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REVIEW ARTICLE

Neurofibromatosis: clinical presentations and anaesthetic implications

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The neurofibromatoses are autosomal dominant diseases that have widespread effects on ectodermal and mesodermal tissue. The commonest member of the group is neurofibromatosis type 1 (NF1) which varies in severity but which can affect all physiological systems. Neurofibromas are the characteristic lesions of the condition and not only occur in the neuraxis but may also be found in the oropharnyx and larynx; these may produce difficulties with laryngoscopy and tracheal intubation. Pulmonary pathology includes pulmonary fibrosis and cystic lung disease. The cardiovascular manifestations of NF1 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. This review documents the aetiology and clinical manifestations of the neurofibromatoses and discusses their relevance to the anaesthetist.

The neurofibromatoses are a group of hereditary diseases transmitted in an autosomal dominant fashion and are characterized by a tendency to formation of tumours of ectodermal and mesodermal tissues. 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.[52]

Although the neurofibromatoses have common characteristics, two distinct forms have been recognized on clinical and genetic grounds. These are designated neurofibromatosis type 1 (NF1) and neurofibromatosis type 2 (NF2).

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

Reports detailing probable cases of neurofibromatosis have appeared since the 16th century.[3] The first review of the disease was published in 1849 by the Dublin Professor of Surgery, Robert W. Smith,[94] who suggested that the origin of the tumours was the connective tissue surrounding small nerves.[34] It was Freidrich von Recklinghausen in 1882 who first recognized that the tumours that characterize the disease arise from nervous tissue;[106] his name has since been inextricably linked with the condition.

Genetics and pathophysiology of NF1

The birth incidence of NF1 lies between 1 in 2500–3300 and its prevalence in the population is 1 in 5000;[13] it is inherited in an autosomal dominant manner. Although the condition shows almost 100% penetrance, it has a variable expressivity (i.e. there may be considerable variation of clinical manifestations within a family). In addition, in 30–50% of cases there is no family history; these 'sporadic' cases probably arise from (usually paternal) germ cell mutations.[68]

Using genetic linkage studies, the gene for NF1 has been localized to chromosome 17q 11.2. The gene spans over 350 kb of genomic DNA and encodes a protein containing 2818 amino acids.[55] This protein has been named neurofibromin and 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.[105]
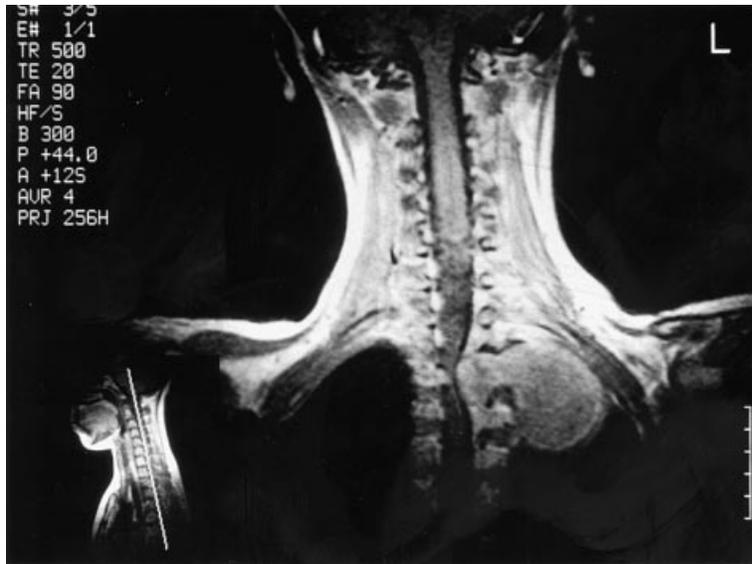
Fig 1 Coronal T_1 weighted MRI showing large dumbbell neurofibroma in T_2/T_3 intervertebral foramen and occupying the apex of the left thoracic cavity and displacing the spinal cord to the right.

