Brief Reports

Anaesthetic management of an adult patient with X-linked adrenoleukodystrophy

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Purpose: Adrenoleukodystrophy (ALD) is a rare genetic disorder. Findings include various central nervous system problems in addition to adrenal insufficiency. We present a case of an adult man with X-linked ALD undergoing surgery.

Clinical features: A 40-yr-old man with X-linked ALD presented with an intertrochanteric femoral fracture. Past medical history included recurrent lung atelectasis, urinary incontinence, mental retardation, seizure disorder, and adrenal insufficiency. No sedative pre-medications were ordered, but perioperative steroid coverage with 100 mg hydrocortisone was initiated. In the operating room, the patient would not allow placement of all monitors. Therefore, 1 mg midazolam then 275 mg thiopentone followed immediately by 40 mg rocuronium were used to induce anaesthesia with the application of cricoid pressure and the remaining monitors. Fentanyl 50 μg *iv* was given soon after induction, and anaesthesia was maintained with nitrous oxide and isoflurane. No further muscle relaxant or opioid was administered and anaesthesia was uneventful. The trachea was extubated with the patient awake and he was taken to the recovery area in stable condition.

Conclusion: Patients with X-linked ALD are rarely seen in a clinical setting because the condition is so uncommon. Adrenal insufficiency, mental retardation, and osteoporosis are major considerations for these patients. In addition, these patients are at risk for reflux, seizures, and major post-operative complications.

Objectif : L'adréno-leucodystrophie (ALD) est une affection héréditaire rare. Ses manifestations comprennent des troubles divers du système nerveux central associés à une insuffisance surrénale. Nous présentons le cas d'un homme atteint d'ALD liée au sexe, devant subir une chirurgie.

Aspects cliniques : Un homme de 40 ans atteint d'ALD génétique s'est présenté souffrant d'une fracture transtrochantérienne du fémur. L'histoire médicale révélait une atélectasie récurrente, de l'incontinence urinaire, un retard mental, des crises convulsives et de l'insuffisance surrénalienne. Aucune prémédication n'a été administrée, mais une dose de protection périopératoire de stéroïde avec 100 mg d'hydrocortisone a été donnée. Dans la salle d'opération, le patient n'acceptait pas la mise en place des différents appareils de surveillance. Par conséquent, on a utilisé 1 mg de midazolam, puis 275 mg de thiopental suivis immédiatement de 40 mg de rocuronium pour induire l'anesthésie avec l'application d'une pression cricoïdienne suivie de la mise en place des autres appareils. Aussitôt après l'induction, on a administré 50 μg *iv* de fentanyl et l'anesthésie a été maintenue avec du protoxyde d'azote et de l'isoflurane. Aucun autre myorelaxant ou opioïde n'ont été administrés et l'anesthésie s'est déroulée sans incident. L'extubation de la trachée s'est faite chez le patient éveillé qui présentait un état stable lors de son transfert à la salle de réveil.

Conclusion : Les patients atteints d'ALD génétique sont rarement traités en clinique, vu leur condition particulière. L'insuffisance surrénalienne, le retard mental et l'ostéoporose constituent d'importantes préoccupations dans le traitement de ces patients. De plus, ce sont des patients qui risquent de présenter du reflux, des crises et des complications postopératoires majeures.

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Accepted for publication July 20, 1998.

ADRENOLEUKODYSTROPHY (ALD) is a term relating to two genetic disorders that affect the central nervous system (CNS), adrenal glands, and occasionally other body tissues. One form, X-linked ALD, will form the major focus of the following discussion. The other form, neonatal ALD, is autosomal recessive and a totally separate entity from X-linked ALD.[1] The anaesthetic implications for neonatal ALD are summarized elsewhere.[2]

X-linked ALD is associated with a total body increase in very long chain fatty acids caused by defective degradation in peroxisomes. The gene responsible for the condition has been mapped to Xq28.[3] The hallmarks of X-linked ALD are CNS demyelination and primary adrenal insufficiency.[3] A phenotypic classification is utilized based on primary CNS site affected and age of onset (Table I).[4]

Case report

A 40-yr-old, 50 kg man with X-linked ALD presented with a fractured femur. Medical history included smoking, recurrent lobar atelectasis, Addison's disease, seizure disorder, mental retardation, and urinary incontinence. Medication included primidone, carbamazepine, and long-term prednisone and fludracortisone. Abnormal blood work included haemoglobin 103 $g \cdot L^{-1}$ and sodium 124 $mmol \cdot L^{-1}$. An endocrinologist felt there was nothing to suggest adrenal insufficiency but recommended perioperative steroid replacement with hydrocortisone.

