orphanaesthesia

Anaesthesia recommendations for patients suffering from

Neuronal ceroid lipofuscinosis

Disease name: Neuronal ceroid lipofuscinoses (NCL)

ICD 10: E75.4

Synonyms: Historically, single NCL forms have been classified according to infantile, late-infantile, juvenile or adult onset and associated with names of investigators such as Santavuori-Haltia, Jansky-Bielschowsky, Batten, Spielmeyer-Vogt, Kufs

The neuronal ceroid lipofuscinoses (NCL) are a heterogeneous group of genetic lysosomal storage diseases causing dementia, epilepsy, motor deterioration and mostly also visual loss through retinal degeneration. Similarities of the different NCL also concern elements of their pathophysiology, which is characterized by loss of neurons and accumulation of a material called ceroid lipofuscin. The single NCL forms differ significantly by the age at manifestation and the progression of neurological deterioration.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Disease summary

The neuronal ceroid lipofuscinoses (NCL) are a heterogeneous group of genetic lysosomal disorders characterized by the accumulation of a waxy intracellular storage material termed ceroid lipofuscin and progressive neurological deterioration, usually associated with dementia and epilepsy, frequently also with visual loss due to retinopathy. Most NCL forms are transmitted autosomal recessively. As a group, NCL represent one of the most frequent etiologies of dementia in children and young adults [1-3]. The classification of the NCL disorders is based on the different genes involved (CLN1-CLN14) and on the age at clinical onset, which can be anytime between the infantile and young adult age. The major NCL forms are shortly described below according to the age at manifestation.

NCL with infantile onset (1st year of life)

Infantile NCL is usually caused by CLN1 mutations. Early development appears normal until around six months of age. At onset, there is typically a decreased muscle tone and decreased social interaction followed by dramatically progressive psychomotor decay, myoclonus, seizures, spasticity and visual failure. By two years of age, blindness has developed with optic atrophy and retinal abnormalities. Patients rapidly reach a vegetative state.

NCL with late-infantile onset (age 2 to 5 years)

The onset of an NCL disease at this age is usually caused by CLN2 mutations, but mutations of other genes are possible. Children with CLN2 disease appear initially healthy and normally developed. Acquisition of speech may be retarded. First symptoms occur generally between the ages of 2 and 4 years and consist in motor decline with clumsiness and ataxia, deterioration of speech and/or epilepsy. Seizures (partial, generalized tonic-clonic, secondarily generalized, or other) are the first symptom in 75% of patients. Non-epileptic myoclonus frequently coexists and has to be distinguished from epileptic seizures as it is treated differently. After the third year of life, loss of motor function and of language ability progress rapidly and uniformly. MR imaging shows progressive brain atrophy. Visual ability declines gradually and leads to blindness. Limb spasticity, truncal hypotonia, and loss of head control lead to complete loss of independent mobility. Children lose the ability to swallow and frequently receive tube feeding. Death usually occurs at the age of 10-15 years.

NCL with juvenile onset (age 5 to 15 years)

Juvenile NCL is mostly caused by CLN3 mutations, rarely also by mutations of other genes. The disease usually starts between ages 4 and 7 years with insidious onset of visual failure due to a pigmentary retinopathy. For several years, patients are regarded as visually handicapped only. Progressive cognitive decline and behavioral problems (angry outbursts, physical violence, and anxiety with features of depression) follow. Seizures develop at around 10 years of age, mostly as generalized tonico-clonic seizures, which are usually well-controlled by medication, at least initially. Any other type of epilepsy may occur, from subtle partial seizures to myoclonic status. A parkinsonian movement disorder develops. Speech becomes affected by a severe dysarthria. Swallowing difficulties frequently lead to tube feeding. A cardiac conduction abnormality is detectable in the second decade of life. Age at death is usually in the third decade.

NLC with onset in adults

Adult onset forms of NCL are all very rare and can be caused by mutations of a variety of genes. In the past, the term Kufs disease was used to designate some of them. Onset is

typically at around 30 years of age, Clinical features include ataxia, dementia, progressive myoclonus epilepsy, but in contrast to most other NCL, there is usually no loss of vison.

Typical surgery

Children who have NCL often require anaesthetic care for diagnostic procedures, gastrostomy, vagus nerve stimulation or other types of surgery. There is limited information available concerning the anaesthetic management of a patient with NCL [4-6]. Because of the profound neurologic abnormalities in these children, the anaesthetic management of these patients requires an understanding of the natural history of the disease.