Diagnostic features of NF1

Despite major advances in the molecular genetics of NF1, diagnosis remains largely based on clinical criteria (Table 1).[35]

Café-au-lait spots are symmetrical flat areas of skin hyperpigmentation with rounded edges and are seen in newborns with NF1; their number and size increase during infancy. By adulthood, about 95% of NF1 patients have café-au-lait spots. Their presence suggests NF1 although familial cafe-au-lait spots do occur rarely. In addition, 70% show freckling of the intertriginous area of the axilla or groin.[45]

Neurofibromas are the major feature of NF1 and fall into three clinically and histologically distinct types.[109] *Cutaneous* neurofibromas occur in more than 95% of patients, and are discrete, benign tumours found within the dermis. *Nodular* neurofibromas arise in peripheral nerves and may be found at any site; despite their size, they do not infiltrate surrounding tissues. Paraspinal neurofibromas may grow to an enormous size, giving rise to the classic thoracic 'dumbbell' tumour (Fig. 1).

Plexiform neurofibromas are the hallmark lesion of NF1. These occur in 30% of NF1 patients, are usually congenital, and affect long portions of the nerve involved; infiltration of the nerve itself and the surrounding tissue may occur, giving rise to extensive disfiguration. It is thought that John Merrick, the Elephant Man, may have suffered from plexiform neurofibromatosis[108] although proteus now appears to be a more likely diagnosis.[100] Apart from the obvious mechanical complications of such tumours, plexiform neurofibromas have a tendency, albeit rare, to undergo malignant change forming *malignant peripheral nerve sheath tumours*. Malignant progression occurs in 2–16%

Table 1 Diagnostic criteria for NF1

The patient should have two or more of the following:
1. Six or more café-au-lait spots
   1.5 cm or larger in post-pubertal individuals
   0.5 cm or larger in pre-pubertal individuals
2. Two or more neurofibromas of any type or one or more plexiform neurofibroma
3. Axillary or groin freckling
4. Optic glioma
5. Two or more Lisch nodules (benign melanotic iris hamartomas)
6. A distinctive bony lesion
   Dysplasia of the sphenoid bone
   Dysplasia or thinning of long bone cortex
7. A first degree relative with NF1

of patients and is the major cause of morbidity and mortality in NF1.[51]

Pilocytic astrocytomas are a benign form of astrocytoma, and when arising from the optic nerve or chiasm, are termed optic gliomas. They are seen in 15% of NF1 patients on MRI and are symptomatic in 2–5%; they are slow growing and generally do not undergo malignant change.[57]

About 95% of individuals with NF1 will develop Lisch nodules—benign multiple melanotic hamartomas of the iris.[46] Finally, distinctive bony lesions including dysplasia of the sphenoid wing and thinning of long bones contribute to the diagnostic criteria of NF1.[28]

Other tumours found in NF1

In addition to the neurofibromas that characterize the disease, other tumours occur more commonly in NF1. Phaeochromocytoma occurs more commonly in NF1 patients than in the general population.[58] Although the features of some of the multiple endocrine neoplasia

Table 2 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 yr 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

Fig 2 Contrast enhanced T_1 weighted image showing bilateral intracanalicular vestibular schwannomas (arrows) projecting into the cerebellopontine angles.
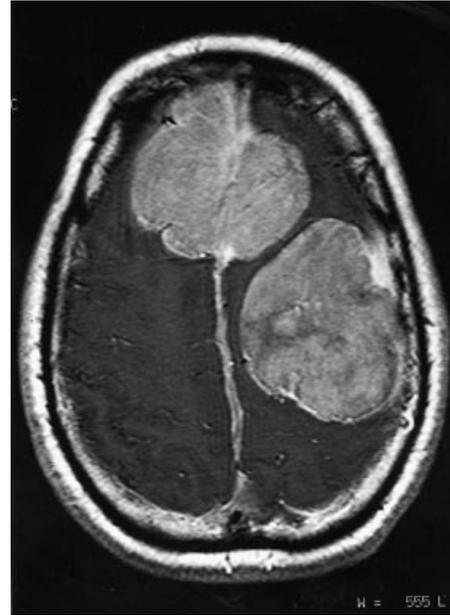

Fig 3 Frontal falx meningioma extending bilaterally and left frontoparietal convexity meningioma in same patient as Figure 2.

syndromes overlap with NF1 (e.g. neural crest origin tumours), no association between the two conditions has been established.[41] Intestinal tumours are commonly seen in NF1 patients and interestingly have a predilection for the duodenum and especially the ampulla of Vater.[50] Malignant gliomas are found in approximately 2% of patients with NF1.[102] 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]

