Anaesthetic implications of nemaline rod myopathy

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Nemaline rod myopathy is an inherited congenital myopathy first described in 1963. Affected patients characteristically present in infancy with a non-progressive hypotonia and symmetrical muscle weakness. The disease affects all skeletal muscles including the diaphragm with sparing of cardiac and other muscle. Facial dysmorphism is common as are skeletal deformities, including kyphosis, scolosis and pectus excavatum.

We present two sisters with nemaline rod myopathy and their anaesthetic management for scoliosis surgery. Facial dysmorphism was a feature of both cases. Preoperatively, both patients demonstrated poor respiratory function on pulmonary function testing. Both cases were successfully managed using controlled ventilation and inhalational anaesthetic agents, avoiding muscle relaxants. Postoperatively, there were no respiratory complications.

Although one case report describes the use of succinylcholine and pancuronium in a patient with nemaline rod myopathy, we feel that neuromuscular blocking agents should be avoided where possible and only used with careful monitoring.

Key words
GENETIC FACTORS: nemaline rod myopathy; ANAESTHETIC TECHNIQUES: inhalational agents, muscle relaxants; COMPLICATIONS: pulmonary function, difficult intubation.

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CAN ANAESTH SOC J 1985 / 32: 5 / pp 543–7

Nemaline rod myopathy belongs to the group of congenital sarcoplasmic myopathies which includes central core disease and mitochondrial myopathy. It was first described in 1963,[1,2] and except for a single case report[3] there is little in the medical literature about the anaesthetic management of these patients.

Myopathic patients can present with decreased respiratory muscle reserve and as such be unable to compensate for the stresses of anaesthesia and surgery. Anaesthesia in these patients may precipitate respiratory failure secondary to the respiratory depressant effects of drugs, sputum retention leading to pneumonia, and ventilatory restriction due to wound pain. We review our anaesthetic experience in two sisters with nemaline rod myopathy, presenting an anaesthetic technique for these patients which appears to be without complications, and avoids the use of muscle relaxants.

Muscular dystrophies and myotonias are associated with abnormal responses to various anaesthetic agents. Succinylcholine has on rare occasions caused cardiac arrest. Although there has been one case report where muscle relaxants were given to a patient with nemaline rod myopathy,[3] we feel that these drugs should be avoided when possible.

Case 1

Sister one was the first born child of a 27-year-old woman. Following a difficult breech delivery, she was found to have severe flexion contractures of both hips and little spontaneous movement in all four limbs. The contractions of her hips were treated with passive stretching and traction without anaesthesia. At age one month a muscle biopsy done using local anaesthesia was normal. The presumptive diagnosis was myodystrophia fetalis or arthrogryposis. One month later a second muscle biopsy and electromyogram were done because of persistent myotonia. On this occasion the biopsy revealed normal muscle and the electromyogram

showed atrophic muscle. The presumptive diagnosis was arthrogryposis and the prognosis for both physical and mental improvement were thought to be poor.

By four years of age Sister one could walk. The myopathy had not progressed. In view of her progress, the diagnosis was changed to non-progressive spinal muscular atrophy. However, at 12 years of age, a review of her disease process changed the diagnosis to nemaline rod myopathy.

Between the ages of six and 16 years, Sister one had four anaesthetics for minor orthopaedic and eye surgery. On each occason, anaesthesia was induced with thiopentone 5 $mg \cdot kg^{-1}$ and atropine 0.02 $mg \cdot kg^{-1}$. An endotracheal tube was passed under deep halothane anaesthesia without the use of muscle relaxants. Anaesthesia was maintained with nitrous oxide, oxygen and halothane with controlled ventilation. On each occasion, anaesthesia and recovery were uneventful.

At 13 years of age, Sister one presented for corrective surgery for a marked thoraco-lumbar scoliosis. A minor degree of facial dysmorphism was noted. Preoperative investigations including blood count, urea, serum electrolytes, prothrombin time, partial thromboplastin time, capillary blood gases and chest *x*-ray were all normal. Pulmonary function studies demonstrated a restrictive defect, with a forced vital capacity of 47 per cent of predicted. The electrocardiogram revealed left atrial hypertrophy without ventricular chamber enlargement; however, the heart size on chest *x*-ray was normal. Anaesthesia was induced with thiopentone 5 $mg \cdot kg^{-1}$ and atropine 0.02 $mg \cdot kg^{-1}$ and an endotracheal tube inserted under deep halothane anaesthesia without muscle relaxant. Anaesthesia was maintained with fentanyl and halothane, and controlled ventilation. No muscle relaxants were used. The blood loss during the scoliosis surgery was 95 per cent of the estimated blood volume. There were no coagulation defects despite the large blood loss. She was extubated in the recovery room. Postoperative pain was treated initially with morphine, and then after two days with codeine. There were no postoperative respiratory complications and she was discharged from hospital 12 days later.

