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Anaesthetic challenges and implications in patient with neurofibromatoses posted for Whipple's surgery: A case report

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Abstract

Background: Neurofibromatosis Type 1 or Von Recklinghausen disease is a group of autosomal dominant disease that have widespread effect on ectodermal and mesodermal tissue. Neurofibromas are the characteristic lesions of the condition that occur not only in the neuraxis but can also be found in the oropharynx and larynx; making laryngoscopy and tracheal intubation difficult. Neurofibromas may also affect the gastrointestinal tract and carcinoid tumours may be found in the duodenum.

Aim: We report a case of 50-year-old male patient with NF1 posted for Whipple's surgery. This study discusses the aetiology, clinical presentation and anaesthetic challenges of neurofibromatosis with its significance to the anaesthetist. We did a brief review so as to optimise anaesthetic management and reduce the complications associated with systemic manifestations of this syndrome.

Case Report: A 50-year-old male patient with neurofibromatosis 1 was diagnosed with periampullary carcinoma. He presented with yellowish discolouration of eyes and urine for one month, associated with abdominal pain but with no h/o fever, GI bleed, abdominal distention. He had multiple small neurofibromas all over the face, body, back, hands and the nape of neck. A difficult yet successful epidural was inserted in T9-T10 space keeping in mind various spinal abnormalities that occurs in these patients. Presuming it to be difficult airway, patient was intubated with C-MAC. The histopathological report of the Periampullary specimen showed mucosa with small areas of neuroendocrine tumour (CK and Synaptophysin positive).

Result and Conclusion: The surgery was conducted successfully and the patient was extubated. This case report demonstrates the importance of knowing the peculiarities of neurofibromatosis presenting for surgery so that a systematic approach to the pre-operative assessment of these patients can result in rational perioperative management.

Keywords: Neurofibromatosis, anaesthetic challenges, complications, Whipple's surgery

Introduction

Neurofibromatosis is a group of autosomal dominant disease that have widespread effect on ectodermal and mesodermal tissue. They represent the most common example of the neurocutaneous syndromes, a group that also includes tuberous sclerosis, von Hippel- Lindau disease and the basal nevus syndrome^[1]. Neurofibromas are the characteristic lesions of the condition and not only occur in the neuraxis but may also be found in the oropharynx and larynx; these may produce difficulties with laryngoscopy and tracheal intubation. Pulmonary pathology includes pulmonary fibrosis and cystic lung disease. The cardiovascular manifestations of NFI include hypertension, which may be associated with phaeochromocytoma or renal artery stenosis. Neurofibromas may also affect the gastrointestinal tract and carcinoid tumours may be found in the duodenum. Although the neurofibromatosis have common characteristics, two distinct forms have been recognized neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2).

Neurofibromatosis type 1 (von Recklinghausen's neurofibromatosis, peripheral neurofibromatosis)

The birth incidence of NF1 lies between 1 in 2500–3300 and its prevalence in the population is 1 in 5000^[2]. The gene for NF1 has been localized to chromosome 17q 11.2 and the protein has been named neurofibromin which appears to have a tumour suppressive role. Mutations at the NF1 gene result in diminished levels of neurofibromin with resultant development of the wide variety of tumours seen in the disease.

Diagnostic Criteria For Nf1: - [3] The patient should have two or more of the following:

- Six or more cafe´-au-lait spots
1.5 cm or larger in post-pubertal individuals
0.5 cm or larger in pre-pubertal individuals
- Two or more neurofibromas of any type or one or more plexiform neurofibroma
- Axillary or groin freckling
- Optic glioma
- Two or more Lisch nodules (benign melanotic iris hamartomas)
- A distinctive bony lesion
- Dysplasia of the sphenoid bone
- Dysplasia or thinning of long bone cortex
- A first degree relative with NF1



Fig 1a: Cafe-au-lait spots



Fig 1b: Axillary freckling



Fig 1c: Plexiform neurofibroma



Fig 2a: Optic glioma



Fig 2b: Lisch nodule

Other tumour found in NF1

Phaeochromocytoma occurs more commonly in NF1 patients than in the general population [4]. Although the features of some of the Multiple Endocrine Neoplasia (MEN)_syndromes overlap with NF1 (e.g. neural crest origin tumours), no association between the two conditions has been established. Intestinal tumours are commonly seen in NF1 patients and interestingly have a predilection for the duodenum and especially the ampulla of Vater [5]. Malignant gliomas are found in approximately 2% of patients with NF1 [6]. Finally, the association of juvenile chronic myeloid leukaemia with NF1 has helped in the identification of the role of the NF1 gene as a tumour suppressive gene [7]. Carcinoid tumours have been described in NF1. An unusual feature of the carcinoid tumour occurring in NF1 is the predilection for the duodenum and especially the ampulla of

vater. Patients may present with jaundice or upper gastrointestinal haemorrhage or obstruction; often, by the time a diagnosis is reached, metastases are present in the liver. The subsequent release of vasoactive peptides may result in patients presenting with the carcinoid syndrome of flushing, diarrhoea, bronchoconstriction and right heart lesions. Anaesthesia and surgery may be hazardous in this situation.