Additional features of NF1

Patients with NF1 often demonstrate relative macrocephaly and tend to be, on average, shorter in stature. Pituitary abnormalities include growth hormone deficiency and central precocious puberty which may occur in the absence of optic chiasm gliomas;[12] radiotherapy treatment of the latter may increase the risk of growth retardation and intellectual deficits.[1] Learning disabilities occur in 50% of patients. However, the relationship between lower range IQ and the presence of so called 'unidentified bright objects' seen in the basal ganglia, thalamus and brainstem on T_2 weighted MRI imaging in 70% of patients remains controversial.[73] Mental retardation (full scale IQ less than 70) is only slightly more frequent than that of the general population. While some social handicap might be expected in severely affected sufferers, no uniform psychiatric syndrome is encountered.[67]

Other conditions which occur more commonly in the NF1 population include epilepsy,[53] headaches,[80] aqueduct stenosis[90] and hydrocephalus. Although the incidence of vestibular schwannoma is probably no greater than that of the general population, deafness is common.[16] Delayed central conduction times of auditory brain stem evoked potentials have been observed[76] and conductive hearing loss may be the consequence of bony deformity or tumour within the auditory meatus.[60]

Table 3 Anaesthetic considerations of NF1

System	Comments
Airway	Neurofibroma of tongue, pharnyx 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 phaeochromocytoma 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

Neurofibromatosis type 2 (bilateral acoustic neurofibromatosis, central neurofibromatosis)

The recognition of a group of patients with familial tendency to pass on bilateral acoustic neuromas (vestibular schwannomas) coupled with genetic studies has resulted in the recognition of NF2 as a distinct entity;[49] this division in the neurofibromatoses is important both in the management and genetic counselling of patients.

Genetics and pathophysiology of NF2

The birth incidence of NF2 lies between 1 in 33 000–40 000 with a prevalence within the population of 1 in 210 000.[44] It is inherited in an autosomal dominant fashion; however, in common with NF1, 50% of cases represent sporadic gene mutations.[27] Using genetic analysis of large pedigrees, the NF2 gene has been shown to reside on chromosome 22q 12.1 and the gene has recently been cloned. It spans 110 kb of genomic DNA and encodes a cytoskeletal protein known as merlin or schwannomin.[20] It appears that the NF2 gene acts as a tumour suppressor, both in NF2, sporadic meningiomatosis and other neuroectodermal tumours.[19] Although there appears to be some correlation between genotype and phenotype, there are exceptions. Limited gene analysis is now available and may be useful for genetic counselling.

Diagnostic features of NF2

As with NF1, diagnosis depends largely on the recognition of clinical features (Table 2). [35]

The defining feature of NF2 is the presence of bilateral vestibular schwannomas—tumours arising from the vestibular branch of the VIII cranial nerve (Fig. 2).

Patients typically present with a gradual, progressive and often asymmetrical hearing loss although sudden hearing loss may occur. The mean age of onset of symptoms is 24 yr whilst non-NF patients with sporadic tumours present in their mid-forties.[26] Whilst the occurrence of bilateral vestibular schwannomas confirms NF2, the presence of a unilateral vestibular schwannoma in conjunction with other NF2 associated features should raise the possibility of NF2.

These features result from abnormal growth in certain cell types and include meningiomas (Fig. 3), other schwannomas, gliomas and juvenile posterior subcapsular lenticular opacities and cortical cataracts. Although neurofibromas can occur, plexiform morphology is not seen in NF2. A non-specific finding in NF2 is intracerebral calcification.

Segmental neurofibromatosis

Both NF1 and NF2 can present as a non-generalized form in which only one body part is affected. This so-called 'segmental neurofibromatosis' appears to represent somatic mosaicism in which only some cells possess the NF1 or NF2 gene mutation. Depending on the segment affected, the risk to offspring may be very much lower than the 50% risk for generalized disease. Other 'incomplete' forms of neurofibromatosis may involve balanced translocations, and may be familial with dominant inheritance patterns. A wide variety of clinical pictures has therefore been described and classified.

Anaesthetic considerations of neurofibromatosis

Because of the relative rarity and the only relatively recent recognition of NF2 as a distinct entity, most of the literature concerning the medical and anaesthetic complications of neurofibromatosis relates to NF1. As the neurofibromatoses affect both ectodermal and mesodermal tissue, it is unsurprising that all systems of the body may be involved (Table 3).

