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Anaesthesia recommendations for

Neurofibromatosis Type 2

Disease name: Neurofibromatosis Type 2

ICD 10: Q85.02

Synonyms: NF2

Disease summary:

Neurofibromatosis Type 2 (NF2) is an autosomal dominant disorder characterized by central nervous system (CNS) tumors. A mutated allele of the *NF2* gene on chromosome 22 accounts for this disorder. Although characterized as autosomal dominant, greater than 50% of cases are new, sporadic mutations. The incidence of NF2 in the general population is 1 in 25,000-40,000. The hallmark feature of NF2 are schwannomas that are classically located at the superior vestibular branch of cranial nerve VIII bilaterally. However, up to 40% may occur in the inferior vestibule. The average age of onset of symptoms is typically in the early twenties. Symptoms include hearing loss, imbalance, and tinnitus, while late symptoms include headache, facial twitching, facial numbness, and elevated intracranial pressure (ICP). Tumors are often found throughout the CNS, including the brain and spinal cord, although peripheral nerves may also be involved. NF2 tumors often include schwannomas, meningiomas, ependymomas, and neurofibromas. Due to the slow growth of some spinal tumors, patients may be asymptomatic for long periods of time. There are many considerations when choosing an anesthetic plan for these patients. Risks of regional anesthesia and general anesthesia must be discussed in detail with the patient.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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A	**AIRWAY / ANAESTHETIC TECHNIQUE**	Nerve sheath tumors in NF2 can obstruct airways in the laryngeal, cervical, and mediastinal regions, complicating intubation. Consider awake fiberoptic intubation for such cases. When a lesion is present or suspected, be prepared for a challenging airway. Vestibular schwannomas may compress the vagus nerve at the cerebropontine angle, so evaluate for hoarseness and dysphagia preoperatively. Anesthetic choices lack strict guidelines, but tumor presence and location should influence the plan. If CNS tumors are suspected, perform radiographic imaging. Engage in a thorough risk-benefit discussion with the patient before finalizing the anesthetic plan.
B	**BLOOD PRODUCTS (COAGULATION)**	NF2 is not linked to systemic bleeding disorders. However, neurofibromas tend to bleed during surgical removal or in response to trauma. Therefore, for patients undergoing neurofibroma resection, it is advisable to order a type and screen ordered.
C	**CIRCULATION**	Cardiac involvement is infrequent in NF2, although it has been documented in certain cases of neurofibromatosis type I. A comprehensive medical history and physical examination should be conducted, and additional diagnostic assessments should be considered accordingly.
D	**DRUGS**	When planning a general anesthetic, avoid drugs that raise intracranial pressure (ICP), particularly in patients with known elevated ICP. Ketamine's use in patients with increased ICP is debated, but some studies suggest doses up to 5 mg/kg IV may not elevate ICP. Ketamine may be beneficial for refractory status epilepticus. Continue home seizure medications when appropriate. Older antiepileptic drugs like carbamazepine, phenytoin, phenobarbital, and primidone induce cytochrome P450 enzymes, potentially reducing plasma levels of cardiovascular drugs (e.g., amiodarone, beta-blockers, calcium channel blockers). Nitrous oxide's ability to trigger seizures in animals has not been consistently observed in humans. Meperidine can induce myoclonus and tonic-clonic seizures and should be avoided if possible. Concerning induction medications, etomidate has the highest reported incidence of seizure activity and can prolong seizures in electroconvulsive therapy (ECT). Consider premedicating with benzodiazepines like midazolam due to the risk of perioperative seizures. There is no evidence suggesting an increased risk of malignant hyperthermia (MH) or rhabdomyolysis in these patients.

E	**EQUIPMENT**	For patients undergoing intracranial tumor resection, consider continuous blood pressure monitoring using an arterial line. The decision to employ intracranial pressure devices should be made by the neurosurgical team and evaluated on a case-by-case basis.

Typical surgery

Often include surgical resection for vestibular schwannoma, meningioma, and spinal tumors. Additionally, cochlear implants and stereotactic radiosurgery (e.g., gamma-knife), all of which commonly require general anesthesia.

