Zhu Y, Chang L, *et al*. Influence of hormones and hormone metabolites on the growth of Schwann cells derived from embryonic stem cells and on tumor cell lines expressing variable levels of neurofibromin. *Developmental Dynamics* 2008; 237(2): 513-24.
7. Košec V, Márton I. Neurofibromatosis type 1 in pregnancy. *Collegium antropologicum* 2006; 30(1): 247-49.
8. Ruggieri M, Huson SM. The clinical and diagnostic implications mosaicism in the neurofibromatoses. *Neurology*2001; 56(11): 1433-43.
9. Colman SD, Rasmussen SA, Ho VT, Abernathy CR, Wallace MR. Somatic mosaicism in a patient with neurofibromatosis type 1. *Am J Human Gen* 58(3), 484.
10. Friedman JM. Epidemiology of neurofibromatosis type 1. *Am J Med Gen Part A* 1999; 89(1), 1-6.


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