CHAPTER 35

Anesthesia for Patients with Neuromuscular Disease

KEY CONCEPTS

1. Weakness associated with myasthenia gravis is due to autoimmune destruction or inactivation of postsynaptic acetylcholine receptors at the neuromuscular junction, leading to reduced numbers of receptors and degradation of their function, and to complement-mediated damage to the postsynaptic membrane.
2. Patients who have myasthenia gravis with respiratory muscle or bulbar involvement are at increased risk for pulmonary aspiration.
3. Many patients with myasthenia gravis are exquisitely sensitive to nondepolarizing neuromuscular blockers (NMBs).
4. Patients who have myasthenia gravis are at risk for postoperative respiratory failure. Disease duration of more than 6 years, concomitant pulmonary disease, a peak inspiratory pressure of less than -25 cm H_2O (ie, -20 cm H_2O), a vital capacity less than 4 mL/kg, and a pyridostigmine dose greater than 750 mg/d are predictive of the need for postoperative ventilation following thymectomy.
5. Patients with Lambert–Eaton myasthenic syndrome and other paraneoplastic neuromuscular syndromes are very sensitive to both depolarizing and nondepolarizing NMBs.
6. Respiratory muscle degeneration in patients with muscular dystrophy interferes with an effective cough mechanism and leads to retention of secretions and frequent pulmonary infections.
7. Degeneration of cardiac muscle in patients with muscular dystrophy is also common, but results in dilated or hypertrophic cardiomyopathy in only 10% of patients.
8. Succinylcholine should be avoided in patients with Duchenne's or Becker's muscular dystrophies because of unpredictable response and the risk of inducing severe hyperkalemia or triggering malignant hyperthermia.
9. Anesthetic management in patients with periodic paralysis is directed toward preventing attacks. Intraoperative management should include frequent determinations of plasma potassium concentrations and careful electrocardiographic monitoring to detect arrhythmias.
10. In patients with periodic paralysis, the response to NMBs is unpredictable, and neuromuscular function should be carefully monitored during their use. Increased sensitivity to nondepolarizing NMBs is particularly apt to be encountered in patients with hypokalemic periodic paralysis.

Although neuromuscular diseases are relatively uncommon, patients with these conditions will present to the operating room and to non–operating room procedure areas for diagnostic studies, treatment of complications, or surgical management of related or unrelated disorders. Overall debility, with diminished respiratory muscle strength and increased sensitivity to neuromuscular blockers (NMBs), predisposes these patients to postoperative ventilatory failure and pulmonary aspiration, and may slow their post-procedure recovery because of difficulty with ambulation and increased risk of falling. A basic understanding of the major disorders and their potential interaction with anesthetic agents is necessary to minimize the risk of perioperative morbidity.

MYASTHENIA GRAVIS

Myasthenia gravis is an autoimmune disorder characterized by weakness and easy fatigability of skeletal muscle. It is classified according to disease distribution and severity (Table 35–1). The prevalence is estimated at 50–200 per million population. The incidence is highest in women during their third decade, and men exhibit two peaks, one in the third decade and another in the sixth decade.

1 Weakness associated with myasthenia gravis is due to autoimmune destruction or inactivation of postsynaptic acetylcholine receptors at the neuromuscular junction, leading to reduced numbers of receptors and degradation of their function, and to complement-mediated damage to the postsynaptic end plate. IgG antibodies against the nicotinic acetylcholine receptor in neuromuscular junctions are found in 85–90% of patients with generalized myasthenia gravis and up to 50–70% of patients with ocular myasthenia. Among patients with myasthenia, 10–15% percent develop thymoma, whereas approximately 70% exhibit histologic evidence of thymic lymphoid follicular hyperplasia. Other autoimmune-related disorders (hypothyroidism, hyperthyroidism, rheumatoid arthritis, and systemic lupus erythematosus) are also present in up to 10% of patients. The differential diagnosis of myasthenia gravis includes a number of other clinical conditions that may mimic its signs and symptoms

TABLE 35–1 Myasthenia Gravis Foundation of America clinical classification of myasthenia gravis.[1]

Class	Definition
I	Any ocular muscle weakness May have weakness of eye closure All other muscle strength is normal
II	Mild weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
IIa	Predominantly affecting limb, axial muscles, or both May also have lesser involvement of oropharyngeal muscles
IIb	Predominantly affecting oropharyngeal, respiratory muscles, or both May also have lesser or equal involvement of limb, axial muscles, or both
III	Moderate weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
IIIa	Predominantly affecting limb, axial muscles, or both May also have lesser involvement of oropharyngeal muscles
IIIb	Predominantly affecting oropharyngeal, respiratory muscles, or both May also have lesser or equal involvement of limb, axial muscles, or both
IV	Severe weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
IVa	Predominantly affecting limb and/or axial muscles May also have lesser involvement of oropharyngeal muscles
IVb	Predominantly affecting oropharyngeal, respiratory muscles, or both May also have lesser or equal involvement of limb, axial muscles, or both
V	Defined by intubation, with or without mechanical ventilation, except when employed during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb

[1]Reproduced, with permission, from Jaretzki III A, Barohn RJ: Myasthenia gravis: Recommendations for clinical research standards. Neurology 2000;55:16.