Type of anaesthesia

There are no definite recommendations for general or regional anesthesia, however the presence and location of tumors should be considered when determining the anesthetic plan. If CNS tumors are suspected by history or physical exam, radiographic imaging is recommended. Before a decision is made on an anesthetic plan, an in-depth risk vs. benefit discussion must occur with the patient.

If CNS tumors are suspected by radiographic exam, or suspected clinically, neuraxial anesthesia may be contraindicated. Complications of neuraxial anesthesia include an epidural hematoma due to the high vascularity of spinal cord tumors, paraplegia or quadriplegia after accidental dural puncture with elevated ICP, patchy block due to the presence of spinal cord tumors, and the risk of spreading mutated cells by incidental puncture. When neuraxial anesthesia is performed, the anesthesiologist should consider reducing the dose or rate to decrease the amount of motor blockade. This allows for frequent neurologic exams to be performed to monitor for complications. If a patient is suspected to have a difficult airway, neuraxial anesthesia may be preferred.

Peripheral regional anesthesia is not contraindicated. However, the anesthesiologist should be aware of the location of known or suspected tumors, and any associated neurological deficit. If peripheral or neuraxial blocks are planned in an area of a known tumor, careful pre-procedural neurological exam should be done and documented to assess for changes post-procedure. A thorough discussion of the risks with documentation in the medical record is warranted.

If a general anesthetic is planned, drugs that increase ICP should be avoided, especially in patients when elevated ICP is known. The use of ketamine in patients with increased ICP is controversial. Some studies suggest ketamine, up to doses of 5 mg/kg IV, did not increase ICP. Systemic blood pressure should be maintained to provide adequate cerebral perfusion pressure. Hypertension should be avoided due to concern for intracranial aneurysm rupture. In those patients with known or suspected CNS tumors requiring general anesthesia with an endotracheal tube, blunting of the laryngeal reflexes with intravenous lidocaine and opioids are recommended to avoid coughing and bucking, which can raise ICP. However, use caution with opioids in the spontaneously breathing patient as hypoventilation can result in high levels of CO2 and increased ICP. Awake fiberoptic intubation may be indicated in patients with pharyngeal masses, tracheal deviation, cervical stiffening, or in cases when cervical manipulation may want to be avoided. Prolonged duration of both depolarizing and nondepolarizing neuromuscular blocking agents has been described in literature, similar to patients with myasthenia gravis. Neuromuscular monitoring must be used in this patient population. Patients may also develop a restrictive lung ventilation pattern depending on the size and location of their tumor. This may increase the risk of post-operative ventilation.

Necessary additional pre-operative testing (beside standard care)

If a patient is suspected of having NF2, genetic testing can confirm the diagnosis. If neuraxial anesthesia is being considered, it is recommended to obtain imaging of the brain and the entire spinal cord prior to the procedure. Contrast enhanced MRI is the gold standard in the evaluation of intracranial and spinal cord tumors.

Particular preparation for airway management

Nerve sheath tumors can be in laryngeal, cervical, and mediastinal regions in NF2. Such tumors can make endotracheal intubation difficult. Awake fiberoptic intubation may be preferred in these cases. If one is aware of or suspects such lesions, one should be prepared for the potential for paralyzed vocal cords and difficult airway. Vestibular schwannomas can compress the vagus nerve at the cerebropontine angle. Thus, preoperative evaluation should include inquiring about hoarseness and dysphagia.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilisation

Positioning of a patient with a CNS tumor or mass effect lesion that will increase ICP, such as trendelenburg, should be avoided if possible. Care must be taken to assess for spinal cord compressing cervical tumors prior to surgery.