Induction of anaesthesia was complicated by the patient's uncooperative and mildly hostile nature. Placement of ECG leads was successful, but the patient would not permit application of the blood pressure cuff nor the plethysmograph probe. In addition, the patient would not tolerate pre-oxygenation by mask. Therefore, 1 mg midazolam, 275 mg thiopentone, and 40 mg rocuronium were administered *iv*. Cricoid pressure was initiated, oxygen was passively administered via mask, and remaining monitors were applied. Tracheal intubation followed without complication. Anaesthesia was maintained with nitrous oxide, isoflurane, and fentanyl 50 μg in total. The patient was carefully positioned on the table and the remainder of the course of anaesthesia ran smoothly. The trachea was extubated with the patient awake and he was taken to the recovery room in stable condition. Post-operatively, he required several transfusions for anaemia and he experienced several seizures. Further investigations resulted in new diagnoses of hypogonadism and osteoporosis.

Discussion

This case describes the first reported anaesthetic for an adult patient with X-linked ALD. Our patient fit the adrenomyeloneuropathy phenotype (Table II).

Anaesthetic considerations begin with the preoperative history during which therapeutic interventions should be elicited. Current therapies for the disease include bone marrow transplantation, low fat diets, glycerol trioleate oil, and Lorenzo's oil (erucic acid).[5] A prior bone marrow transplantation will leave the patient immunosuppressed iatrogenically. Therapy with Lorenzo's oil has caused thrombocytopaenia, which could lead to a coagulopathy.[6] Lorenzo's oil has also produced lipid infiltration in rodent hearts, raising the concern of cardiac dysfunction in humans.[5]

Chronic steroid replacement for adrenal insufficiency may leave these patients unable to compensate for the stress of surgery and extra steroid coverage may be required. As well electrolyte disturbances may occur due to excess or lack of mineralocorticoid effect. Anticonvulsant therapy for seizure disorders can lead to hepatic enzyme induction and the need to alter anaesthetic drug dosages.

These patients can have other morbidities related to their CNS involvement. Our patient had a history of significant atelectasis, which may be due to hypotonia secondary to demyelination rather than primary pulmonary pathology. Another consideration in these

TABLE I Phenotypic classification for X-linked Adrenoleukodystrophy[4]

Phenotype	*Usual Age of Onset - yr*	*CNS Site primarily affected*
Childhood Cerebral	<10	Cerebral Hemispheres
Adolescent Cerebral	10-21	Cerebral Hemispheres
Adult Cerebral	>21	Cerebral Hemispheres
Adrenomyeloneuropathy	Late 20's or early 30's	Spinal Cord
Adrenal-insufficiency only	?	None
Asymptomatic	—	None

TABLE II Findings in the adrenomyeloneuropathy phenotype[1,3]

Site	*Findings*	*Approximate Percent Affected*
Spinal Cord	Spasticity Bladder Incontinence	100%
Peripheral Nerve	Loss proprioception/ vibratory sense	100%
Cerebral Hemispheres	Mental retardation, seizures, Depression	40%
Gonads	Hypogonadism	40%
Adrenal Gland	Adrenal Insufficiency	39%

patients is that of mental retardation which can present as a difficult, uncooperative patient. History of previous anaesthesia and past medical history may be difficult to elicit.

Pre-operative sedation is an issue because it is unknown if these patients are prone to respiratory depression, but the brainstem respiratory centre may be altered in the syndrome. It is probably good practice to avoid any sedative agents until the patient is under direct observation.

There are no reports of adverse effects from anaesthetic agents, but avoiding those which lower the seizure threshold such as ketamine and enflurane is wise. Patients with neuromuscular disease may develop hyperkalaemia if given succinylcholine and it too should be avoided .[7] The response to non-depolarizing muscle relaxants is unknown and clinical monitoring should guide administration.

General anaesthesia should be initiated using the rapid sequence technique with cricoid pressure. These patients are at risk for aspiration because of gastro-oesophageal reflux secondary to gastric dysmotility, and can be treated with H_2 antagonists to decrease gastric acidity. Disagreement exists whether metoclopramide should be used to stimulate gastric emptying because it may cause extrapyramidal symptoms.[8,2]

Utilization of regional techniques could be difficult for several reasons. These patients may have a scoliosis secondary to the CNS involvement with resulting technically difficult anatomy. Patients with mental retardation may be unable or unwilling to consent to a regional technique. Thrombocytopaenia secondary to dietary manipulation could also represent a factor limiting the use of regional techniques.

Another important consideration is patient movement and positioning. A subset of these patients demonstrate hypogonadism which is a known risk factor for osteoporosis. In addition, these patients are often on chronic steroid therapy and immobilized, both of which cause bony mineral density loss.[9] As a result, there exists a risk of iatrogenic fracture during transfer and positioning. With loss of muscle mass secondary to lack of testosterone and disuse atrophy, pressure points are at risk of damage during anaesthesia and should be padded appropriately.

After surgery, the trachea should be extubated with the patient awake. We recommend that the patient be monitored postoperatively for 12 to 24 hr to recognize early postoperative problems such as respiratory failure due to hypotonia. These patients are more at risk for problems such as deep venous thrombosis because their underlying condition may prevent early ambulation, regardless of the type of surgery performed.

In conclusion, X-linked ALD is rare and not often encountered in the operating room. The patient with this condition suffers from various problems centered around the CNS and the adrenal glands. As a result of their condition they are also at high risk of osteoporosis, reflux, and post-operative complications.

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