ANAESTHESIA AND PROGRESSIVE MUSCULAR DYSTROPHY

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The Duchenne form is the most common and severe type of childhood progressive muscular dystrophy (PMD) with an incidence of approximately 30 per 100000 live births. The condition is caused by an x-linked recessive gene, although some of the affected boys are isolated cases with new genetic mutations—presumably occurring in the ovarian cells of the mother or maternal grandmother (Walton, 1983). Becker's muscular dystrophy, which is the other x-linked form, is milder and does not present as early nor run such a progressive course.

Duchenne's PMD usually becomes apparent between 2 and 6 years of age with the onset of a clumsy, waddling gait and frequent falling. Occasionally, affected boys do not develop the ability to walk. A characteristic feature is that of the child "climbing up his legs" on arising from the floor (Gower's sign). There is initial selective involvement of the muscles with, usually, the proximal muscle groups of the pelvis and the shoulders being affected first. The affected muscles may be large, as a result of infiltration by fatty tissue, but are nevertheless weak. This enlargement has led to the disorder being referred to as the pseudohypertrophic type.

Most boys with Duchenne's PMD show steady deterioration and are unable to walk by 8-11 years of age. Characteristically, by 13-14 yr they have difficulty propelling a wheelchair. Contractures are seen in these later stages, probably as a result of the unopposed action of antagonists of the dystrophic muscles. Progressive deformity occurs and kyphoscoliosis is common. Some patients become obese while others have a wasted appearance. Intellectual ability may be reduced. Skeletal atrophy can predispose to fractures of the shafts of the long bones.

SUMMARY

The presentation and features of Duchenne's progressive muscular dystrophy (Duchenne's PMD) are described and the increased risks associated with anaesthesia are considered. Hazards associated with induction of anaesthesia and immediate postoperative recovery have been stressed in recent case reports, and these are summarized. Features of a hyperpyrexia-like response including cardiac arrest, increased serum creatine phosphokinase concentration, myoglobinuria and metabolic acidosis following suxamethonium or halothane, or both, have been described in patients with Duchenne's PMD. Subsequent in vitro muscle tests have suggested that it is possible that a malignant hyperpyrexia response to general anaesthesia may occur. Six children known to have Duchenne's PMD who developed delayed respiratory insufficiency following anaesthesia and required controlled pulmonary ventilation are reported. In five of the children, cardiac arrest occurred despite apparently adequate respiratory support. Suxamethonium was common to the anaesthetic received by all six patients. In one of these patients subsequent anaesthetics, without suxamethonium, were uneventful and delayed muscle weakness did not occur.

Invariably there is myocardial involvement, but this is often masked by the incapacity caused by the skeletal myopathy. Heart and skeletal muscles are thought to share progressive muscular dystrophy abnormalities (Hunsaker et al., 1982). Electrocardiographic changes tend to be typical for Duchenne's PMD and are independent of the duration of the disease (Slucka, 1968). Characteristically these include a tall R wave in lead V1, a deep Q wave in lateral precordial and limb leads, sinus tachycardia, and a shortened P–R interval (Perloff et al., 1967). The electrocardiographic
following surgery has been described by Wislicki.

Acute gastric dilatation occurring 48 h after surgery in the 6 h period when the effects of anaesthesia are still present. Acute gastric dilatation occurring 48 h after surgery may be required. The intensity of management necessary will depend upon the degree of muscle disability.

Anaesthetic considerations

Duchenne’s PMD is a disorder which affects not only striated, but also smooth and cardiac muscle. Weakness of respiratory muscle and the decreased ability to cough can result in loss of respiratory reserve and accumulation of secretions which may lead to repeated chest infection. As the dystrophy progresses, the respiratory weakness becomes more important and the development of spinal deformities adds to the restrictive nature of pulmonary function. Consequently, pre- and post-operative physiotherapy, close observation in the recovery room, and additional oxygen therapy may be required. The intensity of management necessary will depend upon the degree of muscle disability.

Hypomotility of the gastrointestinal tract may lead to slower gastric emptying. Therefore at least 6 h starvation should be allowed before general anaesthesia in elective cases. If swallowing mechanisms and laryngeal reflexes are impaired, there will be a greater risk of aspiration than usual, particularly during the immediate postoperative period when the effects of anaesthesia are still present. Acute gastric dilatation occurring 48 h following surgery has been described by Wislicki (1962) in a patient with advanced Duchenne’s PMD. She suggested that all affected patients requiring supine nursing should have a nasogastric tube passed as a prophylactic measure.

