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Case Report

A rare encounter: Neurofibromatosis and pregnancy—Case insights

Kaviya Vengatesan[1], Maitrayee Sen[1]*, Shubhashree Thiruselvam[1]

[1]Dept. of Obsterics and Gynecology, SRM Insitute of Science and Technology, Chengalpattu, Tamil Nadu, India

Abstract

Neurofibromatosis type 1 (NF-1), or von Recklinghausen disease, is an autosomal dominant disorder caused by mutations in the NF1 gene. It is characterized by cutaneous neurofibromas, café-au-lait spots, axillary/inguinal freckling, and variable systemic involvement. While NF-1 is typically diagnosed in childhood, its course and implications during pregnancy are not well understood due to limited case reports. We present a case of a 25-year-old multigravida (G3P1L1A1) with a known clinical diagnosis of NF-1, who exhibited progressive cutaneous neurofibroma growth during pregnancy. She presented at 24 weeks' gestation for routine antenatal care. Examination revealed multiple non-tender neurofibromas, café-au-lait spots, and palmo-plantar freckling without neurological or skeletal involvement. The lesions increased in size and number throughout gestation, particularly over her previous cesarean scar. A repeat elective lower segment cesarean section was performed at 38 weeks under general anesthesia due to extensive spinal lesions. A healthy female infant (2.475 kg, APGAR 8/10 and 9/10) was delivered with no apparent NF-1 features. Postpartum follow-up revealed significant regression of the maternal lesions within 4–6 weeks. This case highlights the impact of pregnancy-induced hormonal and immunological changes on NF-1 lesion progression. Elevated estrogen and progesterone may stimulate neurofibroma growth, which typically regresses postpartum. Anesthetic and surgical management in such patients pose unique challenges due to lesion location and potential complications. The case underscores the importance of multidisciplinary care and the need for genetic counseling, considering the 50% inheritance risk. NF-1 can exhibit significant progression during pregnancy, requiring tailored antenatal and peripartum management. Awareness of these changes, along with genetic counseling and postpartum follow-up, is essential to optimize maternal and fetal outcomes.

Keywords: Neurofibromatosis type 1, Pregnancy, Hormonal changes, Cesarean section, Cutaneous neurofibromas, Postpartum regression, Multidisciplinary management.

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1. Introduction

Neurofibromatosis type 1 (NF-1), also known as von Recklinghausen disease, is an autosomal dominant genetic disorder characterized by the development of multiple neurofibromas, café-au-lait spots, axillary and inguinal freckling, Lisch nodules, and skeletal abnormalities. It results from mutations in the NF1 gene on chromosome 17, which encodes neurofibromin—a tumor suppressor protein that regulates cell growth and differentiation.[1] The prevalence of NF-1 is approximately 1 in 3,000 individuals, with variable expressivity and penetrance, leading to a broad spectrum of clinical manifestations.[2]

While NF-1 commonly presents during childhood, its course during pregnancy remains underreported. Pregnancy introduces significant hormonal, immunological, and hemodynamic changes that can influence the behaviour of neurofibromas.[3] These changes may lead to the progression, growth, or even malignant transformation of lesions, posing unique challenges in management. Additionally, pregnancy can complicate the anesthetic approach, surgical decisions, and maternal-fetal monitoring in women with NF-1.[4]

Neurofibromatosis Type 2 (NF-2) is an autosomal dominant genetic disorder caused by mutations in the NF2 gene on chromosome 22. It is characterized by bilateral

*Corresponding author: Maitrayee Sen
Email: vkaviya@gmail.com

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vestibular schwannomas (tumors on the nerves responsible for hearing and balance) and other CNS tumors like meningiomas and spinal schwannomas.[5]

This case report describes a patient with NF-1 who experienced progressive cutaneous lesion growth during pregnancy, highlighting the challenges in clinical management and the importance of a multidisciplinary approach. We also discuss the potential implications of pregnancy on the natural history of NF-1, including maternal and foetal outcomes, anesthetic considerations, and the need for genetic counselling.

2. Case Report

A 25 years old multigravida with a obstetric score of G3P1L1A1, booked and immunized presented first to our hospital at 24 weeks of gestation for routine antenatal care.

The patient gave history of multiple nodular cutaneous lesions since childhood and clinically diagnosed as a case of neurofibromatosis.

