Laparoscopic cholecystectomy in Steinert's Myotonic Dystrophy

About two clinical cases

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Myotonic Dystrophy Type 1, or Steinert's Myotonic Dystrophy, is a rare RNA-mediated autosomal dominant disease. Here we describe two clinical cases of patients with Steinert's disease who underwent laparoscopic cholecystectomy under general anaesthesia in conjunction with thoracic peridural anaesthesia, without muscle relaxants. Using such an anaesthesiological technique allowed for rapid recovery from anaesthesia, quick and complete recovery of autonomous breathing, and a significant haemodynamic and arterial blood gases stability, as well as an adequate and complete analgesic coverage over the entire perioperative period.

KEY WORDS: laparoscopic cholecystectomy, Steinert's Myotonic Dystrophy

Introduction

Myotonic Dystrophy (dystrophia myotonica, DM) is a RNA-mediated autosomal dominant disease in which two genetic loci have been associated with different phenotypes: DM type 1 phenotype on chromosome 19 and DM type 2 on chromosome 3 [1].
Steinert's DM has an estimated incidence of 1:8000 newborns, with an estimated prevalence ranging from 2.1 to 14.3 cases per 100.000 inhabitants [2].
The genetic mutation responsible for the development of Steinert's disease in affected subjects is the alteration of a protein (myotonin, the dystrophya myotonica-protein kinase [DMPK]) caused by a mutation in the DMPK gene that controls its expression, located on chromosome 19q13.3.

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This mutation consists of an unstable sequence of three nucleotide bases (cytosine, thymine and guanidine, or CTG), which is expanded in affected subjects. Up to some thousands of triplet repeats may occur, resulting in altered protein synthesis and impaired protein activity [3,4].
Disease severity and age of onset of clinical manifestations correlate with the number of triplet repeats, which tends to increase in successive generations due to the anticipation phenomenon.
Steinert's disease is a progressively worsening disease, and is characterized by myotonia (followed by muscle atrophy), muscle dystrophy, progressive loss of muscle strength and multisystem involvement due to associated dystrophic alterations in non-muscular tissues (crystalline lens, testicles and other endocrine glands, skin, oesophagus and myocardium and, in some cases, brain) causing cardiac, ocular, gastrointestinal (GI), endocrine and cognitive disturbances.
Myotonia, the hallmark phenomenon in Steinert's disease, consists of delayed muscle relaxation after voluntary contraction.

GI symptoms mainly involve the gallbladder, due to formation of stones that lead to frequent biliary colics. This pathological manifestation is caused by smooth muscle dysfunction secondary to impaired MBNL-1 (muscle-blind-like protein 1) function, which reduces smooth muscle contractility [5].

According to Schwindt *et al.*, 25-50% of patients with Steinert's Myotonic Distrophy have symptomatic cholelithiasis secondary to gallbladder smooth muscle insufficiency, which leads to biliary stasis and nucleation [5,6]. Therefore, in patients with Steinert's DM, altered gallbladder smooth muscle contraction, disrupted motility and biliary stasis cause the pathogenesis of cholelithiasis [5,7].

The age of onset and severity of disease are highly variable, even in subjects belonging to the same family. In general, symptoms first appear from the second decade. In the congenital form, the disease manifests at birth. In other cases, it may appear at about the age of 40-50 years.

Here we describe two clinical cases of patients from the same family, both with DM type 1, who underwent video laparoscopic cholecystectomy with integrated anaesthesia, performed by combining continuous segmental thoracic epidural anaesthesia with intravenous general anaesthesia with propofol and remifentanil, avoiding the use of muscle relaxants.

Case Report

A 28-year old male patient with Steinert's DM, weighing 80 kilograms and 175 cm tall, was admitted for acute abdomen due to gangrenous cholecystitis complicated by gallbladder perforation, which was preoperatively diagnosed by a CT-scan performed at the Emergency Department.

Neurological examination revealed facial muscle weakness, with hyposthenia of the orbicularis oculi muscle, hypotrophy of temporalis muscles, initial frontal balding, strength deficit of distal upper limbs, and percussion myotonia of the hand. All cognitive functions were normal. He underwent a transthoracic echocardiogram, which was normal. An ECG revealed sinus tachycardia and a first-degree atrioventricular block. Furthermore, the patient was diagnosed with factor V Leiden syndrome associated with homocysteinuria.