Airway

An estimated 5% of patients with NF1 have an intra-oral manifestation of the disease.[5] Discrete neurofibromas may

involve the tongue[93 94] or the larynx.[10 30] When the latter is involved it is often the aryepiglottic fold or arytenoids that are affected, presumably reflecting those areas most rich in terminal nerve plexuses.[47] Unilateral vocal cord palsy has been reported secondary to involvement of the recurrent laryngeal nerve.[79] Discrete and plexiform neurofibromas commonly occur in the cervical region and large tumours of the parapharyngeal space may result in distortion of the airway. Pathologies in NF1 that affect the tongue, larynx and cervical tissues may cause obstruction, and symptoms of dyspnoea, stridor, loss or change of voice or dysphagia should warn the anaesthetist of potential airway problems. Suspicion warrants specialist examination with indirect laryngoscopy and CT or MR imaging.

Airway obstruction after induction of anaesthesia has been reported in patients with a tongue neurofibroma[14] and a neurofibroma involving the laryngeal inlet.[78] Both patients required emergency tracheostomy. Even if intra-oral pathology is recognized pre-operatively, elective awake fibreoptic tracheal intubation may fail because of a grossly distorted anatomy.[113] However, successful intubation after inhalation anaesthesia with sevoflurane has been described.[107]

In addition, the presence of macroglossia, macrocephaly, specific mandibular abnormalities[54] and cervical spine involvement may contribute to difficulties of airway management. Painless dislocation of cervical vertebrae has been reported in a patient with multiple cervical neurofibroma and it has been suggested that radiographic examination of the neck should be performed before anaesthesia in these patients in order to avoid spinal cord damage during laryngoscopy and tracheal intubation.[59]

Respiratory system

Neurofibromatosis may affect the conducting airways, lung parenchyma, the thoracic cage and the chest wall.

Conducting airways

Mediastinal neurofibromas usually originate in the posterior mediastinum or spread from the retroperitoneal space or cervical paraspinal areas. Tracheal and bronchial compression with rapidly progressive symptoms may occur[74] and may present a difficult challenge to the anaesthetist.[21]

Lung parenchyma

Intrapulmonary neurofibromas are rare, usually asymptomatic and carry a good prognosis. However, they may grow to a large size resulting in cough and dyspnoea. Excision of such tumours is advocated as they carry a risk of malignancy.[96] The association of pulmonary fibrosis and NF1 has long been recognized although estimates of its incidence of 10–20%[17] have probably been overstated. More recent surveys[45] have suggested that the association may even be coincidental. However, reports suggest that the typically bilateral upper lobe pulmonary fibrosis is of adult onset and is progressive,[9 87] and the resulting restrictive defect may culminate in pulmonary hypertension and right ventricular failure.[97] In addition, cystic lung disease may co-exist[63] as a honeycomb lung structure or large apical cysts.[65] Although rare, pneumothorax has been reported.[101]

Chest wall deformities

Thoracic spinal curvatures are common in NF1 and affect approximately 10% of NF1 patients. They appear early in childhood and often require corrective surgery.[2] Dystrophic spinal curvatures are short and sharp and progress throughout life. Severe kyphosis, although uncommon, may be associated with tumours and a high risk of neurological deficit. Scoliosis with rotation may also occur and produces a reduction in lung volume, which if severe, may result in respiratory failure. Although pectus excavatum and carinatum occur in up to 30% of patients with NF1,[81] they do not contribute to respiratory problems. Neurofibromas and schwannomas may produce erosion of the ribs and are a rare cause of flail chest.[40]

It is clear that evaluation of the respiratory system is an essential part of the pre-operative management of patients with NF1, and as well as chest x-ray, may include CT evaluation of the thorax and detailed lung function testing.

Cardiovascular system

Although hypertension is the most commonly occurring cardiovascular manifestation of NF, the disease may also primarily affect the myocardium and the vasculature.

Hypertension

Hypertension occurs in approximately 6% of NF1 patients and may be multifactorial. In the majority of cases, essential hypertension coincidentally coexists with the condition; however, in 30% of cases the hypertension is secondary to renovascular disease,[43] aortic coarctation or phaeochromocytoma.

Hypertension presenting in the young NF1 sufferer is usually because of renal artery stenosis, which may be bilateral.[8] The arterial lesions are of variable morphology with fusiform intimal narrowing, or nodule or aneurysm formation.[88] Surgery to stenosed vessels may be disappointing, possibly as the vessel abnormalities extend to intrarenal tissue. However, success has been reported with percutaneous angioplasty, resulting in remission of hypertension.[32] Regular arterial pressure measurement is thus a vital screen in even young patients with NF1 and mandatory in the pre-operative assessment of these patients. Caution should be taken when treating hypertension with potentially renotoxic drugs.

