Unexpectedly prolonged weaning from mechanical ventilation in a patient with previously undiagnosed dystrophia myotonica type 1

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Abstract - Dystrophia myotonica is the most common hereditary disease of the neuromuscular system in adults and was first identified by Steinert, Batten and Gibb (1909). It is inherited as an autosomal dominant trait and is a clinical syndrome that affects skeletal muscle, the heart, and the neurological-, gastrointestinal- and endocrine systems. Several complications can occur during the course of the disease which often go unrecognized, and can lead to admission to the ICU. We describe the case history of a man who presented with respiratory failure due to aspiration after gastrointestinal surgery, and who was diagnosed with dystrophia myotonica type 1 during a prolonged ICU stay.

Keywords - Morbus Steinert, weaning, respiratory failure

Case report
A 33-year-old man was admitted to the ICU from the surgical ward with respiratory failure due to presumed aspiration after vomiting. Five days earlier, he had undergone a sigmoid resection for intestinal obstruction due to volvulus. He was immediately intubated and developed septic shock. His previous medical history revealed that in 2005 he had been admitted to hospital with gastroenteritis with a distended small intestine and renal insufficiency due to dehydration.

During physical examination he was seen to have small jaws and a typical myopathic facial appearance (long face, frontal baldness, droopy eyes) were noticed, but no other abnormalities were found.

Unexpectedly, his course in the ICU was severely prolonged and complicated. Poorly understood recurrent gastric retention, despite the use of prokinetics, resulted in a rapid and severe weight loss. During placement of a gastric-duodenal tube significant gastric dilatation and atony were seen. Weaning from mechanical ventilation was frustrated by recurrent atelectases. After extubation he suffered from repeated periods of aspiration pneumonia for which he was treated with several courses of antibiotics. Logopedic evaluation showed swallowing dysfunction, disturbed orofacial movement and unintelligible speech. He appeared passive, depressed and unwilling to cooperate. This suggested that mental illness was playing a major part in the course of this admission. Considering the loss of muscle strength and gastrointestinal motility disturbances, suspicion of a neuromuscular disease was raised. The diagnosis of dystrophia myotonica type 1, also known as Steinert’s disease was confirmed by genetic testing.

After discharge to the surgical ward his recovery was slow but complete. Four months later he was re-admitted to the ICU with respiratory failure due to aspiration after reconstructive surgery of the large intestine. This time intubation was not necessary and recovery followed slowly after implementing supportive measures.

Discussion
In general, motor weakness in a patient in the ICU can be related to [1] a pre-existing neuromuscular disorder that leads to ICU admission, [2] a new-onset or previously undiagnosed neurological disorder, or [3] complications of non-neuromuscular critical illness (reviewed in [1]). Motor weakness can be caused by lesions located in the central nervous system, spinal cord and neuromuscular system (including the anterior horn cell, peripheral nerve, neuromuscular junction and muscle). Table 1 summarizes the differential diagnosis of pre-existing and new onset weakness in ICU patients [1].

Dystrophia myotonica type 1 affects 1 in 20 000 individuals and is a neuromuscular disease characterized by myotonia and multi-organ damage [2]. It combines various degrees of muscle weakness, cardiac, gastrointestinal and neurological disorders, with endocrine dysfunction, sleep disorders and cataract. Electromyography (EMG) can reveal signs of myotonia and myopathy and may contribute to making the diagnosis. The sensitivity of the EMG depends on the selection and number of muscles tested [3]. Diagnosis is confirmed by the demonstration of an abnormality at the 19q13.3 locus resulting in the improper amplification of CTG trinucleotides in the DMPK gene. The mechanism by which the unusual genetic mutation results in the clinical syndrome is by derangements in the chloride channels in
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the membrane of the skeletal muscle cells [4]. Common features of dystrophia myotonica include myotonia, i.e. delayed muscle relaxation after a voluntary contraction, and progressive skeletal muscle loss in certain regions of the body (face, neck and distal extremities). On physical examination specific findings such as grip myotonia (after a handshake) or percussion myotonia (hitting the thenar muscle to see whether excessive and prolonged adduction of the thumb will occur) can be seen.

However, due to variable penetration and expression, it can be difficult to recognize a patient suffering from dystrophia myotonica; lack of correlation between severity or duration of the disease and the variety of clinical signs and symptoms contributes to late or misdiagnosis. Also, progression of the as yet unrecognized disease can be mistaken for common problems of physiological aging.