Neurofibromatosis type 2 (bilateral acoustic neurofibromatosis, central neurofibromatosis)

The birth incidence of NF2 lies between 1 in 33000–40000 with a prevalence within the population of 1 in 210000 [8]. NF2 gene has been shown to reside on chromosome 22q 12.1. The defining feature of NF2 is the presence of bilateral vestibular schwannomas—tumours arising from the

vestibular branch of the VIII cranial nerve. Patients typically present with a gradual, progressive and often asymmetrical hearing loss although sudden hearing loss may occur^[9].

Diagnostic criteria for NF2: The following features confirm NF2:

- Bilateral vestibular schwannomas (VS)
Or
- Family history of NF2 (first degree relative) plus:
 1. Unilateral vestibular schwannoma in patient <30-year-old; or
 2. Any two of the following: meningioma, glioma, schwannoma, juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract.
- The following features indicate probable NF2:
- Unilateral vestibular schwannoma in patient <30 yr old plus at least one of the following: meningioma, glioma, schwannoma, juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract.
- Multiple meningiomas (two or more) plus unilateral vestibular schwannoma in patient <30 yr old or one of the following: glioma, schwannoma, juvenile posterior subcapsular lenticular opacities/juvenile cortical cataract.

Clinical Case

We present a case of a 50-year-old patient who came to our hospital with the chief complaints of yellowish discoloration of eyes and urine for one month. It was associated with generalised abdominal pain, mild in intensity and non-radiating in nature but no h/o fever, GI bleed, abdominal distention or significant vomiting. No

fibromas of the oral cavity or predictors of a difficult airway were found during airway exploration. The patient did not report dyspnoea, dysphagia or changes in voice tone that could suggest the presence of laryngeal fibromas. No signs and symptoms of carcinoid syndrome like flushing, diarrhoea, bronchoconstriction, right heat lesions were noted and neither was there any history of DM, HTN, CAD, BA, TB, Thyroid dysfunction, Seizure, Stroke, Covid infection, Visual disturbances. Patient also did not receive any Chemotherapy, Radiotherapy in the past & nor were there any past surgical history. CECT W/A: showed an ampullary mass measuring 2.3*1.9 cm causing gross upstream dilatation of CBD, bipolar IHBRD, ventral pancreatic duct and distension of gall bladder. Histopathology & Cytology of the Periapillary specimen showed mucosa with small areas of neuroendocrine tumour (CK and Synaptophysin positive). Additional tests included biochemistry, whole blood count, coagulation tests and a chest radiograph, all of which came back normal. So, depending upon the S/S, investigations and examination, the diagnosis of Ca periampullary carcinoma was made and the patient was planned on Whipple's Pancreaticoduodenectomy.

On the day of surgery my patient was given premedication in the form of tablet Pantocid (40mg) and tablet Granicep (2mg), 1 hour prior to shifting him in the OT. After taking him inside, on the table, all non-invasive monitors were applied (ECG, Pulse oximeter, NIBP) and in sitting position his spine was again evaluated for the possibility of epidural anaesthesia. Thereafter a challenging yet successful epidural anaesthesia was administered at (T9-T10) level via LOR technique at a depth of 5 cm. Successful epidural placement was confirmed with the test dose of 3ml (Lox+adr).