A recent review of the literature suggests that phaeochromocytoma affects between 0.1–5.7% of patients with NF1 but almost 25% of patients with phaeochromocytoma have the disease.[64] The mean age of presentation in NF1 patients is 42 yr and most patients have solitary, non-malignant tumours. The tumours are more commonly seen in association with other neurocutaneous syndromes such as

the Von Hippel-Lindau syndrome.[72] Sudden, short-lasting frontal or occipital headache occurs in 60% of patients while other common symptoms include anxiety attacks, weight loss, palpitations and night sweats.[84] Sustained or paradoxical hypertension that proves resistant to treatment should raise the suspicion of phaeochromocytoma and appropriate investigations such as urinary catecholamine estimation and abdominal CT scanning should be performed. It is vital to exclude phaeochromocytoma as a cause of hypertension as anaesthesia, surgery and pregnancy are particularly hazardous if it is undiagnosed pre-operatively. Death during orthopaedic surgery as a result of phaeochromocytoma has been reported in NF1 patients.[28 48] The subject of anaesthesia for the patient with phaeochromocytoma has been recently reviewed.[75]

Coarctation of the thoracic[22] or abdominal[110] aorta is a rare cause of hypertension in the NF1 patient.

Vasculopathy and cardiac pathology

In addition to the renal arterial lesions, in some cases of NF1 a generalized vasculopathy exists. Micronodular vascular proliferation may be seen in the nervous system and visceral organs: when a prominent feature, this is termed vascular neurofibromatosis. In spite of varying histological appearances, it has been proposed that the primary mechanism is that of schwann cell proliferation with secondary degeneration or fibrosis of the vessel wall. This process may result in formation of both aortic and cerebral aneurysms.[85]

Although initial studies suggested congenital heart defects were more common in the NF1 population,[71] a subsequent review[56] found no clear evidence of a link.

Idiopathic hypertrophic cardiomyopathy has been reported in NF1[25 86] but doubt exists as to whether this is a coincidental finding in two conditions that have a similar incidence. Fitzpatrick[31] suggests that the left ventricular hypertrophy may be secondary to neurofibromatosis and because of the abnormal metabolism of catecholamines or nerve growth factor, or that both diseases represent defects of neural crest tissue. In addition, neurofibromas may involve the heart causing both hypertrophy and outflow obstruction;[77] the development of an endocardial fibromuscular band giving rise to right ventricular failure has also been described.[83]

The presence of coronary artery aneurysms has been documented[15] and may represent a vascular manifestation of the disease; coronary vasospasm has been associated with sudden death in such a patient.[38]

Superior vena caval obstruction resulting from large mediastinal tumours is well recognized in NF1[74] and vascular lesions involving the subclavian artery may result in life-threatening haemothorax.[66 99] A high index of suspicion is required to diagnose the involvement of mediastinal structures and radiological examinations may need repeating at frequent intervals to exclude significant intrathoracic tumours.

The autonomic nervous system is not immune to the condition and sudden death has been reported in a patient with neurofibromatosis who was found to have a neurofibroma of the vagus nerve.[11]

It is clear that careful questioning concerning cardiovascular disease coupled with appropriate investigations is an integral part of the assessment of the patient with neurofibromatosis.

Central nervous system

As tumours of the central nervous system account for the major portion of the morbidity and mortality of patients with neurofibromatosis, it is unsurprising that patients often present for cranial or spinal neurosurgery. Anaesthesia for such patients follows normal neuroanaesthetic practice although surgery to plexiform neurofibromas may result in severe haemorrhage.

Anaesthetic assessment of such patients should take into account the increased incidence of epilepsy, learning difficulties and the possibility of undiagnosed CNS tumours. Clinicians should be open to the possibility of multiple lesions and not necessarily attribute new symptoms to a pre-existing tumour. Fatal neurogenic pulmonary oedema has been reported in a child with NF1 with unsuspected cerebral involvement when undergoing spinal surgery.[103]

Although an uncommon manifestation of NF1, cerebrovascular disease has been reported and probably represents similar pathology of vascular structures as described earlier. The most common disorder is a progressive narrowing of the internal carotid artery at the origin of the anterior and middle cerebral arteries.[95] Although it is not clear that there is an increase in the incidence of cerebrovascular accident in NF1 patients once the risk factor of hypertension is excluded, symptomatic ischaemic disease has been reported and confirmed by cerebral angiography. Furthermore, cerebral aneurysm formation has been reported and affects both the anterior and posterior circulations.[89] Control of arterial pressure perioperatively must be carefully considered in the light of arterial occlusive disease and the potential presence of aneurysms.

