Case Report

Anaesthetic complications associated with myotonia congenita: case study and comparison with other myotonic disorders

E. FARBU1, E. SOFTELAND2 and L. A. BINDOFF1

1Department of Neurology and 2Department of Anaesthesiology and Intensive Care Medicine, Haukeland University Hospital, Bergen, Norway

Myotonia congenita (MC) is caused by a defect in the skeletal muscle chloride channel function, which may cause sustained membrane depolarisation. We describe a previously healthy 32-year-old woman who developed a life-threatening muscle spasm and secondary ventilation difficulties following a preoperative injection of suxamethonium. The muscle spasms disappeared spontaneously and the surgery proceeded without further problems. When subsequently questioned, she reported minor symptoms suggesting a myotonic condition. Myotonia was found on clinical examination and EMG. The diagnosis MC was confirmed genetically. Neither the patient nor the anaesthetist were aware of the diagnosis before this potentially lethal complication occurred. We give a brief overview of ion channel disorders including malignant hyperthermia and their anaesthetic considerations.

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MYOTONIA congenita (MC) is an inherited disorder of skeletal muscle excitability. It is caused by mutations in the muscle chloride channel gene (CLCN1) and can be inherited either as an autosomal dominant (Thomsen’s myotonia) or autosomal recessive (Becker’s myotonia) trait (1). Becker’s myotonia is more common than Thomsen’s myotonia and usually presents with more severe symptoms and at an earlier age (2). The disorder is characterised by myotonia (prolonged muscular contraction) and muscular hypertrophy due to prolonged involuntary activation. Patients with myotonia usually report muscular stiffness as their major complaint. The severity is highly variable ranging from EMG-detectable myotonic discharges only to disabling stiffness. The worldwide prevalence of MC is approximately 1/100,000, but in Northern Scandinavia a figure of 1/10,000 has been reported (3).

Symptomatically, the stiffness is most pronounced in the extremities, ameliorates with continuous activity (warm-up phenomenon) and worsens after a period of rest (1). Handgrip and percussion myotonia are easily elicited and blepharospasm can be disabling (4). No extramuscular involvement is seen in MC.

The muscular stiffness is caused by increased excitability of the muscle fibre plasma membrane due to impaired chloride conductance (1, 2). The binding of acetylcholine (Ach) to the Ach receptors causes influx of sodium and a depolarisation that propagates along the muscle membrane opening sodium channels. Sodium influx stimulates calcium release from the sarcoplasmatic reticulum, which initiates muscular contraction. Under normal conditions, influx of chloride stabilises the action potential (1, 5), but in MC the impaired chloride conductance sustains it causing prolonged contraction.

Depolarising muscle relaxants such as suxamethonium bind to Ach-receptors and cause sodium and calcium influx (6). Suxamethonium has a brief duration of action and is metabolised by plasma-pseudocholinesterase, not by acetylcholinesterase. As there is little or no plasma-pseudocholinesterase at the neuromuscular junction, the neuromuscular block induced by suxamethonium is ended by diffusion from the neuromuscular junction (7). This may lead to a prolonged depolarisation of the muscle end-plate. The opening of perijunctional sodium channels is, however, time-limited and after initial excitation and...
opening they close. Once the sodium channels close, the action potential disappears and muscle relaxation occurs (8).

Case report

The patient was a 32-year-old previously healthy woman with no known allergies. Previously, she had undergone epidural anaesthesia, but not general anaesthesia. Following delivery of a healthy baby she had a postpartum haemorrhage and a partially retained placenta, and cervical laceration was suspected. She was admitted for an intrauterine revision and cervical suture under general anaesthesia. During anaesthesia, vital signs were monitored in accordance with the Standard of the Society of Norwegian Anaesthesiologists. After preoxygenation, a rapid sequence induction was performed using 0.2 mg of fentanyl, followed by 500 mg of thiopental and 100 mg of suxamethonium i.v. Soon after the injection of suxamethonium she developed a generalised muscle spasm involving the jaw, chest, abdomen and extremities with arcing of the cervical and lumbar spines. Opening of the mouth for intubation was impossible due to masseter spasm, and mask ventilation using 100% oxygen was initially difficult.

She developed serious hypoxia and became cyanotic with oxygen saturation down to 50% (measured by pulsoxymetry). Blood pressure changed rapidly from 150/60 to 180/60 and heart rate from 85 to 110 (sinus rhythm). No hypotension or arrhythmias were evident and she developed no signs of bronchospasm, urticaria or erythema. The muscle spasms subsided, and as mask ventilation adequately maintained oxygenation there were no further attempts to intubate. Propofol 10 mg kg⁻¹ min⁻¹ (132 mg) was given to maintain anaesthesia and the short operation proceeded with no further complications. The recovery period was uneventful. During the postoperative period, she had elevated levels of creatine kinase (1645–1126 U l⁻¹) and myoglobin (443–190 U l⁻¹). Haemoglobin fell from 12.1 to 9.0 g dl⁻¹. Electrolytes were not examined.