Myocardial involvement always occurs in patients with Duchenne’s PMD. Tachycardia (Miller et al., 1978), ventricular fibrillation (Okada et al., 1982; Brownell et al., 1983) and cardiac arrest (Genever, 1971; Seay, Ziter and Thompson, 1978; Boltshauser et al., 1980; Linter et al., 1982) have been reported during the induction of anaesthesia. In all these patients in these case reports, Duchenne’s PMD was unsuspected until further investigation was prompted by the occurrence of the cardiac manifestations. Ventricular fibrillation or cardiac arrest has also been described in patients known to have Duchenne’s PMD, following a return of consciousness while the patient was still in the recovery room (Boba, 1970; Kelfer, Singer and Reynolds, 1983). The general anaesthetics which resulted in cardiac complications at induction all involved the use of suxamethonium. The majority used halothane as the induction agent, although one patient described by Seay, Ziter and Thompson (1978) had anaesthesia induced with cyclopropane. The patients described by Boba (1970) and Kelfer, Singer and Reynolds (1983) with postoperative complications, received only halothane for anaesthesia. Rhabdomyolysis as shown by myoglobinuria and markedly increased CPK concentrations was evident in the patients with cardiac problems following suxamethonium. This evidence of muscle breakdown was associated either with excess muscle rigidity after suxamethonium (Genever, 1971; Seay, Ziter and Thompson, 1978; Boltshauser et al., 1980; Linter et al., 1982; Brownell et al., 1983), or without rigidity (Miller et al., 1978; Seay, Ziter and Thompson, 1978; Oka et al., 1982). Brownell and colleagues (1983) and Kelfer, Singer and Reynolds (1983) obtained blood samples at the time of cardiac arrest and found marked hyperkalaemia. Metabolic acidosis was usually a feature (Miller et al., 1978; Boltshauser et al., 1980; Linter et al., 1982; Brownell et al., 1983; Kelfer, Singer and Reynolds, 1983), but was not always found (Oka et al., 1982).

Recently, it has been suggested that there may be an association between Duchenne’s PMD and malignant hyperpyrexia (Oka et al., 1982; Brownell et al., 1983; Kelfer, Singer and Reynolds, 1983; Rosenberg and Heiman-Patterson, 1983). Malignant hyperpyrexia (MH) is characterized by a progressive increase in body temperature; muscle...
contracture, usually after suxamethonium or in response to halothane or another inhalation anaesthetic vapour; myoglobinuria; hyperkalaemia; acidosis; cyanosis and tachycardia (Ellis, 1980). Episodes of MH may occur without significant fever or acidosis, but to support the diagnosis there must be evidence of increased aerobic or anaerobic metabolism (Gronert, 1980). Some features of MH were shown by many of the above case reports and in vitro tests for MH were carried out in some instances. Following cardiac arrest during anaesthesia, Oka and colleagues (1982) and Brownell and co-workers (1983) showed increased caffeine sensitivity of biopsied muscle fibres, from a 21-month-old boy and a 5-year-old boy, respectively. Rosenberg and Heiman-Patterson (1983) showed halothane sensitivity of biopsied muscle from a 4-year-old boy with Duchenne's PMD which they interpreted as being consistent with sensitivity to MH. Kelfer, Singer and Reynolds (1983), using a muscle biopsy from their patient, found decreases in the calcium uptake and adenosine triphosphatase activity of the sarcoplasmic reticulum. The results of this test, though, are not comparable to the usual halothane and caffeine contraction tests.

Some of the children described did not develop fever with the anaesthetic agents and the highest temperature recorded was 38.5 °C. Ellis (1980) stated that children with Duchenne's PMD may develop an increase in temperature which does not progress to malignant hyperpyrexia and can be managed by surface cooling. However, the in vitro muscle tests outlined above suggest that it is possible that an MH response to general anaesthesia may occur in Duchenne's PMD. Possibly these patients with their underlying cardiac muscle dysfunction are at greater risk from the increase in serum potassium concentration which occurs following suxamethonium administration. It may be that the high incidence of survival following cardiac arrest in these patients is the result of the transitory nature of the increase in serum potassium concentration (cf. burns patients).

Suxamethonium is known to release potassium from cells, increase serum CPK concentrations (Tammisto and Airaksinen, 1966) and cause myoglobinuria (MacLaren, 1968) in normal patients, including children. Halothane potentiates the enzyme-releasing effects of suxamethonium, but may also produce this result to a lesser degree when administered as a sole agent to normal patients (Lewandowski, 1982). The potassium- and enzyme-releasing effects are potentiated in patients with Duchenne's PMD and in patients with subclinical myopathy, as demonstrated by increased resting CPK and lactic dehydrogenase (LD) concentrations in serum (Lewandowski, 1981). Lewandowski (1982) described a boy with normal resting serum CPK concentration and increased serum LD concentrations who developed rhabdomyolysis, myoglobinuria, acidosis, tachycardia and hyperpyrexia following halothane and suxamethonium. Both the patient and a brother had strabismus and a cousin suffered from severe Duchenne's PMD. It was suggested that "the family is affected by subclinical dystrophy" and "may be prone to MH and/or rhabdomyolysis".