In addition to the respiratory pathology described above, involvement of brainstem structures by neurofibroma or glioma may result in central hypoventilation syndromes which may require respiratory support even in childhood.[91] Such patients may exhibit protracted weaning from mechanical ventilation post-operatively.

Gastrointestinal and genitourinary systems

Gastrointestinal tumours in NF1 may present with disordered gut motility, abdominal pain, haematemesis or melaena; although neurofibromas, usually affecting the jejunum or stomach, are the most common lesions, leiomyoma, ganglioneuroma and sarcoma have been described. All may result in intestinal perforation.

Gastrointestinal symptoms may be the first manifestation of neurofibromatosis.[33]

Carcinoid tumours have been described in NF1 and authors agree that the association is not coincidental. Fernandez[29] has suggested that neurofibromas and carcinoid tumours in NF1 have a common neuroendocrine origin, and this is supported by a case in which an intestinal neurofibroma showed histological transition into a carcinoid tumour.[4]

An unusual feature of the carcinoid tumour occurring in NF1 is the predilection for the duodenum and especially the ampulla of vater—an uncommon site in the non-NF1 population.[18] 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. Perioperative management of patients with carcinoid syndrome has been comprehensively reported by Veall.[104] It is important to note that carcinoid tumours and phaeochromocytoma may co-exist and, therefore, patients with phaeochromocytoma require imaging of the duodenum to exclude pathology in this region.[111]

The genitourinary tract may be involved in NF1 and retroperitoneal neurofibromas may result in ureteric obstruction and hydronephrosis. Similarly, bladder outflow obstruction has been reported[92] and bladder catheterization may be difficult.

Pregnancy

Although neurofibromatosis appears to have no intrinsic effect on fertility, a high rate of spontaneous abortion and stillbirth has been reported.[24 112] There is little documentation of difficult or obstructed labour because of uterine or vaginal neurofibroma but pre-term labour may occur in up to 30% of patients.[36] Pregnancy is often associated with an increase in the number and size of dermal neurofibromas and the potential for rapid increase in the size of CNS tumours must be considered.

Hypertension occurs commonly in pregnant NF1 sufferers[98] and arterial pressure must be carefully monitored throughout pregnancy. Both phaeochromocytoma and renal artery stenosis may present during pregnancy, perhaps with a lethal outcome.[42] Furthermore, renal artery stenosis may be induced by pregnancy when it may be associated with the haemolysis, elevated liver enzymes and low platelets (HELPP) syndrome.[37]

Anaesthesia for the pregnant patient with neurofibromatosis is not well documented. In the majority of patients with mild disease, the question of regional versus general anaesthesia is the same as that for patients without neurofibromatosis. In those patients with more extensive disease, regional techniques may be more appropriate, especially if airway problems are present. However, regional anaesthesia may be technically difficult if spinal neurofibromas or scoliosis are present. In addition, the presence of raised intracranial pressure must be excluded before regional anaesthesia is considered, even if this requires CT scanning with its radiation risk.[23] Anaesthesia for phaeochromocytoma in pregnancy carries its own particular difficulties.[39]

Pharmacology

There have been many reports suggesting an increased sensitivity of patients with NF1 to non-depolarizing neuromuscular blocking drugs.[6 61 62 69 70 114] In addition, the sensitivity to succinylcholine has been reported as increased,[61 62 114] decreased[6] or normal.[62 69] However, these reports are marred by a paucity of detail preventing a definite diagnosis of neurofibromatosis to be established; in addition, with the exception of one study,[6] no neuromuscular monitoring was performed. 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.[82] It was 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.

Conclusion

The neurofibromatoses are a group of conditions that vary in their severity but which have fundamental implications for the anaesthetist, physician and surgeon. NF1 is one of the most common genetically transmitted diseases and anaesthetists with a general practice are likely to encounter patients with the condition. Although the manifestations of NF1 are often mild, there may be associated pathology of direct relevance and importance to the anaesthetic management of patients with the disease. It is therefore important to have a working knowledge of the clinical manifestations of the disease (Table 3) so that a systematic approach to the pre-operative assessment of these patients can result in rational perioperative management.

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