No H/O headache, visual or hearing disturbances, hypertension or poor balance. No skeletal deformities noted and IQ normal.

Patient had no significant family history or past medical history.

2.1. Obstetric history

The patient is a G3 woman with a history of one full-term lower segment caesarean section (LSCS) performed for fetal distress. The delivery resulted in a healthy female infant weighing 2.7 kg, who is now six years old. During that pregnancy, the patient had a history of exaggerated cutaneous lesions, which showed noticeable improvement postpartum.

Spinal anesthesia was initially planned for the LSCS but was unsuccessful, and general anesthesia was subsequently administered.

The patient's second pregnancy ended in early pregnancy failure and was managed medically. The current (third) pregnancy is a spontaneous conception. The patient presented for the first antenatal visit at 24 weeks of gestation. The antenatal period has been uneventful so far.

On physical examination she was moderately built and nourished with normal vitals.

Few dark brown papules of 0-.5 – 1 cm noted primarily in the back, chest abdomen and arms – clinically consistent with neurofibromatosis. Lesions were non – tender, soft in consistency and with no history of itching.

Hyperpigmented patches suggestive of café au lait [> 6 in number] and palmo-plantar freckling noted with no tenderness. No kyphosis / scoliosis.

Ophthalmologic and neurologic examination revealed no abnormality.

Patient came for regular antenatal checkup and lesions found to progressively increase in size and number compared to the first trimester. There were no constitutional symptoms.

Routine investigations / ultrasonography for fetal well being – normal.

Dark brown papules increased in number and reached the size of a lemon. Lesions were soft, few lesions were cystic in consistency. Multiple neurofibroma lesions seen over the suprapubic transverse scar as seen in **Figure 1**.

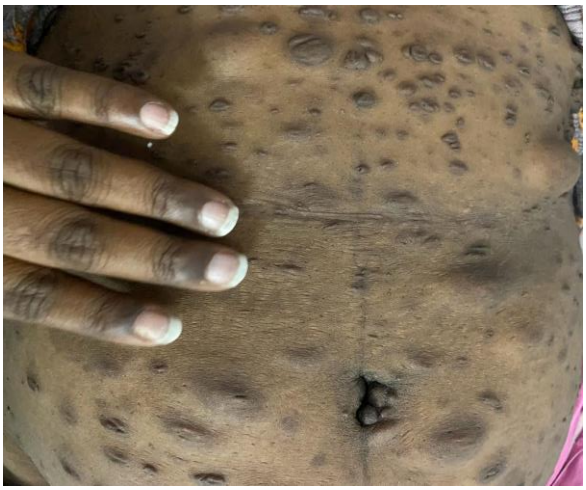

Figure 1: Multiple neurofibroma lesions seen over the suprapubic transverse scar

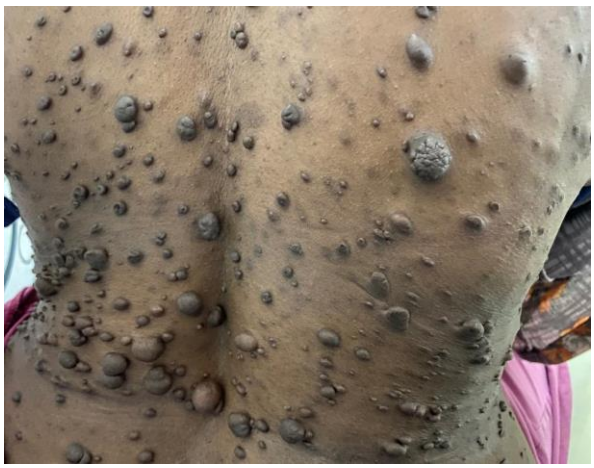

Figure 2: GA given as extensive lesions present over the spinal region

Obstetric examination revealed a term fetus in cephalic presentation with good FHR.

The patient was planned for elective repeat LSCS at 38 weeks of gestation.

Anesthetist opinion was taken for the choice of anesthesia. GA given as extensive lesions present over the spinal region as seen in **Figure 2**.

Conventional pfannensteil incision could not be given due to presence of extensive lesions. Hence skin incision given over the suprapubic region, free of lesions.

2.2. Baby details

Alive term healthy female baby, 2.475 kgs and APGAR of 8/10, 9/10. No skin lesions present in the baby. She was advised regular post natal follow up and also for genetic testing for NF-1 mutations for baby.