Recent experimental work suggests there is a spectrum of susceptibility to MH (Nelson, Flewellen and Gloyna, 1983). In addition, the presentation of MH is not always classical and confusion can easily develop as to whether this disorder is occurring. The diagnosis of MH susceptibility in patients with Duchenne's PMD should not be made without muscle biopsy and in vitro contracture studies, as the response to suxamethonium in particular, and inhalation agents, may be rapid breakdown of muscle giving a biochemical and clinical picture very similar to MH.

Although this discussion implies these patients are extremely vulnerable to anaesthesia, large series have been described in which no unexpected problems occur with anaesthesia provided the general state of fitness is reasonable (Cobham and Davis, 1964; Richards, 1972; Morris, personal communication (1984)). A variety of anaesthetic techniques was utilized in these patients, including the use of suxamethonium in some.

Delayed effects of general anaesthesia

In addition to the side effects during or immediately after general anaesthesia, instances of delayed muscle weakness leading to respiratory failure have been described (Watters, Karpati and Kaplan, 1977; Bush, 1979; Linter et al., 1982). There follows a more complete description of the patients previously referred to by Bush (1983). All these patients were known to be severely affected with Duchenne's PMD before anaesthesia.

Patient 1. Diagnosed as Duchenne's PMD aged 7 yr. At 9 yr he was admitted for left plantar fasciotomy and wedge removal from the lateral side of the left os calcis under general anaesthesia.
Thiopentone, suxamethonium, halothane, nitrous oxide and oxygen were administered, and endotracheal intubation performed. Uneventful anaesthesia and recovery occurred. On the 2nd day after operation, inadequate cough and the presence of secretions in his airway were noted. The following day there was no improvement despite conventional treatment. On the 4th day after operation, sudden cardiorespiratory collapse occurred. The patient was resuscitated, requiring tracheal intubation to allow suction and assisted ventilation. Tracheotomy was advised, but on induction of anaesthesia sudden cardiac arrest occurred. On this occasion there was no response to resuscitative efforts.

**Patient 2.** Diagnosed as Duchenne’s PMD aged 9 yr. At 10 yr he was admitted for right plantar fasciotomy. Uneventful recovery from operation followed, but 9 months later he was described as having great difficulty in walking. When aged 13 yr he was admitted for dental treatment under general anaesthesia which consisted of thiopentone, suxamethonium, halothane, nitrous oxide and oxygen, and endotracheal intubation. After good recovery from anaesthesia he was discharged from hospital. However, readmission was required because of the onset of swallowing difficulties on the 2nd day after operation. The next day he developed a weak cough and tachypnoea. On the 4th day after operation, cardiorespiratory collapse occurred, requiring endotracheal intubation and controlled ventilation. Tracheotomy was performed on the same day. The following day sudden cardiac arrest occurred with resuscitative attempts being unsuccessful.

**Patient 3.** Admitted for dental treatment as a day case aged 14 yr. He had previously been diagnosed as having Duchenne’s PMD. Thiopentone, suxamethonium, nitrous oxide and oxygen and possibly halothane were administered. Attempts at intubation were unsuccessful. He was discharged home later the same day. Admission was required again the next day because of difficulty in swallowing and breathing. He suffered a cardiac arrest from which he could not be resuscitated.

**Patient 4.** Diagnosed as Duchenne’s PMD by muscle biopsy aged 6 yr. When aged 14 yr he was admitted for drainage of dental abscess. Before operation he was completely bedridden and unable to feed himself, but his chest movement was good and his lungs clear to auscultation. General anaesthesia consisted of methohexitone, suxamethonium, nitrous oxide and oxygen, halothane, nasotracheal intubation and spontaneous respiration. Following good immediate recovery from anaesthesia he developed respiratory insufficiency 9 h later. The trachea was intubated, 100% oxygen administered and artificial ventilation instituted. However, cardiac arrest supervened which failed to respond to treatment. Postmortem showed typical evidence of Duchenne’s PMD.