TABLE 35–2 Differential diagnosis of myasthenia gravis.[1]

Other neuromuscular disorders
Congenital myasthenic syndromes
Botulism
Lambert–Eaton syndrome
Cranial nerve palsies
Diabetes
Intracranial aneurism
Trauma (eg, orbital factures)
Congenital (eg, Dwayne syndrome)
Infections (eg, basilar meningitis)
Inflammation (eg, cavernous sinus syndromes)
Neoplasm (eg, basilar meningioma)
Horner's syndrome
Muscle disease
Myotonic muscular dystrophy
Oculopharyngeal muscular dystrophy
Mitochondrial myopathies (eg, chronic progressive external ophthalmoplegia)
Central nervous system pathology
Stroke
Demyelinating disease
Other
Motor neuron disease
Metabolic disease (eg, thyroid disease)

[1]Reproduced, with permission, from Mahadeva B, Phillips II L, Juel VC: Autoimmune disorders of neuromuscular transmission. Semin Neurol 2008;28:212.

TABLE 35–3 Drugs that may potentiate weakness in myasthenia gravis.[1]

Cardiovascular agents
β-Blockers
Lidocaine
Procainamide
Quinidine
Verapamil
Antibiotics
Ampicillin
Azithromycin
Ciprofloxacin
Clarithromycin
Erythromycin
Gentamycin
Neomycin
Streptomycin
Sulfonamides
Tetracycline
Tobramycin
Central nervous system drugs
Chlorpromazine
Lithium
Phenytoin
Trihexyphenidyl
Immunomodulators
Corticosteroids
Interferon-α
Rheumatological agents
Chloroquine
D-Penicillamine
Miscellanous
Iodinated radiocontrast agents
Magnesium
Nondepolarizing neuromuscular blockers

[1]Data from Mahadeva B, Phillips II L, Juel VC: Autoimmune disorders of neuromuscular transmission. Semin Neurol 2008;28:212; and Matney S, Huff D: Diagnosis and treatment of myasthenia gravis. Consult Pharm 2007;22:239.

(Table 35–2). *Myasthenia gravis crisis* is an exacerbation requiring mechanical ventilation and should be suspected in any patient with respiratory failure of unclear etiology.

The course of myasthenia gravis is marked by exacerbations and remissions, which may be partial or complete. The weakness can be asymmetric, confined to one group of muscles, or generalized. Ocular muscles are most commonly affected, resulting in fluctuating ptosis and diplopia. With bulbar involvement, laryngeal and pharyngeal muscle weakness can result in dysarthria, difficulty in chewing and swallowing, problems clearing secretions, or pulmonary aspiration. Severe disease is usually also associated with proximal muscle weakness (primarily in the neck and shoulders) and involvement of respiratory muscles. Muscle strength characteristically improves with rest but deteriorates rapidly with exertion. Infection, stress, surgery, and pregnancy have unpredictable effects on the disease but often lead to exacerbations. A number of medications may exacerbate the signs and symptoms of myasthenia gravis (Table 35–3).

Anticholinesterase drugs are used most commonly to treat the muscle weakness of this disorder. These drugs increase the amount of acetylcholine at the neuromuscular junction through inhibition of end plate acetylcholinesterase. Pyridostigmine is prescribed most often; when given orally, it has an

effective duration of 2–4 h. Excessive administration of an anticholinesterase may precipitate *cholinergic crisis*, which is characterized by increased weakness and excessive muscarinic effects, including salivation, diarrhea, miosis, and bradycardia. An *edrophonium (Tensilon) test* may help differentiate a cholinergic from a myasthenic crisis. Increased weakness after administration of up to 10 mg of intravenous edrophonium indicates cholinergic crisis, whereas increasing strength implies myasthenic crisis. If this test is equivocal or if the patient clearly has manifestations of cholinergic hyperactivity, all cholinesterase drugs should be discontinued and the patient should be monitored in an intensive care unit or close-observation area. Anticholinesterase drugs are often the only agents used to treat patients with mild disease. Moderate to severe disease is treated with a combination of an anticholinesterase drug and immunomodulating therapy. Corticosteroids are usually tried first, followed by azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil, and intravenous immunoglobulin. Plasmapheresis is reserved for patients with dysphagia or respiratory failure, or to normalize muscle strength preoperatively in patients undergoing a surgical procedure, including thymectomy. Up to 85% of patients younger than 55 years of age show clinical improvement following thymectomy even in the absence of a tumor, but improvement may be delayed up to several years.

