

Anaesthesia recommendations for patients suffering from

Pantothenate kinase-associated neurodegeneration

Disease name: Pantothenate kinase-associated neurodegeneration

ICD 10: G23.0

Synonyms: Hallervorden-Spatz disease; neurodegeneration with brain iron accumulation type 1

Disease summary: Pantothenate kinase-associated neurodegeneration (PKAN) is a rare autosomal recessive disorder that was first described by the neuropathologist Julius Hallervorden and the neurologist Hugo Spatz in 1922 [1]. The active involvement of Hallervorden in euthanasia in Germany during World War II and the discovery of the defective gene (mutation in pantothenate kinase 2 gene, located on chromosome 20p13) removed the name "Hallervorden Spatz disease" to PKAN (2,3). Prevalence is estimated at 1-3/1,000,000 [4]. It has variable phenotype that is mainly age dependent. The classic form has early onset (usually before six years of age) and rapid progression. Children usually present with gait abnormalities, followed by severe dystonia, seizures, dysarthria, spasticity, retinopathy and learning disorders [5]. Atypical PKAN (25% of cases) has later onset and slower progression. Speech abnormality and psychiatric symptoms are more common in this form. Dyskinetic symptoms may be mild [5]. PKAN has a characteristic brain MRI pattern called "eye of the tiger sign", which is a low signal intensity region surrounding a central high signal intensity region in the globus pallidus [6]. Histopathologic findings reveal iron deposition in the globus pallidus and pars reticulata of the substantia nigra [7]. Oropharyngeal dystonia can lead to pulmonary aspiration, dynamic upper airway obstruction and breathing difficulty [8]. Severe dystonia usually fails to respond to pharmacological therapy and intrathecal baclofen pump or stereotactic pallidotomy can be considered. Patients requiring general anaesthesia with this syndrome may have many symptoms that influence the pre-anaesthetic management, the induction of anaesthesia and the postoperative care.

Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong



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Typical surgery

- Stereotactic procedures, deep brain stimulation, pallidotomy
- Intrathecal baclofen pump implantation
- Orthopaedic surgery (for bone fractures)
- Oro-dental surgery (for self-mutilation of the oro-facial mucosa due to intense spasms)
- Spine surgery
- Sedation (for MRI, gastric tube placement, tracheostomy)
- Ophthalmologic surgery

Type of anaesthesia

Regional anaesthesia is not suitable for these patients because of presence of involuntary movements, rigidity and seizures. Scoliosis and contractures, causing position difficulties, are common late complications of dystonia. Patients may be mentally disabled and uncooperative.

General anaesthesia with volatile or intravenous anaesthetics can be performed [9-12].

Sedative agents must be chosen carefully because of risk of dynamic airway. Dexmedetomidine can be a viable option without comprising airway and hemodynamics [13].

Necessary additional diagnostic procedures (preoperative)

Detailed pre anaesthetic evaluation is very important in patients with PKAN. However, because of compromised articulation, dementia or severe mental retardation, medical history usually cannot be obtained from the patient and cooperation with family members is necessary. The presence of medical personnel may induce anxiety leading to exaggerated dystonic movements. Assessment of auscultation, respiratory rate, chest X-ray and arterial blood gases are limited. Sedation of the patient is sometimes needed for this evaluation.

Patients in an advanced stage of the disease show severe involvement of the pulmonary system. Dystonia may involve oromandibular muscles leading to dysphagia and impairment of swallowing. Malnourishment, chronic pulmonary aspiration, pneumonia and compromised gas exchange can be seen [8]. Blood gas analysis and X-ray of the thorax should be done. Cardiac function tests including electrocardiography and echocardiography should be performed looking for cardiomyopathy and arrhythmias due to electrolyte imbalance.

Rhabdomyolysis and myoglobinaemia, causing acute renal failure and metabolic acidosis may occur after dystonic storms as well as hyperpyrexia and dehydration [14]. Renal function tests are important in these patients.

Particular preparation for airway management

PKAN is characterized by periods of life-threatening dysfunctional breathing that can include dynamic upper airway obstruction. Mouth opening is reduced with oromandibular rigidity. Extrapyraximal signs like chorea, dystonia, rigidity and tremor usually disappear with the induction of anaesthesia [8,9]. However, chronic repeated dystonic movements can lead to excessive stress on the cervical spine, resulting in degenerative changes [15]. Muscle contractures may fix the jaw or cervical spine, so that mobility could be limited even in the presence of muscle relaxants. Endotracheal intubation may be difficult. Awake intubation techniques are not suitable as noxious stimulation intensify the dystonia and involuntary movements. Physicians should be aware that emergency tracheostomy can be necessary.

Increased risk of gastric aspiration in patients with PKAN makes endotracheal entubation the gold standard for securing the airway. There is one single report about the successful administration of ProSeal laryngeal mask airway in a child with PKAN undergoing ophthalmic surgery [16].