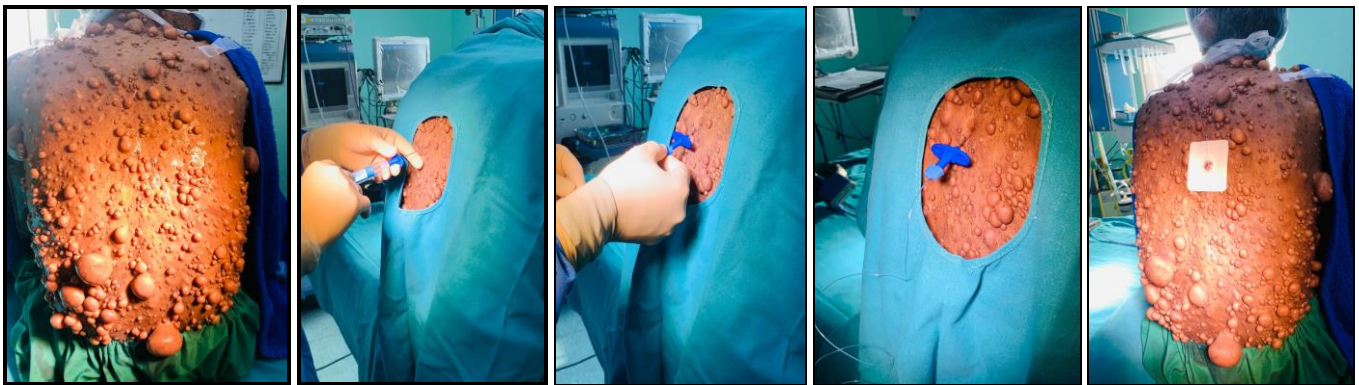


Fig 3: Patient positioning for epidural insertion, Part preparation and epidural needle with catheter insertion

After a difficult epidural anaesthesia we next decided to intubate the patient, keeping in mind the possibility of difficult airway with all equipments ready, in case of an emergency. The patient was induced with injection fentanyl 130mcg, injection propofol 120mg and injection succinylcholine 75mg. There was no airway obstruction after induction during manual ventilation with a facial mask.

Endotracheal intubation proceeded uneventfully with the help of videolaryngoscope (Cmac with D blade) and mechanical ventilation was instituted. The correct position of the tube was confirmed with capnography and auscultation. Laryngoscopy did not reveal gross laryngeal fibromas. Sevoflurane at 1 MAC and fentanyl according to analgesic needs were used during anaesthetic maintenance.



Fig 4: ETT Insertion, Left Radial artery Cannulation

WPD is a major abdominal surgery with risk of many hemodynamic fluctuations and blood loss, so we decided to use invasive monitoring for this case by inserting a CVP line and an intra-arterial line (preferably Radial artery). Triple lumen CVP line was inserted into the right internal jugular vein under USG guidance. Similarly, after

performing an Allen's test on both sides, left sided radial artery cannulation was done using USG probe. Insertion of all invasive monitors along with IV cannulation was yet another challenging task because of numerous neurofibromas present at the site of cannulation.



Fig 5: 16 G IV Cannulation, Right IJV Central line insertion

The entire surgery lasted for about 6.5 hrs during which, there was an inadvertent lesion of the superior mesenteric artery which evolved with hemodynamic instability, haemorrhagic shock and the need for clipping of the vessels. The mean arterial pressure fell to 42mmhg but with the administration of colloids and norepinephrine (0.3mcg/kg/min) rapidly increased to 60mmhg. Once the patient was stabilised, an ABG was sent showing the haemoglobin concentration of 7.2g/dl. As the baseline haemoglobin of the patient was low and considering the possibility of further blood losses because of the type of the surgery, we decided to transfuse 2 units of PRBC's and 2 units of FFP to the patient. Thankfully, the bleeding was well controlled and the rest of the surgery proceeded uneventfully. At the end of the surgery, after repeating an ABG showing the hb of 8.9 g/dl and patient being hemodynamically stable with no requirement of any further vasopressors/inotropes, the decision was made to extubate the patient. He was given Inj Ranitidine 50mg, Inj ondansetron 4mg, Inj Glycopyrrolate 0.5mg and Inj. neostigmine 2.5mg, and was extubated upon reaching a train-of-four value of 0.9. Upon extubation VAS score recorded was 0 and the recovery was smooth. The patient was then taken to the SICU and had a favourable course.

Discussion

Neurofibromatosis (NF) is a group of autosomal dominant neurocutaneous phakomatoses which includes tuberous sclerosis complex, Hippel–Lindau syndrome and the basal-cell nevi syndrome^[10]. It is possible to distinguish two types of neurofibromatosis on the basis of the phenotypical and genetic characteristics: NF1 or VR and neurofibromatosis type 2 (NF2).

The incidence of VR is 1 in every 2500–3300 births^[11] and the prevalence is 1 in every 5000 inhabitants. Although it has a 100% penetrance, expression varies^[12] with 50% of the patients having no family history, which implies a spontaneous mutation^[12].

Café-au-lait spots are found in 95% of adults with VR. Neurofibromas are the most characteristic lesion^[13] representative of this disorder.