Case 2

Sister two presented at the age of 14 years for Luque rod instrumentation to correct a thoraco-lumbar scoliosis. Her past medical history was unremarkable except for a history of nemaline rod myopathy. Preoperative investigations including blood count, urea, serum electrolytes, urinalysis, prothrombin time, partial thromboplastin time, capillary blood gases, chest *x*-ray and electrocardiogram were all normal. Pulmonary function tests showed a severe restrictive defect with a fixed vital capacity of 34 per cent of predicted.

Sister two had dysmorphic facial features including a very narrow mandible and high arched palate. Anaesthesia was induced with nitrous oxide, oxygen and halothane. At laryngoscopy only the posterior arytenoids were visualized and the trachea was intubated with the aid of a stylet. Anaesthesia was maintained with nitrous oxide, oxygen and isoflurane, and controlled ventilation. Muscle relaxants were not used. Because surgery lasted seven hours and the blood loss was 2.5 times the patient's estimated blood volume, Sister two was ventilated overnight in the intensive care unit. She was extubated the next morning. There were no postoperative respiratory complications or coagulation problems, and the patient was discharged home ten days later.

Discussion

Nemaline rod myopathy often presents in the neonatal period with hypotonia, a weak cry, poor sucking reflex and dysphagia. These problems may lead to respiratory distress and cyanosis. Motor development is delayed, and crawling and walking are characteristically late. Most patients with nemaline rod myopathy present in the newborn period with only a small number presenting later in life.[4]

The trunk and proximal limb muscles are most commonly affected. Distal limb muscles,[5,6] palatal, pharyngeal and facial muscles may also be involved. Engel described one patient in whom there was loss of muscle bulk in all muscle groups, and in particular in the paraspinal and proximal limb muscles.[5] In that patient, the muscle groups most severely affected were considerably stronger than expected when tested. In autopsy studies, extensive diaphragmatic involvement is reported,[6–9] with sparing of cardiac and smooth muscle.

Although the nervous system is not commonly involved, deep tendon reflexes may be absent.

In addition to skeletal muscle involvement, dysmorphic features are common. The face is

characteristically long and slender, with a high arched palate. Micrognathia and dental malocclusion are also common. Skeletal deformities including kyphosis, scoliosis, pes cavus and pectus excavatum are often present. It is the latter orthopaedic problems which usually require surgery. The presence of arachnoidactyly in one patient, has suggested that the disease resembles Marfan's syndrome without the cardiac lesion.[10]

It has been suggested that nemaline myopathy is a non-progressive muscle disease. However, there have been several reports of a severe form of nemaline rod myopathy which resulted in death in the first year of life.[7–9] The first fatal case occurred in a patient with severe involvement of the bulbar and respiratory muscles, including the diaphragm.[9] Death was due to pulmonary aspiration, and respiratory failure again is a potential problem. A patient with a positive muscle biopsy for nemaline rod myopathy may also be symptom free.[12] Sudden progression of the disease in late middle life has also been reported.[6] Because the clinical manifestations of the infantile nemaline myopathy and the late onset rod body myopathy are different it has been suggested that they are distinct entities. In the adult, rod body myopathies have been associated with other diseases of muscle including dermatomyositis and polymyositis.[13] These diseases may represent a single disease spectrum with an early or late onset.[6]

Laboratory investigations may help to confirm the diagnosis of nemaline rod myopathy. Creatinurea has been found in a number of cases, but the non-specific nature of the test limits its usefulness.[6] Electromyography usually reveals a non-specific myopathy which is not diagnostic for nemaline rod myopathy. Microscopy of a muscle biopsy specimen is the only diagnostic test. Microscopy usually reveals aggregates of rods in the sarcolemma of the muscle fibre. The rods may be identified with Gormori's trichrome stain. Negative muscle biopsies have been explained by the variability of affected fibres in different muscle groups.[6] Nevertheless, microscopy of a muscle biopsy specimen remains the only definitive test of the disease.

The inheritance pattern is thought to be autosomal dominant with variable penetrance. Nemaline rod myopathy may affect both parents and children.[1,6] In one case, the mother had both central core disease and nemaline myopathy, and the daughter had only central core disease.[11] There have been no extensive pedigrees described for nemaline rod myopathy to date and sporadic cases of the disease have also been recorded.[12]

Patients with nemaline rod myopathy can present three main problems to the anaesthetist – facial dysmorphism, the adequacy of pulmonary function, and the question of which anaesthetic agent may be used safely. Preoperative assessment of these patients should include an examination of the airway for a high arched palate, micrognathia and dental malocclusion, which suggest a potentially difficult intubation. Pulmonary function studies will be useful in assessing the severity of the restrictive lung disease due to a combination of the myopathy and scoliosis. Blood gases indicate the adequacy of oxygenation and ventilation. In those patients with pulmonary problems, chest physiotherapy should commence preoperatively and continue in the postoperative period. Preoperative chest infection should be actively treated and elective surgery delayed until the infection resolves. A complete anaesthetic management including a technique for securing the airway in view of a difficult intubation, difficulty in ventilating the patient during surgery and contingency plans for postoperative ventilation must be considered.