Anesthetic Considerations

Patients with myasthenia gravis may present for thymectomy or for unrelated surgical or obstetric procedures, and medical management of their condition should be optimized prior to the intended procedure. Myasthenic patients with respiratory and oropharyngeal weakness should be treated preoperatively with intravenous immunoglobulin or plasmapheresis. If strength normalizes, the incidence of postoperative respiratory complications should be similar to that of a nonmyasthenic patient undergoing a similar surgical procedure. Patients scheduled for thymectomy may have deteriorating muscle strength, whereas those undergoing other elective procedures may be well controlled or in remission. Adjustments in anticholinesterase medication, immunosuppressants, or steroid therapy in the perioperative period may be necessary. Patients with advanced generalized disease may deteriorate significantly when anticholinesterase agents are withheld. These medications should be restarted when the patient resumes oral intake postoperatively. When necessary, cholinesterase inhibitors can also be given parenterally at $\frac{1}{30}$ the oral dose. Potential problems associated with management of anticholinesterase therapy in the postoperative period include altered patient requirements, increased vagal reflexes, and the possibility of disrupting bowel anastomoses secondary to hyperperistalsis. Moreover, because these agents also inhibit plasma cholinesterase, they could *theoretically* prolong the duration of ester-type local anesthetics and succinylcholine.

Preoperative evaluation should focus on the recent course of the disease, the muscle groups affected, drug therapy, and coexisting illnesses. **2** Patients who have myasthenia gravis with respiratory muscle or bulbar involvement are at increased risk for pulmonary aspiration. Premedication with metoclopramide or an H_2 blocker or proton pump inhibitor may decrease this risk. Because patients with myasthenia are often very sensitive to the respiratory depressant effect of opioids and benzodiazepines, premedication with these drugs should be done with caution, if at all.

With the exception of NMBs, standard anesthetic agents may be used in patients with myasthenia gravis. Marked respiratory depression, however, may be encountered following even moderate doses of propofol or opioids. When general anesthesia is required, a volatile agent–based anesthetic is frequently employed. Deep anesthesia with a volatile agent alone in patients with myasthenia may provide sufficient relaxation for tracheal intubation and most surgical procedures, and many clinicians routinely avoid NMBs entirely. The response to succinylcholine is said to be unpredictable, but we have not found this to be so in practice. Patients may manifest a relative resistance, or a moderately prolonged effect (see Chapter 11). The dose of succinylcholine may be increased to 2 mg/kg to overcome any resistance, expecting that the duration of paralysis could be increased by 5–10 min.

3 Many patients with myasthenia gravis are exquisitely sensitive to nondepolarizing NMBs. Even a defasciculating dose in some patients may result in nearly complete paralysis. If NMBs are

necessary, small doses of a relatively short-acting nondepolarizing agent are preferred. We have not found nondepolarizing NMBs to be necessary during thymectomy with volatile anesthesia. Neuromuscular blockade should be monitored very closely with a nerve stimulator, and ventilatory function should be evaluated carefully prior to extubation.

4 Patients who have myasthenia gravis are at risk for postoperative respiratory failure. Disease duration of more than 6 years, concomitant pulmonary disease, peak inspiratory pressure of less than −25 cm H_2O (ie, −20 cm H_2O), vital capacity less than 4 mL/kg, and pyridostigmine dose greater than 750 mg/d are predictive of the need for postoperative ventilation following thymectomy.

Women with myasthenia can experience increased weakness in the last trimester of pregnancy and in the early postpartum period. Epidural anesthesia is generally preferable for these patients because it avoids potential problems with respiratory depression and NMBs related to general anesthesia. Excessively high levels of motor blockade, however, can also result in hypoventilation. Infants of myasthenic mothers may show transient myasthenia for 1–3 weeks following birth, induced by transplacental transfer of acetylcholine receptor antibodies, which may necessitate intubation and mechanical ventilation.