Patients with recognized or unrecognized dystrophia myotonica can present to the intensive care specialist with several problems that we will discuss below.

Respiratory failure

Respiratory failure is a major factor contributing to mortality although dyspnoea and orthopnoea are often relatively late findings. Approximately half of the patients die from pneumonia or acute respiratory failure [5] after aspiration due to dysphagia and swallowing disorders. Weaning from mechanical ventilation can be difficult due to muscle weakness of the respiratory pump, decreased diaphragmatic function and impaired coughing which result in recurrent pneumonia. Predictive weaning parameters such as the rapid shallow breathing index have not been evaluated in this group of patients. Clearing airway secretions can be accomplished by spontaneous coughing or with the help of a mechanical device. A limited number of studies show longer survival, less need for reintubation or occurrence of atelectasis with the use of a cough assist device in patients with various forms of neuromuscular disease [6]. There is no evidence to support other suggested supportive measures to optimize weaning strategies. Administration of anabolic hormones may have positive effects on muscle protein content, but recombinant human growth hormone did not improve muscle strength or decrease the duration of ventilatory support [7] and may even increase mortality in the critically ill [8]. A Cochrane review shows no general benefits from moderate-intensity physical exercise in patients with dystrophia myotonica [9], and no studies regarding the influence of exercise on weaning these patients from the ventilator are available yet.

Chronic ventilation failure is found in about half of the patients, resulting in hypercapnia as a result of muscle weakness, diaphragmatic dysfunction, altered respiratory patterns and sleep apnoea syndrome. The incidence of severe complications such as pulmonary hypertension due to chronic hypercapnia in this group of patients is unclear, but could possibly contribute to the reduction in life expectancy. Nocturnal noninvasive positive pressure ventilation (NPPV) leads to a remarkable recovery of daily performance although a survival benefit has not been shown [10].

Cardiac disturbance

Specific cardiac complications of dystrophia myotonica type 1 include conduction disturbances predominantly of the infra-nodal conduction system, focal myocarditis, mitral valve prolapse and sudden death. Asymptomatic electrocardiographic abnormalities are seen in 90% of patients suffering from myotonic dystrophy. Atrial tachyarrhythmias are the most common arrhythmias. Ventricular tachycardia with a bundle branch re-entry mechanism

Table 1. Classification of neurological causes of muscular weakness in ICU patients (depicted from 1)

<table>
<thead>
<tr>
<th>LOCALIZATION</th>
<th>PRE-EXISTING</th>
<th>PREVIOUSLY UNDIAGNOSED / NEW-ONSET</th>
<th>CRITICAL ILLNESS RELATED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal cord</td>
<td>Trauma</td>
<td>Acute ischemia</td>
<td>Not described</td>
</tr>
<tr>
<td></td>
<td>Infarction</td>
<td>Epidural abscess</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transverse myelitis</td>
<td>Acute transverse myelitis</td>
<td></td>
</tr>
<tr>
<td>Anterior horn cell</td>
<td>Amyotrophic lateral sclerosis</td>
<td>Amyotrophic lateral sclerosis</td>
<td>Hopkins syndrome</td>
</tr>
<tr>
<td></td>
<td>Polymyelitis (West Nile virus)</td>
<td>Polymyelitis (West Nile virus)</td>
<td></td>
</tr>
<tr>
<td>Peripheral nerve</td>
<td>Guillain-Barré syndrome</td>
<td>Guillain-Barré syndrome</td>
<td>Critical illness polyneuropathy</td>
</tr>
<tr>
<td></td>
<td>Chronic inflammatory demyelinating polyneuropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuromuscular junction</td>
<td>Myasthenia Gravis</td>
<td>Myasthenia Gravis</td>
<td>Prolonged neuromuscular blockade</td>
</tr>
<tr>
<td></td>
<td>Lambert-Eaton syndrome</td>
<td>Toxic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Botulism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>Muscular dystrophy</td>
<td>Rhabdomyolysis</td>
<td>Critical illness myopathy</td>
</tr>
<tr>
<td></td>
<td>Polymyositis</td>
<td>Toxic myopathies</td>
<td></td>
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<tr>
<td></td>
<td>Periodic paralysis</td>
<td>Polymyositis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metabolic/congenital</td>
<td>Myotonic dystrophy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mitochondrial</td>
<td>Adult-onset acid maltase deficiency</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Pyomyositis</td>
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<td></td>
<td></td>
<td>Hypokalaemic</td>
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<td>Hypophosphatasaemic</td>
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</tbody>
</table>
is very rare. A significant portion of patients have heart failure, which may not be clinically apparent. Therefore, a low threshold for echocardiography should be advised especially in patients who are unable to be weaned from the ventilator [11]. The risk of sudden death due to rhythm disturbances is estimated to be between 4 - 10 %, which might be a reason to consider pacemaker treatment[ 12].

