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## Pregnancy and neurofibromatosis type 1- challenges in anesthesia: A case report

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### Abstract

Neurofibromatosis is a multisystem disorder with a relentless course. It poses a particular challenge to the anesthesiologist due to involvement of airway, spine, central and peripheral nervous system with systemic neurohormonal implications that can all lead to an adverse intraoperative course. Hence an understanding and detailed evaluation of systemic and local involvement of NF-1 is essential. Pregnancy has additional implications in a patient of NF-1, with an increase in size of neurofibromas, IUGR, preterm labour, hypertension secondary to pheochromocytoma, to name a few. We present the case of a 38 weeks pregnant 29-year-old female with NF-1 who underwent LSCS under spinal anesthesia and had an uneventful recovery. Our aim is to understand the anesthesia implications of NF-1 and present our unusual case.

**Keywords:** Neurofibromatosis, hyperbaric ropivacaine, spinal anesthesia

### Introduction

Neurofibromatosis is a hereditary, single gene, neurocutaneous disorder that is inherited in an autosomal dominant pattern <sup>[1]</sup>. Although half of the cases of NF1 are familial, the other half result from spontaneous new mutations, and hence may be seen in families with no history of the disease <sup>[2]</sup>. NF-1 has multisystem manifestations involving CNS, cardiovascular, respiratory, cutaneous and musculoskeletal systems to name a few <sup>[3]</sup>. These ultimately influence airway management and respiratory, cardiovascular, central and peripheral nervous system involvement, vertebral anomalies thereby make the choice of general versus regional anesthesia complex. Co-existing cranial or spinal neuromas can worsen the neurological status of even an asymptomatic patient in regional anesthesia and make GA the preferred method <sup>[4]</sup> Patients of NF-1 during pregnancy need extensive preoperative examination and work up, planned method of anesthesia considering systemic and local manifestations of the disease and critical monitoring during the Intraoperative period for an uneventful anesthesia and recovery <sup>[5]</sup>.

### Case Report

A 29 year old, G2P2L1 female was admitted to Obstetrics Department of PDMMC, Amravati with history of 38 weeks of amenorrhea. She also had pregnancy induced hypertension (PIH) diagnosed during 6th month of gestation. She did not give history of vomiting, blurring of vision, seizures or loss of consciousness. Her blood pressure was controlled with tablet Nicardipine 100 mg twice a day along with tablet Labetalol 100 mg thrice a day. She had NF-1 for 14 years of age, without any multisystem involvement or neurodeficits. She didn't have any issues in previous full-term vaginal delivery four years ago. Although she met NF-1 criteria, she didn't have any family history for the same and there was no flare up of the disease during both pregnancies. She had no past surgical history and was never exposed to anesthesia. On examination, a 75 kg female, with BMI of 26 kg/m<sup>2</sup>, conscious and well oriented to time, place and person. Her heart rate was 89 beats/min, blood pressure was 140/70 mmHg, respiratory rate 18 cycles/min. Her oxygen saturation was 98% on room air and she had pedal edema. She had adequate urine output. CNS examination didn't reveal any signs of raised intracranial pressure and she had a normal sensory and motor examination. Cardiovascular and respiratory examinations were normal. Per abdomen examination was consistent with 38 weeks gestation, cephalic presentation and present fetal heart sounds.

Patient had mouth opening of 3 fingers, MPG 2, thiopental distance of > 5 cm, normal neck movements, no or pharyngeal edema, no gum hypertrophy, and no visible neurofibromas on airway examination. On examination of spine, there were multiple neurofibromas from cervical to sacral region. There was presence of lumbar lordosis and no presacral edema. Patient's hemogram, liver and kidney function, coagulation profile were all within normal limits. Ultrasound abdomen suggested a single live intrauterine fetus, no IUGR and normal Doppler. MRI spine was planned but patient went into spontaneous labor before that could be done. However labor did not progress, leading to fetal deceleration, making emergency LSCS a strong indication. Patient was posted for emergency LSCS.

