Clinical Reports

Anaesthetic considerations for the child with leukodystrophy

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The author presents a four-year-old boy with Pelizaeus-Merzbacher disease who required anaesthesia during placement of PE (pressure equalization) tubes and a permanent silastic intravascular device (Broviac catheter). Pelizaeus-Merzbacher is one of a group of progressive, degenerative disorders of the cerebral white matter known as the leukodystrophies. They include metachromatic leukodystrophy, adrenoleukodystrophy, Krabbe's disease, Canavan's disease, Alexander's disease and Pelizaeus-Merzbacher disease. Due to the progressive nature of the disorders and their devastating effects on the central nervous system, these children frequently require anaesthesia during imaging procedures such as MRI or during various surgical procedures. Of concern to the anaesthetist is the high prevalence of seizure disorders, gastroesophageal reflux with the risk of aspiration, and airway complications related to poor pharyngeal muscle control and copious oral secretions. In addition, adrenal involvement and hypofunction may be seen in patients with adrenoleukodystrophy. Identification of these associated conditions during the preoperative examination will allow safe anaesthesia for these children.

L'auteur décrit et commente l'anesthésie générale administrée à un garçon de quatre ans atteint de la maladie de Pelizaeus-Merzbacher pour la mise en place de tubes de tympanostomie et d'un accès veineux permanent (catheter de Broviac). La maladie Pelizaeus-Merzbacher fait partie du groupe des affections

progressives et dégénératives de la substance blanche connues sous le nom de leucodystrophies. En plus de la maladie de Pelizaeus-Merzbacher, celles-ci comprennent la leucodystrophie métachromatique, l'adrénoleucodystrophie, les maladies de Krabbe, de Canavan et d'Alexander. A cause de la nature progressive de ces affections et leurs effets dévastateurs sur le système nerveux central, ces jeunes malades doivent souvent subir des interventions chirurgicales ainsi que des démarches diagnostiques comme l'imagerie par résonnance magnétique nucléaire. L'anesthésiste doit se préoccuper de l'incidence élevée de crises comitiales, du reflux gastro-oesophagien avec risque d'aspiration et de difficultés respiratoires éventuelles par absence de contrôle de la musculature pharyngée et la présence de sécrétions orales copieuses. On peut aussi retrouver une atteinte surrénalienne dans l'adrénoleucodystrophie. L'identification de ces désordres associés à la maladie lors de la consultation pré-opératoire permettra de conduire l'anesthésie avec plus de sécurité.

Key words

ANAESTHESIA: pediatric;

BRAIN:

SYNDROMES: Pelizaeus-Merzbacher disease.

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Myelin, the major component of cerebral white matter, is composed of lipid membranes that wrap around axonal processes thereby increasing the speed and efficiency of neuronal conduction. Myelin formation and/or degradation may be affected by several hereditary or acquired degenerative disorders. The degenerative disorders of cerebral white matter may be divided into those involving defective formation of myelin (the leukodystrophies) and the demyelinating diseases (multiple sclerosis). The leukodystrophies compose a group of progressive, degenerative disorders that include metachromatic leukodystrophy, adrenoleukodystrophy, Krabbe's disease, Canavan's disease, Alexander's disease and Pelizaeus-Merzbacher disease.¹ In general, these diseases present during the first year of life with spasticity, arrest of motor development, and gait disturbances. Due to their progressive nature with devastating effects on the central nervous system, such children frequently require anaesthesia during imaging procedures such as MRI or during surgical procedures to correct the sequelae of their disease.

TABLE I Summary of the inheritance and biochemical defects of the leukodystrophies

<i>Disorder</i>	<i>Inheritance</i>	<i>Enzymatic defect</i>
Pelizaeus-Merzbacher	X-linked recessive and autosomal dominant	Not identified
Metachromatic leukodystrophy	Autosomal recessive	Aryl sulfatase A
Krabbe's disease	Autosomal recessive	Galactocerebrosidase
Adrenoleukodystrophy	X-linked recessive	Defective metabolism of long chain fatty acids
Canavan's disease	Autosomal recessive	Not identified
Alexander's disease	Autosomal recessive	? Mitochondrial defect