PARANEOPLASTIC NEUROMUSCULAR SYNDROMES

Paraneoplastic syndromes are immune-mediated diseases associated with an underlying cancer. Myasthenia gravis is often considered a paraneoplastic syndrome because it is an autoimmune disorder associated with thymic hyperplasia, including thymoma. Other neurological or neuromuscular paraneoplastic syndromes include Lambert–Eaton myasthenic syndrome, limbic encephalitis, neuromyotonia, stiff person syndrome, myotonic dystrophy, and polymyositis.

Lambert–Eaton Myasthenic Syndrome

The Lambert–Eaton myasthenic syndrome (LEMS) is a paraneoplastic syndrome characterized by proximal muscle weakness that typically begins in the lower extremities but may spread to involve upper limb, bulbar, and respiratory muscles. Dry mouth, male impotence, and other manifestations of autonomic dysfunction are also common. LEMS is usually associated with small cell carcinoma of the lung but may also be seen with other malignancies or as an idiopathic autoimmune disease. The disorder results from a presynaptic defect of neuromuscular transmission in which antibodies to voltage-gated calcium channels on the nerve terminal markedly reduce the quantal release of acetylcholine at the motor end plate. Small cell lung carcinoma cells express identical voltage-gated calcium channels, serving as a trigger for the autoimmune response in patients with paraneoplastic LEMS.

In contrast to myasthenia gravis, muscle weakness associated with LEMS improves with repeated effort and is improved less dramatically by anticholinesterase drugs. Guanidine hydrochloride and 3,4-diaminopyridine (DAP), which increase the presynaptic release of acetylcholine, often produce significant improvement in LEMS. Corticosteroid or other immunosuppressive medications, or plasmapheresis, may also be of benefit.

Limbic Encephalitis

Limbic encephalitis is a degenerative central nervous system disorder characterized by personality changes, hallucinations, seizures, autonomic dysfunction, varying degrees of dementia, and asymmetric loss of sensation in the extremities. It may involve the brain, brainstem, cerebellum, and spinal cord. In approximately 60% of cases, limbic encephalitis is paraneoplastic. There is a strong association with small cell lung carcinoma, and neurological dysfunction often precedes the cancer diagnosis. Therapy includes treatment of the underlying cancer, if present, and administration of immunosuppressive medications.

Neuromyotonia

Neuromyotonia is a condition of peripheral nerve hyperexcitability that is frequently associated with an underlying cancer but may also be inherited or associated with diabetic, drug- or toxin-induced, or other acquired neuropathies. Its features

include *myokymia* (a continuous undulating movement of muscles described as being like a "bag of worms"), stiffness, impaired muscle relaxation, painful muscle cramping, hyperhidrosis, and muscle hypertrophy. Treatment includes immunoglobulin therapy, plasma exchange, and administration of anticonvulsants.

Stiff Person Syndrome

Stiff person syndrome is a progressive disorder characterized by axial stiffness and rigidity that may subsequently involve the proximal limb muscles. In advanced cases, paraspinal rigidity may cause marked spinal deformities, and the patient may have difficulty with ambulation and a history of frequently falling. Although stiff person syndrome is rare, when it occurs it is frequently associated with cancer. Therapy includes treatment of the underlying cancer, if present, and administration of immunoglobulin and benzodiazepines.

Myotonic Dystrophy

See next page.

Polymyositis

Polymyositis is an inflammatory myopathy of skeletal musculature, especially proximal limb muscles, characterized by weakness and easy fatigability. Patients are prone to aspiration and frequent pneumonias because of thoracic muscle weakness and dysphagia secondary to oropharyngeal muscle involvement. They may also exhibit cardiac dysrhythmias due to conduction defects. Therapy includes treatment of the underlying neoplasm, if present; plasma exchange; and administration of immunoglobulin, corticosteroids, and immunomodulators such as methotrexate, cyclosporine, and tumor necrosis factor-α inhibitors.

Anesthetic Considerations for Patients with Neuromuscular Paraneoplastic Syndromes

5 Patients with LEMS and other neuromuscular paraneoplastic syndromes are very sensitive to both depolarizing and nondepolarizing NMBs. Volatile agents alone are often sufficient to provide muscle relaxation for both intubation and most surgical procedures. NMBs should be given only in small increments and with careful neuromuscular monitoring. Because these patients frequently exhibit marked debility, benzodiazepines, opioids, and other medications with sedative effects should be administered with caution.