When asked subsequently about muscular symptoms, the patient explained she had always had stiffness of her muscles particularly releasing her fingers after handgrip. Her symptoms were most prominent in her hands and feet, but she had also noticed it in her facial muscles. Continuous muscular activity ameliorated her symptoms, whereas repetitive muscular activity after a period of rest led to worsening. She had no worsening of her symptoms by cold nor any muscular weakness. Her mother and sister had the same symptoms, but neither of them had consulted a doctor nor had they received general anaesthesia.

The patient was examined neurologically after delivery. Both grip and percussion myotonia were present, but no muscular hypertrophy or weakness was found; the examination was otherwise normal. EMG showed frequent myotonic discharges. The diagnosis of myotonia congenita was made and genetic analysis showed that she was homozygous for a known mutation involving the chloride channel gene CLCN1 (IVS1 + 3 > T). At follow up 8 months later, she had not experienced any changes in her condition.

Discussion

We describe a patient who developed life-threatening muscular spasms following the administration of a depolarising muscle relaxant (suxamethonium). Subsequent evaluation revealed typical symptoms and signs of myotonia congenita and the diagnosis was confirmed by genetic analysis. The striking feature of this case is that neither the patient nor the anaesthetist were aware of the diagnosis before exposure to a potentially lethal complication occurred. In the acute phase of this case, differential diagnoses like allergic reactions, bronchospasm, and malignant hyperthermia had to be considered.

Myotonia congenita belongs to a group of genetically determined disorders that affect ion channel function (Table 1). Patients with MC are at high risk of developing a severe myotonic response with generalised muscle spasms whenever depolarising muscle relaxants are used. The myotonic response may be stronger in pregnant women and patients with hypothyroidism (6). Any increase in serum potassium following administration of suxamethonium may contribute to the myotonic response. The myotonia is primarily caused by lack of compensation by normal chloride influx during repolarisation. Non-depolarising muscle relaxants seem to behave normally in myotonic patients, but will not counteract a myotonic response caused by suxamethonium (4, 6). Suxamethonium should be avoided in myotonic patients. Myotonic conditions can also be caused by defects in the sodium channels, which open later and more persistently after membrane depolarisation, leading to repeated initiation of the membrane depolarisation cycle (5).

Many of the clinical syndromes listed in Table 1 can be directly explained by the mutation effect on ion
<table>
<thead>
<tr>
<th>Disorder</th>
<th>Symptoms</th>
<th>Gene defect</th>
<th>Diagnosis</th>
<th>MH susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myotonia congenita, Thomsen (AD)</td>
<td>Generalised myotonia, warm-up phenomenon, muscle hypertrophy, muscle weakness (Becker)</td>
<td>CLCN1 Chloride channel</td>
<td>Family history, myotonia on examination EMG</td>
<td>No</td>
</tr>
<tr>
<td>Paramyotonia congenita (AD)</td>
<td>Paradoxical myotonia, cold-induced muscle weakness followed by muscle weakness</td>
<td>SCN4A Sodium channel</td>
<td>Family history, cold provocation EMG</td>
<td>No</td>
</tr>
<tr>
<td>Potassium activated myotonia (AD)</td>
<td>Generalised myotonia, aggravation by potassium administration</td>
<td>SCN4A Sodium channel</td>
<td>Family history, potassium administration in milder cases EMG</td>
<td>No</td>
</tr>
<tr>
<td>Hyperkalemic periodic paralysis (AD)</td>
<td>Episodic weakness after rest or potassium intake</td>
<td>SCN4A Sodium channel</td>
<td>Family history, trigger factors, potassium serum level ictally EMG</td>
<td>No</td>
</tr>
<tr>
<td>Hypokalemic periodic paralysis (AD)</td>
<td>Episodic weakness triggered by exercise or carbohydrate-rich food</td>
<td>CACN1AS, SCN4A, KCNE3 (sodium channel)</td>
<td>Family history, trigger factors, potassium serum level ictally EMG</td>
<td>No</td>
</tr>
<tr>
<td>Central core disease (AD)</td>
<td>Proximal muscle weakness and hypotonia in childhood, delayed motor milestones, normalization in adulthood</td>
<td>MYH7, RYRI (calcium channel)</td>
<td>Family history, Muscle biopsy</td>
<td>Yes</td>
</tr>
<tr>
<td>‘True’ malignant hyperthermia (AD)</td>
<td>Hyperthermia, accelerated muscle metabolism, contractures, metabolic acidosis and tachycardia triggered by common anaesthetics and muscle relaxants. Can give asymptomatic elevated levels of creatine kinase (CK).</td>
<td>RYRI (calcium channel)</td>
<td>In vitro contracture test</td>
<td>Yes</td>
</tr>
<tr>
<td>Dystrophia myotonica (AD)</td>
<td>Myotonia in hands, ptosis, peripheral muscular weakness, cataracts, premature balding, cardiac muscle conduction defect, diabetes mellitus.</td>
<td>Expanded CTG 19q 13.3, Expanded MG 3q21.3 (DM1, DM2)</td>
<td>Family history, Clinical findings DNA test EMG</td>
<td>Not established</td>
</tr>
</tbody>
</table>
channel function. The disorders show great variety ranging from subclinical findings and periodic symptoms to disabling muscle weakness; they may therefore be unknown to both the patient and the anaesthetist prior to surgery.