TABLE II Summary of the clinical characteristics of the leukodystrophies

<i>Disorder</i>	<i>Clinical manifestations</i>
Pelizaeus-Merzbacher	Onset in infancy, progressive CNS deterioration
Metachromatic leukodystrophy	Most common type of leukodystrophy, onset at one to two years, associated with bouts of fever and abdominal pain, gall bladder dysfunction
Krabbe's disease	Also known as globoid cell leukodystrophy, onset at four to six months of age
Adrenoleukodystrophy	Also known as sudanophilic cerebral sclerosis, onset at 5 to 10 years of age, accompanied by hypoadrenalism
Canavan's disease	Onset at two to four months of age, increased water content of brain, questionable defect in mitochondrial function leading to increased plasma membrane permeability to water and cations; children have macrocephaly without evidence of hydrocephalus
Alexander's disease	Onset within first year of life

Case report

The patient initially presented at three months of age with loss of developmental milestones and nystagmus. Family history was positive for the diagnosis (made at autopsy) of Pelizaeus-Merzbacher in an older sibling. Other important past medical history included a seizure disorder controlled with phenytoin and phenobarbital. Previous surgical history included a fundoplication and gastrostomy tube placement performed six months earlier for gastroesophageal reflux (GER). Previous anaesthesia was uneventful: airway management during the previous anaesthetic was uncomplicated. Physical examination revealed a small for age child (11 kg, <5% for age) with nystagmus, choreoathetoid movements, and marked hypotonia. The child showed markedly delayed development. He did not interact with his environment. He had poor head control and was unable to sit without assistance. Preoperative medications included the usual morning doses of phenobarbital and phenytoin in addition to glycopyrrolate and ranitidine. Anaesthetic induction was with propofol ($3 \text{ mg} \cdot \text{kg}^{-1}$) and fentanyl ($2 \mu\text{g} \cdot \text{kg}^{-1}$). Muscle relaxation was achieved with vecuronium ($0.15 \text{ mg} \cdot \text{kg}^{-1}$) and the trachea was intubated with a 4.5 uncuffed tracheal tube. An air leak was noted at 20 cm H_2O . Maintenance of anaesthesia was with N_2O in 50% O_2 and isoflurane (expired concentration 0.4 to 1.0%). Following the surgical procedures, which lasted 90 min, residual neuromuscular blockade was reversed with neostigmine ($0.04 \text{ mg} \cdot \text{kg}^{-1}$) and glycopyrrolate ($0.01 \text{ mg} \cdot \text{kg}^{-1}$), the trachea was extubated, and the patient was transported to

the recovery room with 40% oxygen by mask. The patient was weaned from O_2 to room air and admitted to the Intermediate Care Unit for observation overnight. He did well and was discharged to the inpatient ward the following morning.

Discussion

We present a four-year-old boy with Pelizaeus-Merzbacher disease who required general anaesthesia during placement of PE tubes and a Broviac catheter. Several variants of leukodystrophy have been described clinically and identified biochemically. The disorders, their inheritance, and biochemical defects are summarized in Table I. The clinical characteristics are summarized in Table II. Children with these disorders frequently require general anaesthesia during surgical procedures aimed at correcting the sequelae of the disease. They include orthopaedic procedures to improve function and facilitate nursing care, fundoplication for GER, and spinal fusion to prevent pulmonary dysfunction and cor pulmonale from progressive scoliosis.

Our patient was an inpatient since he had been admitted the week before to change anticonvulsant therapy due to poor seizure control. However, there are no contraindications to same day surgery in these children. Although admission to hospital following surgery is recommended, due to concerns for postoperative respiratory status, preoperative evaluation may be accomplished as an outpatient. In such cases, these children should be evaluated by an anaesthetist the week before the anticipated surgery

so that concerns may be addressed and evaluated. Arrival in the outpatient surgery area should be arranged so that preoperative aspiration prophylaxis may be administered if deemed necessary.

Although there are minor clinical differences, such as age of onset, between the leukodystrophies, the common features of concern to the anaesthetist include seizures and poor airway tone with the risk of aspiration. As with our patient, many of these children have a severe seizure disorder that requires two or three anticonvulsant medications for effective control. Therapeutic levels should be documented preoperatively and anticonvulsant doses should be continued up to the time of the operation and during the immediate postoperative period. When oral or nasogastric administration is not feasible due to the recent surgical procedure, intravenous administration is an acceptable alternative for phenobarbital or phenytoin while therapeutic levels may be maintained with rectal administration of carbamazepine or valproic acid.^{2,3} Intraoperative doses of intravenous anaesthetic agents and muscle relaxants may need to be increased due to the increased hepatic enzyme function seen in patients on chronic anticonvulsant therapy.⁴

Other associated neurological manifestations include choreoathetoid and other extrapyramidal movement disorders. Phenothiazines, butyrophenones and other agents with dopaminergic blocking activity should be avoided since they may exacerbate these movement disorders. The newly released serotonin antagonist, ondansetron, may be the drug of choice to control postoperative nausea and vomiting⁵ since it should not exacerbate movement disorders due to its lack of effect on the dopaminergic system.