MUSCULAR DYSTROPHIES

Preoperative Considerations

Muscular dystrophies are a heterogeneous group of hereditary disorders characterized by muscle fiber necrosis and regeneration, leading to muscle degeneration and progressive weakness. Anticipated anesthetic risk is increased by the patient's overall debilitated status, which may impede clearance of secretions and postoperative ambulation, as well as by increased risk of respiratory failure and pulmonary aspiration. Duchenne's muscular dystrophy is the most common and most severe form of muscular dystrophy. Other muscular dystrophy variants include Becker's, myotonic, facioscapulohumeral, and limb-girdle dystrophies.

Duchenne's Muscular Dystrophy

An X-linked recessive disorder, Duchenne's muscular dystrophy affects males almost exclusively. It has an incidence of approximately one to three cases per 10,000 live male births and most commonly presents between 3 and 5 years of age. Affected individuals produce abnormal dystrophin, a protein found on the sarcolemma of muscle fibers. Patients characteristically develop symmetric proximal muscle weakness that is manifested as a gait disturbance. Fatty infiltration typically causes enlargement (pseudohypertrophy) of muscles, particularly the calves. Progressive weakness and contractures eventually result in kyphoscoliosis. Many patients are confined to wheelchairs by age 12. Disease progression may be delayed by up to 2–3 years with glucocorticoid therapy in some patients. Intellectual impairment is common but generally nonprogressive. Plasma creatine kinase (CK) levels are 10–100 times normal even early in the disease and may reflect an abnormal increase in the permeability of muscle cell

membranes. Female genetic carriers often also have high plasma CK levels, variable degrees of muscle weakness, and, rarely, cardiac involvement. Plasma myoglobin concentration may also be elevated. The diagnosis is confirmed by muscle biopsy.

6 Respiratory muscle degeneration in patients with muscular dystrophy interferes with an effective cough mechanism and leads to retention of secretions and frequent pulmonary infections. The combination of marked kyphoscoliosis and muscle wasting may produce a severe restrictive ventilatory defect. Pulmonary hypertension is common with

7 disease progression. Degeneration of cardiac muscle in patients with muscular dystrophy is also common, but results in dilated or hypertrophic cardiomyopathy in only 10% of patients. Mitral regurgitation secondary to papillary muscle dysfunction is also found in up to 25% of patients. Electrocardiogram abnormalities include P–R interval prolongation, QRS and ST-segment abnormalities, and prominent R waves over the right precordium with deep Q waves over the left precordium. Atrial arrhythmias are common. Death at a relatively young age is usually due to recurrent pulmonary infections, respiratory failure, or cardiac failure.

Becker's Muscular Dystrophy

Becker's muscular dystrophy is, like Duchenne's, an X-linked recessive disorder but is less common (1:30,000 male births). Manifestations are nearly identical to those of Duchenne's muscular dystrophy except that they usually present later in life (adolescence) and progress more slowly. Mental retardation is less common. Patients often reach the fourth or fifth decade, although some may survive into their 80s. Death is usually from respiratory complications. Cardiomyopathy may occur in some cases and may precede severe skeletal weakness.

Myotonic Dystrophy

Myotonic dystrophy is a multisystem disorder that is the most common cause of *myotonia*, a slowing of relaxation after muscle contraction in response to electrical or percussive stimuli. The disease is autosomal dominant, with an incidence of 1:8000, and usually becomes clinically apparent in the second to third decade of life, but it has also been reported as a paraneoplastic disorder in association with thymoma. Myotonia is the principal early manifestation; muscle weakness and atrophy become more prominent as the disease progresses. This weakness and atrophy usually affect cranial muscles (orbicularis oculi and oris, masseter, and sternocleidomastoid), and in contrast to most myopathies, distal muscles more than proximal muscles. Plasma CK levels are normal or slightly elevated.

Multiple organ systems are involved in myotonic dystrophy, as evidenced by presenile cataracts, premature frontal baldness, hypersomnolence with sleep apnea, and endocrine dysfunction leading to pancreatic, adrenal, thyroid, and gonadal insufficiency. Respiratory involvement leads to decreased vital capacity, and chronic hypoxemia may cause cor pulmonale. Gastrointestinal hypomotility may predispose patients to pulmonary aspiration. Uterine atony can prolong labor and increase the incidence of retained placenta. Cardiac manifestations, which are often present before other clinical symptoms appear, may include cardiomyopathy, atrial arrhythmias, and varying degrees of heart block.

The myotonia is usually described by patients as a "stiffness" that may lessen with continued activity—the so-called "warm-up" phenomenon. Patients often report that cold temperatures worsen stiffness. Antimyotonic treatment may include mexiletine, phenytoin, baclofen, dantrolene, or carbamazepine. A cardiac pacemaker may be placed in patients with significant conduction defect, even if they are asymptomatic.