The lesions began to reduce post partum. The size and number of the lesions were found to be considerably decreased by about 4-6 weeks.

3. Discussion

3.1. Neurofibromatosis type 1 (NF-1) in pregnancy: A brief overview

NF-1 is typically diagnosed in childhood, with its progression during pregnancy less well understood due to limited case reports. Although common in the general population, newly diagnosed NF-1 during pregnancy is rare, as most cases are identified early due to characteristic features like café-au-lait spots and neurofibromas.

Pregnancy-related hormonal changes can unmask previously undiagnosed NF-1 or exacerbate symptoms. This case underscores the challenges of managing NF-1 during pregnancy, including lesion progression, anesthetic considerations, and risks to both mother and fetus.[3]

3.2. Pathophysiology and impact of pregnancy on NF-1

Pregnancy-induced hormonal changes, especially elevated estrogen and progesterone, can stimulate fibroblast proliferation, leading to growth and increased neurofibromas.[6] These changes also affect lesion vascularity, causing edema and cystic degeneration, as observed in this case. Pregnancy-related immunological shifts towards a Th2-dominant response may influence neurofibroma growth and progression.[7] While most lesions remain benign, there is a rare theoretical risk of malignant transformation to malignant peripheral nerve sheath tumors (MPNSTs).[8]

The patient had a history of a term lower segment cesarean section (LSCS) with extensive cutaneous lesions and an early pregnancy loss. The current pregnancy was managed with routine antenatal care, with a healthy fetal outcome.

Given the extensive lumbar and sacral lesions, an elective repeat LSCS was advised. Spinal anesthesia was deemed unsafe due to potential infection and anatomical challenges. A suprapubic incision, free from lesions, provided safe surgical access, with general anesthesia selected to minimize risks to both mother and fetus.

NF-1 is an autosomal dominant disorder with a 50% chance of transmission to offspring if one parent carries the mutation.[9] The newborn in this case was healthy at birth, with no signs of NF-1, though manifestations may appear later. Fetal complications can arise from genetic inheritance or maternal health issues during pregnancy.

NF-1 symptoms vary in severity, even among individuals with the same mutation, with some showing no signs at birth and others developing symptoms later. The condition is associated with increased risks of pregnancy complications, including miscarriage, preterm delivery, pre-eclampsia, IUGR, stillbirth, and HELLP syndrome.[4]

Our patient experienced no major pregnancy complications, except for a low birth weight baby. Vigilant monitoring and follow-up are essential. NF-1 manifestations include café-au-lait spots, neurofibromas, freckling, Lisch nodules, skeletal abnormalities, and optic pathway gliomas. Inherited NF-1 may lead to learning disabilities, ADHD, cognitive delays, and increased preterm birth risk.[10] Regular follow-ups, including growth assessments and ophthalmologic screening, are crucial. Genetic counseling and testing were recommended for the newborn to enable early detection and management of potential complications.

The patient showed significant regression of neurofibromas within 4–6 weeks postpartum, likely due to the rapid decline in estrogen and progesterone levels, which had previously promoted lesion growth. Reduced vascularity and hormonal stimulation contributed to this improvement.[6]

Anesthetic management in NF-1 patients is challenging due to extensive cutaneous lesions, with general anesthesia posing risks like airway complications and drug interactions, necessitating multidisciplinary care.[11] Monitoring for rare malignant transformation to MPNSTs is crucial, especially with rapid lesion growth, pain, or neurological changes. The psychosocial impact of NF-1, particularly during pregnancy, requires supportive counseling and care.[12]

4. Future Directions and Research Implications

This case highlights the need for further research on NF-1 management during pregnancy, focusing on longitudinal studies of disease progression, anesthetic safety protocols for pregnant patients, and genetic studies to identify modifiers affecting disease severity.

5. Conclusion

This case highlights the dynamic nature of NF-1 during pregnancy, with potential for rapid progression of cutaneous lesions due to hormonal and immunological changes. It emphasizes the need for multidisciplinary management involving obstetricians, dermatologists, anesthesiologists, and genetic counselors to ensure optimal maternal and fetal outcomes. Additionally, it underscores the importance of genetic counseling and follow-up for offspring to monitor for signs of NF-1.

Future research should focus on larger cohorts to better understand the long-term outcomes of NF-1 in pregnancy and the impact of hormonal changes on disease progression.

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7. Conflict of Interest

None.

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