Involuntary movements may reappear on emergence from anaesthesia. Reentubation or a delayed tracheal extubation can be needed [9,12]. Patients should be monitorized longer than usual in the recovery room or admitted to the intensive care unit and sedated to allow slow, gradual emergence. However, there is a case regarding that intrathecal baclofen may help postanesthetic pulmonary care by attenuating dystonia and rigidity and can be an adjuvant for anesthesia care in patients with PKAN [17].

Particular preparation for transfusion or administration of blood products

There is no special consideration for transfusion or administration of blood products in patients with PKAN. Acanthocytosis has been reported in some patients [18]. This is a condition of the blood that presents with some red blood cells that are spiked, or possess various abnormal thorny projections. Acanthocytes have a reduced red blood cell survival. This may give rise to a mild hemolytic anemia. But it usually does not require special treatment.

Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation. But the impaired mobility of patients may suggest a higher risk of postoperative thrombosis.

Particular precautions for positioning, transport or mobilisation

Repeated dystonic movements cause extra stress to the spine, leading to degenerative changes and neurologic symptoms. Positioning of the neck during intubation and surgery must be performed with extreme care.

Muscle spasms combined with decreased bone mass can result in bone fractures, not caused by trauma or accident [19]. Patients with PKAN are often malnourished and accordingly, the skin is at risk of injury from compressive and shearing forces of surgical positioning. Meticulous patient positioning and padding is important.

Probable interaction between anaesthetic agents and patient's long-term medication

Patients of PKAN could be on any one or more of the following medications: Anticholinergics, antiepileptics, baclofen, deferiprone, levodopa and benzodiazepines. These drugs are to be continued during perioperative period. Any discontinuation can precipitate withdrawal. Baclofen withdrawal is a life-threatening condition that may be associated with reflex spasticity, dysautonomia, hyperthermia, rhabdomyolysis, multiorgan dysfunction, and death [20].

Sedation with an increased dose of benzodiazepines can be helpful at the day of surgery controlling for involuntary movements. But risk of aspiration and respiratory depression on the treatment of sedatives should not be forgotten.

Anaesthesiologic procedure

Sedative premedication with benzodiazepines and the presence of the parents during induction may be helpful in controlling involuntary movements of children with PKAN [12].

Propofol, thiopental, fentanyl, remifentanyl, N₂O and volatile anaesthetics have been used without adverse effects [8]. When venous conditions are difficult, inhalational induction of anaesthesia can be considered. The agent mostly used is Sevoflurane [9].

Non-depolarizing neuromuscular blocking agents can be used safely. Hyperkalemic cardiac arrest induced by succinylcholine is always a possibility, because skeletal muscle wasting and diffuse axonal changes in the brain that involve upper motor neurons could accentuate the release of potassium [8,10]. However, Keegan et al. reported administration of succinylcholine without problems [9]. Possibility of the difficulty in intubation determine the anaesthetic management.

Madhusudhana et al reported a successful use of dexmedetomidine, without comprising airway and hemodynamics, as a sole sedative agent for MRI in a patient with PKAN [21].

In most case reports, dystonia reappeared postoperatively after the anaesthetics wore off. Re-intubation may be required due to muscular rigidity, spasticity and respiratory disability. Patients should be monitored longer than usual in the recovery room or admitted intubated to the intensive care unit [12]. Emergency tracheostomy may even be needed [9].

Particular or additional monitoring

Standard monitoring is indicated. Arterial cannulation for invasive blood pressure measurement is recommended in case of highrisk surgery, major fluids shifts, advanced disease or multipl blood sampling.

A urinary catheter may be beneficial to assess fluid status during anaesthesia.

Possible complications

Patients with PKAN requiring surgery under general anesthesia are usually in a status of uncontrolled dystonia and rigidity. This state is life-threatening and often requires intensive care.

Involuntary movements and seizures can complicate catheter cannulations. Dystonia may lead to spontaneous fractures, rhabdomyolysis and renal failure.

Oromandibular rigidity, contractures and severe tongue protrusion can cause difficult airway. Emergency tracheostomy may be needed.

Due to immobility, hyperkalemic cardiac arrest induced by succinylcholine is always a possibility.

Dysphagia and difficulties in swallowing raise the risk of aspiration and pneumonia. Sedatives used for the control of dystonia can also cause respiratory depression.

Hayashi et al. described spontaneous presentation of neuroleptic malignant syndrome in a patient with PKAN in the absence of neuroleptic drugs and suggested that dopaminergic hypoactivity, which was characteristic of PKAN, could trigger episodes of this syndrome [22].

Postoperative care

Anaesthetists should be aware that delayed tracheal extubation or re-intubation may be required due to muscular rigidity, spasticity and respiratory disability. Patients should be monitored longer than usual in the recovery room or admitted to the intensive care unit. Emergency tracheostomy may be needed.

Information about emergency-like situations / Differential diagnostics

caused by the illness to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

- Postoperative respiratory problems (DD of dynamic upper airway obstruction corresponding to the underlying disease versus residual opiate or neuromuscular blockers effect)
- Emergency tracheostomy

Ambulatory anaesthesia

Due to the significantly higher risk for post anaesthetic adverse airway events, ambulatory anaesthesia is not recommended.

Obstetrical anaesthesia

Not reported.

Literature and internet links

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