Facioscapulohumeral Dystrophy

Facioscapulohumeral dystrophy, an autosomal dominant disorder with an incidence of approximately 1–3:100,000, affects both sexes, although more females than males are asymptomatic. Patients usually present in the second or third decade of life with weakness that is confined primarily to the muscles of the face and the shoulder girdle. Muscles in the lower extremities are less commonly affected, and respiratory muscles are usually spared. The disease is slowly progressive with a variable course. Plasma CK levels are usually normal or only slightly elevated. Cardiac involvement is rare, but loss of all

atrial electrical activity with an inability to atrially pace the heart has been reported; ventricular pacing is still possible in these patients. Longevity is minimally affected.

Limb-Girdle Dystrophy

Limb-girdle muscular dystrophy is a heterogeneous group of genetic neuromuscular diseases. Limb-girdle syndromes include severe childhood autosomal recessive muscular dystrophy and other incompletely defined autosomal recessive syndromes such as Erb's (scapulohumeral type) and Leyden–Mobius (pelvifemoral type) dystrophies. Most patients present in childhood to the second or third decade of life with slowly progressive muscle weakness that may involve the shoulder girdle, the hip girdle, or both. Plasma CK levels are usually elevated. Cardiac involvement is relatively uncommon but may present as frequent arrhythmias or congestive heart failure. Respiratory complications, such as hypoventilation and recurrent respiratory infections, may occur.

Anesthetic Considerations

A. Duchenne's and Becker's Muscular Dystrophies

The anesthetic management of these patients is complicated not only by muscle weakness but also by cardiac and pulmonary manifestations. An association with malignant hyperthermia has been suggested but is unproven. Preoperative premedication with sedatives or opioids should be avoided because of increased aspiration risk due to respiratory muscle weakness, gastric hypomotility, or both. Intraoperative positioning may be complicated by kyphoscoliosis or by flexion contractures of the extremities or neck. Succinylcholine should be avoided in patients with Duchenne's or Becker's muscular dystrophies because of unpredictable response and the risk of inducing severe hyperkalemia or triggering malignant hyperthermia. Although some patients exhibit a normal response to nondepolarizing NMBs, others may be very sensitive. Marked respiratory and circulatory depression may be seen with volatile anesthetics in patients with advanced disease, and regional or local anesthesia may be preferable in these patients. Perioperative morbidity is usually due to respiratory complications. Patients with vital capacities less than 30% of predicted appear to be at greatest risk and often require temporary postoperative mechanical ventilation.

B. Myotonic Dystrophy

Patients with myotonic dystrophy are at increased risk for perioperative respiratory and cardiac complications. Most perioperative problems arise in patients with severe weakness and in those cases in which surgeons and anesthesiologists are unaware of the diagnosis. The diagnosis of myotonic dystrophy has been made in some patients in the course of investigating prolonged apnea following general anesthesia.

Patients with myotonic dystrophy have altered responses to a number of anesthetic medicines. They are often very sensitive to even small doses of opioids, sedatives, and inhalation and intravenous anesthetic agents, all of which may cause sudden and prolonged apnea. Premedication should therefore be avoided. Succinylcholine is relatively contraindicated because it may precipitate intense myotonic contractions, complicating orotracheal intubation. Myotonic contraction of respiratory, chest wall, or laryngeal muscles may make ventilation difficult or impossible. Other drugs that act on the motor end plate, such as decamethonium, neostigmine, and physostigmine, can aggravate myotonia. Regional anesthesia may be preferentially employed, but does not always prevent myotonic contractions.

The response to nondepolarizing NMBs is reported to be normal; however, they do not consistently prevent or relieve myotonic contractions. As reversal of nondepolarizing NMBs can induce myotonic contractions, the use of short-acting nondepolarizing agents is recommended. Postoperative shivering commonly associated with volatile agents, particularly when associated with decreased body temperature, can induce myotonic contractions in the recovery room. Small doses of meperidine can often prevent such shivering and may preempt myotonic contractions.

Induction of anesthesia without complications has been reported with a number of agents including

inhalation agents and propofol. Neuromuscular blockade, if needed, should employ short-acting NMBs. An association between myotonic dystrophy and malignant hyperthermia has been suggested but not established. Nitrous oxide and inhalation agents can be used as maintenance anesthesia. Reversal with anticholinesterases should be avoided, if possible.