Facial dysmorphism, a common feature of the disease, was present in both our sisters to a lesser or greater degree. This dysmophism may give rise to concern as to the ease of intubation in these patients, and an inhalation induction or awake intubation may be preferred. Sister two was correctly assessed as presenting an intubation problem, because of her long narrow face, small mandible and high arched palate. An inhalational induction was performed and intubation was accomplished with minor difficulty.

The respiratory function of patients with nemaline rod myopathy presenting for scoliosis surgery may be compromised in two ways. Firstly, the myopathy itself may affect the respiratory muscles reducing respiratory reserve. Secondly, severe scoliotic curves cause changes in pulmonary function because of chest wall deformity, pulmonary gas exchange is affected by ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch, producing increases in the alveolar/arterial oxygen difference ($A\text{-}aDO_2$) and the dead space/tidal volume ratio (VD/VT). Increasing maldistribution increases the patient's ventilatory requirements and a rising arterial carbon dioxide

tension reflects an inability to compensate for this. In long-standing cases, pulmonary hypertension may be present. In addition to chest wall deformity and loss of motor function in these patients, there may be an abnormality of central respiratory control causing sensitivity to depressant drugs such as narcotics, sedatives and general anaesthetics. Preoperative pulmonary function tests should include vital capacity, forced expiratory volume and its derivatives, and resting arterial gas levels. These will serve as a baseline against which to compare postoperative results. The presence of a bulbar palsy may further complicate anaesthetic management because of the tendency to regurgitation and pulmonary aspiration.

Because myotonias and muscular dystrophies are associated with abnormal responses to neuromuscular blocking agents, we felt that they were best avoided. Heard and Kaplan, however, have reported a single case in whom succinylcholine 1 $mg \cdot kg^{-1}$ and pancuronium $0.08\,mg \cdot kg^{-1}$ were used.[3] The patient had an abnormal response to succinylcholine with 95 per cent twitch depression only developing after four minutes. Intubating conditions were good and there were no associated rises in the serum potassium level. The response to pancuronium was normal. We have shown that patients with nemaline rod myopathy can be safely managed without the use of muscle relaxants, which may be preferable in view of their poor respiratory reserve and potentially difficult intubation. Although many muscle diseases including central core disease and Duchenne muscular dystrophy are associated with an increased incidence of malignant hyperthermia,[14,15] there has been no reported association between nemaline rod myopathy and malignant hyperthermia.

If a "wake-up" test is performed during scoliosis surgery, the use of inhalational agents may prolong the time to awakening, but this is not a contraindication to their use in these patients. However, if somatosensory cortical evoked potentials are used to assess spinal cord function, inhalational agents do affect the results.

The use of hypotensive anaesthesia to reduce blood loss in scoliosis surgery remains a controversial subject. In myopathic patients deliberate hypotension is probably best avoided in view of the unpredictability of the patients' response to anaesthetic agents. Although both sisters had large blood losses during their scoliosis surgery, this had no adverse effects on postoperative morbidity.

Summary

We have described the anaesthetic management of six operative procedures in two sisters with nemaline rod myopathy. Special problems associated with this disease are the presence of dysmophism, poor pulmonary reserve and the choice of anaesthetic technique. Inhalational agents appear to be well tolerated in these patients with no side-effects. Although one case report has described the use of muscle relaxants in a patient with nemaline rod myopathy we feel that these agents should be avoided if possible. Postoperative ventilatory support may be required in severely affected patients; however, a meticulous anaesthetic technique can produce little postoperative morbidity.

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Résumé

La myopathie à la nemaline est une myopathie congénitale décrite pour la première fois en 1963. Les patients affectés présentent dès l'enfance une hypotonie non progressive et une faiblesse musculaire symétrique. Cette maladie affecte tous les muscles squelettiques incluant le diaphragme à l'exception du muscle cardiaque. Le dysmorphisme facial est fréquent de même que des difformités squelettiques incluant une cyphose, scoliose et pectus excavatum.

On présente le cas de deux sœurs atteintes de myopathie à la nemaline qui se sont présentées pour une correction de scoliose. La conduite anesthésique est discutée. La déformité du visage a été un problème dans les deux cas. En période préopératoire, les deux patientes avaient une fonction respiratoire perturbée. La conduite anesthésique s'est effectuée avec succès en utilisant la ventilation contrôlée et des agents anesthésiques d'inhalation sans relaxant musculaire. En période postopératoire, aucune complication respiratoire fut notée.

Même si un cas a été rapporté où la succinylcholine et le pancuronium ont été utilisés, on croit que les relaxants musculaires doivent être évités si possible et utilisés uniquement avec une surveillance soutenue.