**Patient 5.** This patient had spina bifida and Duchenne’s PMD. An early operation closed the spina bifida and calipers allowed walking until aged 12 yr. When aged 17 yr he was admitted for dental treatment under general anaesthesia. Marked weakness of arms, chewing and swallowing was noted. Anaesthesia consisted of thiopentone, suxamethonium, nitrous oxide in oxygen and halothane. The trachea was intubated. Initially, he recovered well from anaesthesia, but 5 h later, developed difficulty in breathing with retention of secretions. The trachea was re-intubated, the secretions were removed, and with the onset of satisfactory spontaneous respiration the endotracheal tube was removed. Further respiratory difficulties developed 12 h into the postoperative period and intubation was required again. Mechanical ventilation, utilizing a trigger mechanism, was commenced. At 24 h into the postoperative period, he was breathing spontaneously for brief periods. After 6 days tracheotomy was performed and artificial ventilation continued. On the 12th day after operation there was a sudden deterioration of the cardiovascular system with eventual cardiac arrest.

**Patient 6.** Diagnosed as Duchenne’s PMD by muscle biopsy under general anaesthesia aged 7 yr. He was dependent on a wheelchair 2 yr later. When aged 13 yr the patient was admitted for bilateral elongation of tendoachilles for equinus deformity of feet. General anaesthesia consisted of methohexitone, suxamethonium, nitrous oxide in oxygen and halothane. Endotracheal intubation was performed. Twenty-four hours after recovery from anaesthesia he developed difficulty in swallowing, requiring frequent pharyngeal aspiration. The weakness showed progressive deterioration so that, 3 h later, he was in extremis. Tracheal intubation was performed and artificial ventilation commenced. By the 3rd day after operation he was maintaining satisfactory spontaneous respiratory
effort with a tidal volume of 250 ml. The trachea was extubated but required re-intubation, and the re-introduction of mechanical ventilation, 2 h later. On the 4th day after operation collapse of the right lung occurred but the patient was able to trigger the ventilator. Tracheotomy was performed under fentanyl and diazepam anaesthesia on the 5th postoperative day. By the 10th postoperative day he could tolerate 15 min per hour off the ventilator. Two days later he could manage without ventilatory support and the tracheostomy tube was removed on the 23rd day. Three weeks later he was noted to have a cough, stridor, and was described as “chesty”. X-ray showed tracheal stenosis and he was readmitted for tracheal inspection and dilatation of the stricture under general anaesthesia.

Subsequently, over the next 4 months tracheal dilatation was required on five occasions and anaesthetic agents used included thiopentone, diazepam, fentanyl, nitrous oxide and halothane. Excellent recovery occurred from all anaesthetics without subsequent ventilatory embarrassment.

These six patients with Duchenne’s PMD all had uneventful anaesthesia with postoperative muscle recovery to the level present in the preoperative period. However, delayed respiratory insufficiency developed 5–36 h following anaesthesia. Of the five patients who subsequently received apparently adequate pulmonary ventilation, four suffered a fatal cardiac arrest which may reflect the underlying cardiac myopathy. All six patients received suxamethonium at induction of anaesthesia. Patient 6, who was the only survivor of this delayed respiratory insufficiency, subsequently had anaesthesia on several occasions without suxamethonium, and no problems were encountered. The explanation for the onset of severe muscle weakness after a period of good recovery from anaesthesia must be speculative and further investigation of muscle function during such an episode is needed before any definitive conclusion can be drawn.

All these patients showed severe Duchenne’s PMD, and perhaps this complication will be seen only at such a stage. This suggestion would be compatible with the experience of others who have not found difficulty with anaesthesia in patients with Duchenne’s PMD. However, in view of the above case reports, extreme care should obviously be exercised for longer than is usual in the postoperative period. The delayed development of pulmonary insufficiency is a most unusual clinical feature, and this has drawn our attention to the problems of anaesthesia in Duchenne’s PMD.

CONCLUSIONS
(a) Suxamethonium should be avoided in patients known to have Duchenne’s PMD. Myocardial complications may follow suxamethonium during induction of anaesthesia. Suxamethonium was the common agent in the patients who developed delayed respiratory insufficiency after full recovery from anaesthesia. Patient 6 was managed uneventfully when suxamethonium was not used.

(b) Any untoward myocardial reaction in boys during induction of anaesthesia should alert the anaesthetist to exclude Duchenne’s PMD.

(c) Recent case reports in the literature suggest that some patients with Duchenne’s PMD are at risk of developing malignant hyperpyrexia.

(d) Precautions with patients with Duchenne’s PMD should include temperature and electrocardiographic monitoring throughout anaesthesia. Dantrolene should be available in theatre and readily used if events consistent with a malignant hyperpyrexial response to anaesthesia occur.

(e) Where possible, local anaesthesia should be used to provide surgical analgesia.

REFERENCES