Under all aseptic precautions, spinal anesthesia was given in right lateral position in a single prick with 25g needle at L3-L4 intervertebral space with Injection Ropivacaine 0.75% (heavy), 2 ml with 60 mcg Buprenorphine. The onset of action was 3-5 minutes and level achieved was T4. Post LSCS bilateral TAP block was given with 20ml 0.375% Ropivacaine which covered somatic pain off nearly 10 hours with a VAS score of 2-3. LSCS was uneventful, patient delivered a 2.8kg healthy child and both mother and baby got discharged 3 days post operation.



**Fig 1:** Oral cavity no visible neurofibromas



**Fig 2:** Lumbar spine multiple neurofibromas

## Discussion

The earliest reports of neurofibromatosis date back to 16th century [6]. Although Robert W. Smith from Dublin was the first person to review the disease in 1849, it was Friedrich Von Recklinghausen, a German pathologist who ascertained that the tumor arises from nervous tissue in 1882, thereby giving the disease its alias of Von Recklinghausen's disease [7]. Neurofibromatosis 1 has an autosomal dominant pattern of inheritance, with a single gene mutation on chromosome 17q11.2 [8]. NF1 expresses complete penetrance and variable expressivity [9]. NF1 is characterized by a loss of function mutation in one NF1 allele which encodes the protein Neurofibromin, that is involved in regulation of development and growth of a variety of tissues [10]. Diagnostic criteria for NF-1 developed by National Institute of Health (NIH) Consensus Conference in 1987, need 2 or more of the following; 6 or more CALMs > 5mm in prepubertal children or >15mm in post pubertal patients, 2 or more of any type of neurofibroma or 1 plexiform neurofibroma, axillary or inguinal freckling, 2 or more Lisch nodules of iris, a distinct bony lesion, an optic nerve glioma, or a first degree relative with NF-1 [11]. In addition to cutaneous manifestations, NF-1 has skeletal, neurological, cardiac and vascular manifestations. Cumulatively these pose a challenge to the anesthesiologist. Detailed pre-operative assessment and evaluation of systemic manifestations of NF-1 is necessary due to airway, neuraxial and other systemic manifestations that may preclude smooth anesthesia and recovery.

NF-1 has varied effects on the nervous system. CNS tumors may warrant surgery. Brainstem tumor's may result in hypoventilation and delayed weaning from mechanical ventilation [12]. NF-1 associated vasculopathy of major cerebral vessels can lead to stenosis/ aneurysm and pose a risk for aneurysm rupture and stroke if careful control of arterial pressure is not exercised. NF-1 in oropharynx and trachea can interfere with intubation. Fiber optic bronchoscopy may aid such situations [13]. Upper airway obstruction may even warrant an emergency cricothyroidotomy or tracheostomy [14, 15]. NF-1 can also occur in nasal, sinus and maxillo facial cavities and test the anesthesiologist [16]. A detailed cardiovascular examination of NF-1 patients is essential as multiple heart defects, cardiomyopathy, vasculopathy and hypertension have been reported in these patients [17]. Vena cava compression leading to decrease preload and hence hypotension, delayed response to fluid resuscitation and co existing undiagnosed pheochromocytoma may all lead to an intraoperative catastrophe. Preoperative echocardiography, chest X-ray, CT scan of chest, blood pressure screening and close Intraoperative monitoring of heart rhythm and blood pressure is necessary. The anesthesiologist should be wary of a coexisting pheochromocytoma or carcinoid tumor. NF-1 associated vasculopathy may involve any and every major vessel presenting with stenosis, aneurysms and arteriovenous malformations. Neurofibromin deficiency in the vessel endothelial and smooth muscle cells may lead to diseases of aortic, renal, mesenteric, iliofemoral, intra cerebral, carotid, vertebral, subclavian, axillary and coronary vessels [18]. Neurofibromin is also crucial for hemostasis as it regulates cellular- endothelial interaction post vessel injury and these patients have poor hemostasis. [19] Musculoskeletal sequelae of NF-1 such as kyphoscoliosis, pseudarthroses and spinal cord tumours

pose a challenge during spinal anesthesia. Additionally, chest wall deformities can cause a reduction in lung volume and capacity and compromise respiratory function during anesthesia [20, 21]. Gastrointestinal tumors associated with NF-1 such as pheochromocytoma, GIST, carcinoid are associated with neurohumoral consequences that may result in hypertensive crisis, arrhythmias, bronchoconstriction and multiorgan dysfunctions [22, 23]. Alpha antagonist for pheochromocytoma and octreotide for carcinoid need to be considered, particularly when planning their excision.