Gastro-intestinal disturbances
Most gastro-intestinal disorders are located in pharynx and oesophagus, with a prevalence of dysphagia and swallowing disorders of 25-80% [13]. Delayed gastric emptying and complete gastroparesis may preclude adequate gastric feeding although metoclopramide seems effective in restoring gastric emptying[14]. Major intestinal motility disorders such as intestinal pseudo-obstruction or volvulus may herald the onset of muscular weakness. Diarrhoea, episodic or due to malabsorption, is attributed to hypoactive peristalsis and possibly due to pancreatic dysfunction. Constipation is usually treated with prokinetics, laxatives and enemas.

Neurological/Cognitive disorders
The central nervous system symptoms of dystrophia myotonica include cognitive impairment, hydrocephalus, hypersonmolence, heightened sensitivity to anaesthetic agents, central hyperventilation, neuroendocrine dysfunction, and personality and behavioural disturbances. The specific cognitive defects are supported by neuropsychological and magnetic resonance imaging findings that suggest a slow demyelinating process and cortical atrophy [15].

Depression is often documented, although patients usually present with emotional deficits.

Endocrine disorder
Myotonic dystrophy is associated with several endocrine disorders, including derangements in the hypothalamic-pituitary-adrenal axis, insulin resistance and genital dysfunction. Dysfunction in the hypothalamic-pituitary-adrenal axis comprises increased serum cortisol levels without increased urine excretion, enhanced adrenal cortex reactivity to ACTH and hypoaldosteronism, leading to catabolic stress, metabolic syndrome and occasionally hyperkalaemia [16].

Insulin resistance is a common metabolic feature in dystrophia myotonica (with typically normal basal insulin levels but excessive insulin release after a glucose load, indicating a compensatory beta-cell response to tissue insulin insensitivity [17]. Metformin or other insulin sensitizers may reduce the insulin resistance and hyperglycaemia. Thyroid function may also be abnormal with a slight but significant decrease of serum FT3 and reduced TSH response to TRH [18].

Sedation and analgesia
Muscular and extramuscular organ involvement in dystrophia myotonica increases the risk of postoperative complications. Retrospective studies of perioperative complications in patients with dystrophia myotonica reveal an overall frequency of complications of 8.2-52% [19], mostly pulmonary. The risk of perioperative pulmonary complications is significantly higher after upper abdominal surgery and for patients with severe muscular disability, as assessed by the presence of proximal limb weakness. The likelihood of perioperative pulmonary complications is not related to any specific anaesthetic drug.

Patients with dystrophia myotonica show increased sensitivity to sedative and anaesthetic agents. In addition, numerous stimuli such as cold, shivering and depolarizing neuromuscular blocking drugs may induce generalized myotonia leading to difficulty in intubation, ventilation, fasciculations, rhabdomyolysis and sometimes life-threatening hyperkalaemia.

Conclusion
Faced with patients with unexplained and complex problems in the ICU we should consider the differential diagnosis of a neuromuscular disease. Particularly in younger patients with unexpected weaning difficulties and signs of disturbed motility of the gastrointestinal tract and/or unexpected rhythm disturbances, the differential diagnosis should include Steinert’s disease. When a diagnosis of dystrophia myotonica is made, one should not only manage the acute complications, but also instigate a multidisciplinary approach to annually evaluate cardio-respiratory function, start non-invasive ventilation if hypercapnia is present, and seek genetic counselling for the patient and his family. The early involvement of a neurologist is mandatory in these cases.

Figure 1. Facial features of DM: long face, frontal baldness, droopy eyes and loss of facial muscles (picture printed with permission of the patient)
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References