Myotonic dystrophies are common muscular disorders. They are multisystem disorders in which involvement of smooth muscles (gastrointestinal tract, uterus), heart, eye (lens), brain and endocrine glands occurs (10). Myotonic dystrophy type 1 (DM1) also shows wide clinical variation from asymptomatic myotonia to a congenital disorder with hypotonia, respiratory insufficiency, dysphagia and mental retardation. Myotonic dystrophy type 2 (DM2) has several clinical similarities to DM1, and the clinical distinction between DM1 and DM2 can be difficult (9, 10). Patients with myotonic dystrophies can also develop myotonic responses to anaesthetic drugs and this together with multisystem affection and respiratory insufficiency pose a great challenge to the anaesthetist (4, 11, 12).

Malignant hyperthermia (MH) is a well known and one of the most feared syndromes related to anaesthesia. The incidence in children is approximately 1:15,000 and in adults 1:50,000 (13). Malignant hyperthermia, which can be life threatening, is characterised by hyperthermia, accelerated muscle metabolism, contractures, metabolic acidosis and tachycardia. It is triggered by volatile anaesthetics and/or depolarising muscle relaxants (14). If sustained muscle contractions (rigidity) occur during induction or the course of anaesthesia, MH should always be suspected. The cause is most often a mutation involving the sarcoplasmic reticulum (SR), calcium release channel (ryanodine receptor: RYR1 gene) (15), but genetic heterogeneity exists (13). During an MH episode, the SR calcium channels open persistently and the resulting calcium influx causes sustained muscle contraction, hyperthermia and increased metabolism (5, 13). Due to the low incidence of MH, careful selection of patients to have an in vitro contracture test performed is recommended to avoid a false-positives (16). In our case no further signs of MH developed during the postanaesthetic course. However, MH could not be excluded at the outset.

Predisposition to MH is confirmed in three muscular disorders apart from true MH: central core disease, Evans myopathy, and King Denborough syndrome [short stature, mental retardation, and musculoskeletal abnormalities (13)]. Central core disease is an autosomal dominant disorder characterised by hypotonia (floppy infant syndrome), delayed motor development, proximal weakness and elevation of CK. Central core disease has also been mapped to the RYR1 gene (17). Other myotonic conditions can mimic MH-like disorders including rigidity and sustained contractions, but are not associated with ‘true’ MH.

Difficulties in ventilation during anaesthesia can also be caused by bronchospasm. Bronchospasm is most frequently related to airway irritation by the endotracheal tube or aspiration of gastric contents (18). If bronchospasm and/or ventilation difficulties are present together with hypotension and circulatory collapse, an anaphylactic or anaphylactoid reaction is likely (8, 19). There are reports that bronchospasm may be the only clinical feature of an anaphylactic reaction and that hypertension may occur before hypotension (18–20). Moreover, large boluses of opioids can induce severe chest wall rigidity because of centrally mediated muscular contraction. This effect may be abolished by muscle relaxants (8). Our patient developed trismus and chest wall rigidity, which prevented adequate ventilation after the injection of suxamethonium. In addition, her blood pressure increased. Clinically, her acute symptoms were in line with a myotonic response, but an anaphylactic/anaphylactoid reaction or opioid-induced rigidity could not be excluded at the outset.

In conclusion, some myotonic patients may have subclinical and discrete muscular symptoms of which they are not aware. Patients who develop masseter rigidity during induction of anaesthesia or who are difficult to ventilate may have an underlying myotonic disorder, particularly if allergies to latex and anaesthetic drugs with negative results are already excluded. A careful preoperative history with questions directed at muscular symptoms and family history are vital. If this is suspected, depolarizing muscle relaxants should be avoided during future anaesthesia.

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References


Address:
E. Farbu
Department of Neurology
Haukeland University Hospital
N-5021 Bergen
Norway
e-mail: elisabeth.farbu@helse-bergen.no