An important consideration is giving anesthesia to a pregnant female with NF-1. Neurofibromas may increase in size in pregnancy and consequently increase intracranial pressure, cause IUGR, still births and even preterm labor [24]. Pregnancy may attenuate NF-1 associated hypertension. It is ideal to perform lumbosacral imaging prior to anesthesia in such patients [25, 26]. Since our patient had NF-1 with PIH, she needed a more thorough planning. Let us consider the pros and cons of both Spinal and General anesthesia in our patient. We used ropivacaine 0.75% heavy for spinal anesthesia in this patient, also since the patient had PIH, ropivacaine provided more hemodynamic stability.

**Table 1:** General Anesthesia

Pros	Cons
Better control of vital parameters	In full stomach, chances of aspiration
Useful in cases of raised ICT	Difficult airway in NF-1
Indicated in NF-1 with brain/spinal tumours	Pulmonary edema in PIH
coagulopathy in PIH is an absolute contraindication for spinal	Poor lung compliance due to vertebral anomalies in NF-1
For airway protection in active seizures with NF-1/ PIH	In PIH, MgSO <sub>4</sub> can cause delayed recovery due to NMDR action prolongation
In acute fetal distress	Increased uterine atony
Extensive neurofibromatosis over the back with no space for spinal/epidural	Increased LOS
NF-1 with kyphoscoliosis (relative indication)	

**Table 2:** Spinal Anesthesia

Pros	Cons
Avoid difficult airway (pregnancy, PIH, NF)	NF often associated with kyphosis and scoliosis making spinal anesthesia difficult
Safer in parturient and PIH cases	Intracranial and spinal tumours with raised ICT is an absolute contraindication
Less risk of aspiration (parturient with full stomach)	Risk of hemorrhage, stroke, death
Relative contraindication in NF-1 (with spinal cutaneous lesions)	Risk of local infection and bleeding from NF.
if MRI brain and spine normal, no contraindication	Partial/ inadequate effect as nerve roots are involved.
	Epidural technically difficult

Ayoub *et al*, report a case of emergency LSCS under general anesthesia for a patient with NF-1 [27]. Yong Lee *et al* report a case of NF-1 with preeclampsia comparable to ours where spinal anesthesia was given [28]. Another case reported by Singh *et al*, where spinal anesthesia was given to a patient of neurofibromatosis 1 with preeclampsia for

LSCS, considering complications of general anesthesia in a parturient hypertensive such as intracranial hemorrhage or pulmonary edema due to rise of blood pressure during endotracheal intubation [29]. Demir *et al* report a similar case of emergency LSCS in a patient if NF-1 with severe kyphoscoliosis where subarachnoid block was preferred [30]. Another important consideration is drugs used to anaesthetize such patients. We used ROPIN heavy which is 0.75% hyperbaric Ropivacaine which has comparable efficacy but better safety profile when compared to 0.5% hyperbaric bupivacaine when given by spinal route.

### Conclusion

Due to multisystem involvement of NF-1, it's management should have a multidisciplinary approach. Decision of type of anesthesia depends on patient presentation, systemic manifestations and local involvement. Anesthesiologist must exercise extreme caution and vigilance due to its widespread and varied presentations and unpredictability. We suggest spinal anesthesia for a patient of NF-1 for LSCS in the absence of central and peripheral nervous system involvement.

### Abbreviations

Neurofibromatosis 1 (NF1), CNS- central nervous system, GA- General Anesthesia, MPG- Mallam Patti Grade, IUGR- intrauterine growth retardation, MRI- Magnetic Resonance Imaging, LSCS- Lower segment caesarean section, TAP- Transversus abdominus plane block, VAS- visual analogue scale for pain, CALM- cafe-au-lait macules, CT- computed tomography, GIST- Gastrointestinal stromal tumours, LOS- length of hospital stay, ICT- intracranial tension, NMDR- non depolarizing muscle relaxants

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