Since these patients have copious oral secretions, preoperative administration of an anti-sialogogue such as glycopyrrolate is suggested. In addition to increased secretions, airway management may be further complicated by bulbar involvement with poor control of pharyngeal musculature. Due to the risks of airway compromise especially in the presence of residual anaesthetic agents, extended postoperative monitoring (24 hr) with pulse oximetry is recommended. This may be best accomplished in an intermediate care unit since many of these children will require frequent suctioning and positioning to avoid postoperative respiratory complications.

Progressive CNS deterioration is frequently accompanied by GER and recurrent aspiration. Our patient had previously a Nissen fundoplication and no clinical symptoms of reflux. However, many patients will present for anaesthesia with signs or symptoms suggestive of GER. In such patients, preoperative administration of metoclopramide and an H₂-antagonist is recommended and rapid sequence induction with cricoid pressure is advo-

cated. Metoclopramide may also cause extrapyramidal effects and should be used only in patients with documented GER who are at risk for aspiration. At the conclusion of the surgical procedure, tracheal extubation should occur only when airway protective reflexes are present.

Any of the several available induction agents may be used. Likewise several choices exist for maintenance anaesthesia and we can find no advantage of any particular agent. One exception is dorsal rhizotomy surgery for severe spasticity unresponsive to medical management.⁶ For this procedure, ketamine offers the advantage of providing anaesthesia while maintaining muscle tone thereby allowing intraoperative evaluation of the surgical results.

Intraoperative monitoring should be determined by the anticipated surgical procedure. We chose to use routine intraoperative monitoring including precordial stethoscope, pulse oximetry, electrocardiogram, non-invasive blood pressure cuff, and end-tidal carbon dioxide measurement. Invasive monitoring may be indicated for more involved surgical procedures. In addition, careful monitoring of body temperature is recommended as well as measures to avoid hypothermia such as warming of infused fluids, regulation of the operating room temperature, and humidification of inhaled gases. This is particularly relevant in children with CNS damage since there may be a disruption of the normal homeostatic mechanisms to maintain body temperature. In addition, the general cachectic state of many of these patients leaves them with little or no body fat and therefore at risk for hypothermia.

Malnutrition also impacts on positioning of these patients on the operating table. Care must be taken to pad bony prominences to prevent pressure necrosis even during brief operative procedures.

The choice of muscle relaxant (depolarizing versus non-depolarizing) is more controversial. We were unable to find any discussion concerning the use of succinylcholine in patients with leukodystrophies. However, due to the risks of hyperkalaemia following succinylcholine in patients with upper motor neurone diseases,⁷ we recommend non-depolarizing agents even when rapid-sequence intubation is required.

As with any patient, the provision of postoperative analgesia should be part of the anaesthetic technique. Whenever possible, we recommend regional anaesthetic techniques to avoid parenteral narcotics. Caudal or lumbar epidural anaesthesia can be used to provide analgesia following orthopaedic procedures on the lower extremities or abdominal procedures such as fundoplication. When regional anaesthetic techniques are not feasible, we recommend the administration of small doses of *iv* narcotics (e.g., morphine 0.03 to 0.05 mg · kg⁻¹) repeated as needed to provide analgesia. Although no studies have evaluated the effects of narcotics in these patients, we

speculate that due to altered central control of respiration, they may have an increased sensitivity to the respiratory depressant effects of narcotics. Therefore, monitoring of respiratory function (pulse oximetry, respiratory rate) is recommended when administering narcotics in this setting.

A few subtle differences exist between the various leukodystrophies that are of concern, particularly the occurrence of adrenal hypofunction with adrenoleukodystrophy. Perioperative administration of adrenocorticoid hormones may be necessary and preoperative evaluation of adrenal function (ACTH stimulation testing) is recommended if the patient's function is not known. One minor consideration exists in patients with Canavan's disease who frequently have macrocephaly. Careful positioning with elevation of the remainder of the body may be necessary to obtain the correct "sniffing position" for intubation and facilitate airway management.

In summary, we have presented the anaesthetic management of a four-year-old boy with a degenerative cerebral white matter disorder (leukodystrophy). Of concern to the anaesthetist is the high prevalence of seizure disorders, poor pharyngeal co-ordination, and the presence of GER with the risk of aspiration. Identification of these associated conditions during the preoperative examination will allow the safe provision of anaesthetic care to these children.

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