Type of anaesthesia

In the literature, there is insufficient data to recommend a specific type of anaesthesia. NCL patients are frequently blind, demented and tend to have seizures. They may have severe neurologic abnormalities, including difficulty swallowing with the consequence of an increased risk for aspiration. Patients are prone to bradycardia and may develop hypothermia during anaesthesia.

Necessary additional diagnostic procedures (preoperative)

Preoperative assessment should be conducted with special focus on epilepsy and other coexisting medical problems. The type and pattern of seizures, frequency and control of seizures, antiepileptic therapy, and complications of antiepileptic drugs (AEDs) need to be sought. Laboratory tests should screen for the side-effects of AEDs. Patients on sodium valproate, carbamazepine, and ethosuximide should have their liver function, platelet count, and coagulation indices checked. In poorly controlled epilepsy, plasma levels of AEDs should be measured and optimized before operation. Patients on valproate may develop a severe exacerbation of a complex movement disorder leading to hyperthermia, hyper-CK-emia and prolonged decreased consciousness [7]. Electrocardiogram is necessary to rule out cardiac conduction disorders. X-ray or blood gas analysis should be considered in cases with suspected recurrent aspiration. Consultation with specialists may be advised (cardiology, paediatric neurology, respiratory care [8]).

Particular preparation for airway management

Preoperative physiotherapy may be advisable to remove excessive tracheobronchial secretions due to a swallowing disorder. There are no good data on the use of specific premedication.

Particular preparation for transfusion or administration of blood products

There are no particular recommendations.

Particular preparation for anticoagulation

The presence of an impaired mobility may predispose to deep venous thrombosis, so compression stockings and/or low molecular weight heparin may be indicated in the perioperative period.

Particular precautions for positioning, transport or mobilisation

These patients may suffer spinal rigidity, scoliosis, and limb contractures, although uncommon; for this reason, positioning in the operating room must be careful. Immobile patients may have breakable bones and fractures can be caused by inadequate handling.

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

The use of preoperative AEDs may have significant impact on anaesthetic management. Cytochrome p450 enzyme induction by AEDs (e.g., phenytoin, a drug not recommended in NCL patients) may alter the metabolism of anaesthetic drugs. AEDs may also affect neuromuscular relaxants by causing acetylcholine receptors to be up-regulated at the neuromuscular junction.

Anaesthesiologic procedure

Regional anaesthesia is not formally contraindicated, and general anaesthesia has been used in several surgical procedures. Although there are muscular changes (increased muscle tone and myoclonus) in these patients, the use of nondepolarizing neuromuscular blockers (NMBs) for endotracheal intubation may be very helpful, provided the possibility of abnormal pharmacokinetics and interaction with other drugs is being considered. As most patients suffer from epilepsy, anaesthetists should be aware of the potential risk of seizures associated with volatile anaesthetics. All opioids (alfentanil, fentanyl and remifentanil) activated epileptic discharges and had a dose-related effect on spike activity.

Particular or additional monitoring

Patients with NCL may have a lower baseline body temperature and be at risk for significant hypothermia during general anaesthesia. Adequate monitoring should prevent the complication of profound hypothermia.

Possible complications

The main complications that must be ruled out are aspiration, hypothermia, bradycardia and status epilepticus.

Postoperative care

Seizures are more common in the postoperative period. They may be precipitated by the use of proconvulsant anaesthetic agents, hypoxia, hypercapnoea, electrolyte disturbances (hyponatraemia, hypocalcaemia and hypomagnesaemia), hypoglycaemia, uraemia, subtherapeutic levels of AEDs, or local anaesthetic toxicity. Correction of any precipitating factors and checking plasma levels of AEDs are required. It is essential to restart the antiepileptic treatment in the postoperative period as soon as possible.

Additionally, avoiding prolonged mechanical ventilation and temperature control must be among the mains goals in the postoperative period. Non-invasive postoperative ventilation may be needed in this period.

Information about emergency-like situations / Differential diagnostics

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

Not reported.

Ambulatory anaesthesia

Ambulatory anaesthesia, in view of significant risks associated with the severe neurological disease that tend to exacerbate during the postoperative period, can usually not be recommended.

Obstetrical anaesthesia

Not applicable.

Literature and internet links

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Please note that this guideline has not been reviewed by an anaesthesiologist but by two disease experts instead.