The principal postoperative complications of myotonic dystrophy are prolonged hypoventilation, atelectasis, aspiration, and pneumonia. Close postoperative monitoring should be accompanied by aggressive pulmonary hygiene with physical therapy and incentive spirometry. Aspiration prophylaxis is indicated. Patients undergoing upper abdominal surgery or those with severe proximal weakness are more likely to experience pulmonary complications. Perioperative cardiac conduction abnormalities are less likely to occur but still warrant close cardiovascular monitoring.

C. Other Forms of Muscular Dystrophy

Patients with facioscapulohumeral and limb-girdle muscular dystrophy generally have normal responses to anesthetic agents. Nevertheless, because of the great variability and overlap among the various forms of muscular dystrophy, sedative-hypnotics, opioids, and nondepolarizing NMBs should be used cautiously, and succinylcholine should be avoided.

MYOTONIAS

Myotonia Congenita & Paramyotonia Congenita

Myotonia congenita is a disorder manifested early in life with generalized myotonia. Both autosomal dominant (Thomsen's) and recessive (Becker's) forms exist. The disease is confined to skeletal muscle, and weakness is minimal or absent. Many patients have very well developed musculature due to near constant muscle contraction. Antimyotonic therapy includes phenytoin, mexiletine, quinine sulfate, or procainamide. Other medications that have been used include tocainide, dantrolene, prednisone, acetazolamide, and taurine. There is no cardiac involvement in myotonia congenita, and a normal life span is expected.

Paramyotonia congenita is a very rare autosomal dominant disorder characterized by transient stiffness (myotonia) and, occasionally, weakness after exposure to cold temperatures. The stiffness worsens with activity, in contrast to true myotonia, thus the term *paramyotonia*. Serum potassium concentration may rise following an attack similar to hyperkalemic periodic paralysis (see below). Medications that have been used to block the cold response include mexiletine and tocainide.

Anesthetic management of patients with myotonia congenita and paramyotonia is complicated by an abnormal response to succinylcholine, intraoperative myotonic contractions, and the need to avoid hypothermia. NMBs may paradoxically cause generalized muscle spasms, including trismus, leading to difficulty with intubation and ventilation.

Infiltration of muscles in the operative field with a dilute local anesthetic may alleviate refractory myotonic contraction. Among patients with these types of myotonia, none have been reported with positive in vitro tests for malignant hyperthermia. Excised muscle in these patients does, however, display a prolonged myotonic contraction when exposed to succinylcholine. Excessive muscle contraction during anesthesia, therefore, likely represents aggravation of myotonia and not malignant hyperthermia.

PERIODIC PARALYSIS

Periodic paralysis is a group of disorders characterized by spontaneous episodes of transient muscle weakness or paralysis. Symptoms usually begin in childhood, with episodes lasting a few hours and typically sparing respiratory muscle involvement. The weakness usually lasts less than 1 hour but can last several days, and frequent attacks may lead to progressive, long-term weakness in some patients. Hypothermia exacerbates the frequency and severity of episodes. Muscle strength and serum potassium concentrations are usually normal between attacks. The episodes of weakness are due to a loss of muscle fiber excitability secondary to partial depolarization of the resting potential. This partial depolarization prevents the generation of action potentials and thereby precipitates weakness.

Periodic paralysis is classified into primary genetic channelopathies and secondary acquired forms. The genetic types are due to dominantly inherited mutations in the voltage-gated sodium, calcium, or potassium ion channels. Classifications have been based on clinical differences, but these have not been shown to relate to specific ion channels. Different defects in the same channel can cause different clinical pictures, whereas mutations in different channels may have similar clinical pictures. However, the clinical classifications remain useful as guides to prognosis and therapy.

Hypokalemic periodic paralysis is typically associated with low serum potassium levels, and *hyperkalemic periodic paralysis* with elevated serum potassium levels, during episodes of weakness. In these defects, muscle membranes are inexcitable to both direct and indirect stimulation due to either decreased potassium conductance or increased sodium conductance, respectively. Both defects are associated with fluid and electrolyte shifts.

Thyrotoxicosis is associated with a secondary form of hypokalemic periodic paralysis. It resembles the primary form but is much more common in men than women, particularly in persons of Asian descent and in young adults. Once the thyroid condition is treated, the episodes usually cease. The disorder can develop in 10–25% of hyperthyroid Asian men. The metabolic sequelae and fluid and electrolyte shifts seen in the primary form are also seen in secondary hypokalemic periodic paralysis. Treatment involves management of the hyperthyroidism, avoidance of high carbohydrate and low potassium meals, and administration of potassium chloride for acute attacks.