Interactions of chronic disease and anaesthesia medications

Older generation antiepileptic medications such as carbamazepine, phenytoin, phenobarbital, and primidone induce cytochrome P450 enzymes leading to decreased plasma concentrations of cardiovascular drugs especially amiodarone, beta-blockers (propranolol, metoprolol), and calcium channel blockers (nifedipine, felodipine, nimodipine, and verapamil). Nitrous oxide has been shown to provoke seizures in animal models, however this has not been shown in humans. Meperidine can cause myoclonus and tonic-clonic seizure activity and should be avoided in these patients if possible. Regarding induction medications, etomidate has the highest reported incidence of seizure activity. Etomidate has been shown to increase seizure duration when used in ECT procedures. The use of ketamine in patients with increased ICP is controversial. Some studies suggest ketamine, up to doses of 5 mg/kg IV, did not increase ICP. However, ketamine has been shown to be useful in status epilepticus that are refractory to other agents.

Anaesthetic procedure

If a difficult airway is anticipated due to the presence of laryngeal, cervical, or mediastinal tumors, short acting neuromuscular blocking agents, such as succinylcholine, should be considered. As fasciculations associated with the use of succinylcholine can increase ICP, a defasciculating dose of a non-depolarizing neuromuscular blocking agent can be used to negate this.

During induction of a general anesthetic, drugs that increase ICP should be avoided. Alternatives include propofol, etomidate, barbiturates, benzodiazepines, and opioids. Also, if an endotracheal tube is used, adequate blunting of laryngeal reflexes with intravenous lidocaine, LTA, and intravenous opioids should be accomplished. During the termination of anesthesia, a deep extubation can be considered in a patient without a laryngeal or mediastinal tumor to prevent coughing and bucking on the endotracheal tube, and the administration of lidocaine prior to an awake extubation may be beneficial as well.

If neuraxial anesthesia is performed, the anesthesiologist should consider reducing the anesthetic dose or rate to decrease the amount of motor blockade. This allows for frequent neurologic exams to be performed to monitor for complications from the procedure.

Particular or additional monitoring

Due to described prolongation of neuromuscular blockade in this patient population, neuromuscular monitoring must be used when neuromuscular blocking drugs are given.

Possible complications

If one suspects laryngeal, cervical, or mediastinal tumors, a difficult airway may be encountered. Hence, the difficult airway cart should be readily available.

If CNS tumors are present, increased ICP and brain herniation are possible, especially when performing neuraxial anesthesia.

Complications of neuraxial anesthesia include bleeding and epidural hematoma formation due to high vascularity of the spinal cord tumors, paraplegia or quadriplegia after accidental dural puncture with elevated ICP, patchy block due to the presence of spinal cord tumors, bleeding and epidural hematoma formation due to high vascularity of the spinal cord tumors, and the risk of spreading mutated cells by incidental puncture.

Post-operative care

The level of post-operative care should be determined by the surgical team in conjunction with anesthesia based on risk of procedure in addition to patient specific risk factors. In the perioperative period, patients may be at higher risk of seizures and should be monitored for this.

Disease-related acute problems and effect on anaesthesia and recovery

If neuraxial anaesthesia is administered, serial surveillance for epidural hematoma should be carried out, including neurological assessment of motor and sensory function, until the patient returns to baseline neurologic function.

If peripheral regional anaesthesia is used in a region of known or suspected tumor, a neurological workup to document pre-existing pathology should be performed. If clinically indicated, radiological studies may be useful in documenting sites of peripheral tumors. After completion of the procedure, a postprocedural neurological exam should be completed and documented.

Ambulatory anaesthesia

Not reported.

Obstetrical anaesthesia

Neuraxial anesthesia for laboring patients and those in need of a cesarean section involves potential risks of bleeding and epidural hematoma formation, patchy block, raised ICP, and puncture of Schwannomas. We recommend that in high-risk patients, an MRI prior to labor may be prudent to assess for lesions, which tend to enlarge during pregnancy. In certain patients with risk factors for general anesthesia, especially those with potentially difficult airways, neuraxial anesthesia may be preferred. When epidural anesthesia is performed in laboring patients, one should consider reducing the rate of the epidural infusion to decrease the amount of motor blockade. This allows for close neurologic exams to detect complications in the early stages. Pushing during the second stage of labor also can increase ICP. Due to these risks, patients with known or suspected CNS lesions may undergo general anesthesia to avoid the potential complications described above. In general, we would still recommend neuraxial over general anesthesia unless imaging showed severe disease, especially considering airway risks as noted above.

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