Lisch nodules are present in 95% of cases. They may be associated with bone abnormalities, pheochromocytoma^[14, 15], gut tumours^[16], carcinoid tumours, spinal or cerebral^[17], vertebral deformities, juvenile chronic myelogenous leukaemia, and growth and mental retardation. Neurofibromatosis type 2 is diagnosed on the basis of a series of clinical criteria, defined by the presence of bilateral vestibular schwannomas leading to hearing loss, cataracts,

and central nervous system involvement, such as meningioma. VR poses a challenge to anaesthetists, including a potentially difficult airway, abnormalities of the spinal anatomy and peripheral neurofibromas; [18] hence the need for a careful systemic assessment before selecting the anaesthetic technique [19].

Anaesthetic challenges of NF1

Systems	Comments
Airway	Neurofibroma of tongue, pharynx or larynx may interfere with tracheal intubation. Suspicion raised by history of dysphagia, dysarthria, stridor or change of voice.
Respiratory system	Intrapulmonary neurofibroma, pulmonary fibrosis may produce cough and dyspnoea Right ventricular failure may be present Scoliosis/kyphosis may compromise lung function.
Cardiovascular system	Raised arterial pressure usually essential hypertension but consider pheochromocytoma or renal artery stenosis Hypertrophic cardiomyopathy may occur Mediastinal tumours may result in superior vena caval obstruction.
Central nervous system	Cerebral and spinal neurofibromas common. Increased incidence of epilepsy and learning disorders. Cerebrovascular disease may co-exist.
Gastrointestinal tract	Intestinal tumours may present with pain, gastrointestinal haemorrhage or perforation. Carcinoid tumours occur in duodenum and may result in jaundice and carcinoid syndrome.
Genitourinary system	Neurofibromas may cause ureteric/urethral obstruction.
Musculoskeletal system	Vertebral deformities or spinal cord tumours may make spinal/extradural techniques difficult.

Classically, general anaesthesia has been considered safer since the presence of intracranial neuromas or the existence of unknown spinal neuromas (up to 40% of cases) may worsen the neurological picture when locoregional anaesthetic techniques are used [19, 20], with devastating consequences such as haematomas and paralysis.

Therefore, as anaesthetists we are required to perform a thorough assessment to identify difficult airway predictors, as well as an adequate interview designed to detect intraoral lesions [21]. If a difficult airway is expected, awake fibre optic bronchoscopy intubation must be considered as the technique of choice [21]. Multisystem involvement in VR requires special attention to other potential intra-operative findings such as hypertension, which could be related with an unknown pheochromocytoma (up to 20% of patients with VR) or renal artery stenosis. Other causes of pheochromocytoma that need to be ruled out include von Hippel-Lindau syndrome, multiple endocrine neoplasia Type 2B (MEN 2B) and paraganglioma syndromes [22].

Other considerations include respiratory compromise with intrapulmonary fibromas and pulmonary fibrosis, and cardiovascular compromise with hypertrophic cardiomyopathy or mediastinal tumours compressing the superior vena cava, beside hypertension. The presence of scoliosis compromises cardiopulmonary function, leading to right ventricular failure [11]. Also conditions like epilepsy, carcinoid tumours and obstructive ureteral stenosis due to neurofibromas must be ruled out [11]. If we see the pharmacology of drugs there have been many reports

suggesting an increased sensitivity of patients with NF1 to non-depolarizing neuromuscular blocking drugs [23,24, 25, 26, 27, 28]. In addition, the sensitivity to succinylcholine has been reported as increased, decreased or normal. A large retrospective study of patients given succinylcholine and/or a variety of non-depolarizing neuromuscular blocking drugs with neuromuscular monitoring excluded any definite abnormal response to the relaxants given. It was thus concluded that patients with neurofibromatosis react in a normal fashion to neuromuscular blocking drugs. However, patients with neurofibromatosis should have neuromuscular transmission monitored when neuromuscular blocking drugs are used. This is especially pertinent in NF1 patients with renal impairment or those on concurrent medication (e.g. anticonvulsant drugs), which may interfere with the normal pharmacokinetics or pharmacodynamics of neuromuscular blocking drugs.

Summary and Conclusion

We reviewed the existing literature in order to avoid deleterious effects from our clinical anaesthesia practice because of the multi-organ involvement in a disease that may give rise to multiple perioperative adverse events. Despite various challenges that were encountered during epidural placement, invasive lines insertion, induction and intraoperative adverse events, a successful surgery was conducted which once again highlights the importance of knowing the peculiarities of neurofibromatosis presenting for surgery so that a systematic approach to the pre-operative assessment of these patients can result in rational perioperative management.

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