Secondary hypokalemic paralysis can also develop if there are marked losses of potassium through the kidneys or the gastrointestinal tract. The associated weakness is, at times, episodic and potassium levels are much lower than in other variants of hypokalemic periodic paralysis. Management of the primary disease with potassium replacement, and treatment of acidosis or alkalosis, is important in preventing attacks.

Patients who consume large amounts of barium salts, which block potassium channels, can also develop hypokalemic periodic paralysis. This condition is treated by stopping the barium salts and administering oral potassium.

Potassium levels that exceed 7 mEq/L between episodes of weakness suggest a secondary form of hyperkalemic periodic paralysis. Treatment is targeted toward the primary disease and involves restriction of potassium.

Anesthetic Considerations

9 Anesthetic management of patients with periodic paralysis is directed toward preventing attacks. Intraoperative management should include frequent determinations of plasma potassium concentration and careful electrocardiographic monitoring to detect arrhythmias. Because of the potential for glucose-containing intravenous solutions to lower plasma potassium concentration, they should not be used in patients with hypokalemic paralysis, whereas they may benefit patients with hyperkalemic paralysis. The response to NMBs is unpredictable, and neuromuscular function should be carefully monitored during their use. Increased sensitivity to nondepolarizing NMBs is particularly apt to be encountered in patients with hypokalemic periodic paralysis. Succinylcholine is contraindicated in hyperkalemic paralysis and perhaps other variants as well because of the risk of hyperkalemia. Intraoperative maintenance of core temperature is important because shivering and hypothermia may trigger or exacerbate episodes of periodic paralysis.

10

CASE DISCUSSION

Anesthesia for Muscle Biopsy

A 16-year-old boy with progressive proximal muscle weakness is suspected of having a primary myopathy and is scheduled for biopsy of the quadriceps muscle.

What other potential abnormalities should concern the anesthesiologist?

The diagnosis of myopathy can be difficult to make and the differential diagnosis may include any one of several hereditary, inflammatory, endocrine, metabolic, or toxic disorders. A muscle

biopsy may be necessary to supplement clinical, laboratory, nerve conduction, and electromyographic findings and help establish the diagnosis. Although the cause of the myopathy in this case is not yet clear, the clinician must always consider potential problems that can be associated with primary myopathies.

Respiratory muscle involvement should always be suspected in patients with muscle weakness. Pulmonary reserve can be assessed clinically by asking about dyspnea and activity level. Pulmonary function tests are indicated if significant dyspnea on exertion is present. An increased risk of pulmonary aspiration is suggested by a history of dysphagia, regurgitation, recurrent pulmonary infections, or abdominal distention. Cardiac abnormalities may be manifested as arrhythmias, mitral valve prolapse, or cardiomyopathy. A 12-lead electrocardiogram is also helpful in excluding conduction abnormalities. A chest radiograph can evaluate inspiratory effort, the pulmonary parenchyma, and cardiac size; gastric distention secondary to smooth muscle or autonomic dysfunction may also be evident. Preoperative laboratory evaluation should have excluded a metabolic cause with measurement of serum sodium, potassium, magnesium, calcium, and phosphate concentrations. Similarly, thyroid, adrenal, and pituitary disorders should have been excluded. Plasma CK measurement may not be helpful, but very high levels (10 times normal) generally suggest a muscular dystrophy or polymyositis

What anesthetic technique should be used?

The choice of anesthesia should be based on both patient and surgical requirements. Most muscle biopsies can be performed under local or regional anesthesia with supplemental intravenous sedation, using small doses of midazolam. Spinal or epidural anesthesia may be utilized. A femoral nerve block can provide excellent anesthesia for biopsy of the quadriceps muscle; a separate injection may be necessary for the lateral femoral cutaneous nerve to anesthetize the anterolateral thigh. General anesthesia should be reserved for uncooperative patients or for times when local or regional anesthesia is inadequate. The anesthesiologist must therefore always be prepared with a plan for general anesthesia.

What agents may be safely used for general anesthesia?

Major goals include preventing pulmonary aspiration, avoiding excessive respiratory or circulatory depression, avoiding NMBs if possible, and perhaps avoiding agents known to trigger malignant hyperthermia. A normal response to a previous general anesthetic in the patient or a family member may be reassuring but does not guarantee the same response subsequently. General anesthesia may be induced and maintained with a combination of a benzodiazepine, propofol, or an opioid with or without nitrous oxide. Patients at increased risk for aspiration should be intubated. When an NMB is necessary, a short-acting nondepolarizing agent should be used. Succinylcholine should generally be avoided because of the unknown risk of an unusual response (myotonic contractions, prolonged duration, or phase II block), of inducing severe hyperkalemia, or of triggering malignant hyperthermia.

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