A 36-year old female patient with with Steinert's DM, weighing 80 kilograms and 165 cm tall, was admitted for recurrent abdominal pain due to cholelithiasis. She underwent US and MR of the abdomen, which showed several gallstones and no main bile duct or Vater's papilla abnormalities. She was diagnosed with Steinert's DM in 2004, when diagnosis was confirmed by genetic testing that revealed a CTG triplet repeat expansion in the range of 300-500 repeats on chromosome 19q13.3.

Neurological examination revealed facial muscle weakness with bilateral hyposthenia of the orbicularis oculi muscle, bilateral palpebral ptosis, hypotrophy of temporalis muscles, neck flexor weakness and distal muscle weakness of the upper and lower limbs, deep tendon reflexes were diminished and the plantar response was flexor bilaterally.

She was also diagnosed with autoimmune piastrinopenia.

In both cases, premedication was performed with 1 gr intravenous (i.v.) paracetamol infusion in 1000 ml of pre-heated normal saline (37° C). During surgery, hypothermia was prevented by infusing warm i.v. fluids at 20 ml/Kg/h via a counter current heat exchanger, and by using a thermal mattress.

Peridural anaesthesia was performed with the patients in the sitting position, using a 18-gauge needle at the T7-T8 (T8-T9) peridural interspace, identified with the loss of resistance (LOR) to air technique. Peridural block was obtained by peridural injection of 10 ml of ropivacaine 0.5% plus sufentanil 20 mcg, to produce a metameric blockade from L2 to T4. The level of sensory block was determined by the pinprick test and by the hot and cold method (ice test).

After the induction of peridural blockade, general anaesthesia was performed in both patients by an i.v. bolus of propofol 200 mg in the male patient (corresponding to a dose of about 2.5 mg/kg), followed by a continuous IV infusion of remifentanil. Remifentanil infusion was maintained at a rate of 0.15 mcg/Kg/min for 6 minutes prior to perform indirect laryngoscopy (6 minutes is the time needed for this opioid to achieve the steady state). Following the induction of general anaesthesia, patients underwent indirect laryngoscopy and subsequent orotracheal intubation through translaryngeal insertion of a respiratory prosthesis with a diameter of 8.5 mm for the male and of 8 mm for the female patient, with no prior administration of muscle relaxants. Patients were then connected to the mechanical ventilator.

General anaesthesia was maintained with a continuous i.v. infusion of 0.1 mcg/kg/min of propofol in conjunction with a remifentanil infusion at a rate of 6 mg/kg/min as an analgesic adjunct to peridural anaesthesia.

Peridural analgesia was maintained administering a solution of ropivacaine 0.1% and sufentanil 1 mcg/ml, at a rate of 5 ml/h via an elastomeric pump connected to the distal end of the peridural catheter.

The surgical technique for video-assisted laparoscopic cholecystectomy was performed according to the French school. The patient is placed in the supine position with the legs abducted and spread apart. The surgeon stands between the patient's legs, with the first assistant on the right side of the patient and the second assistant on the patient's left side. The 10-mm Hasson trocar is inserted into the abdominal cavity through a supraumbilical incision, according to an "open" technique that allows CO_2 insufflation and insertion of the optical fibre. Pneumoperitoneum was established at a pressure of 10 mmHg, which is slightly below the usual pressure.

In both cases, retrograde cholecystectomy was performed. Dissection of the elements of Calot's triangle was carried out, and the cystic artery and duct were isolated. Both structures were proximally and distally clipped with metallic clips, and subsequently dissected.
The gallbladder was freed from peritoneal adhesions, removed from its anatomical site and placed into the endobag, which allowed its retrieval through the umbilical port. Performing haemostasis control and peritoneal lavage concluded the surgical procedure. Trocars were then removed and all incisions were closed with layered sutures.
Continuous ECG, invasive arterial pressure and body temperature (with an endo-oesophageal temperature sensor) monitoring was performed throughout the procedure in both patients. The PaO_2/FiO_2 ratio and airways pressures were monitored, and serial arterial blood sampling was carried out for blood gas analysis and assessment of acid-base balance.
Epidural analgesic infusion was continued for further 60 hours. Prior to discharge, patients underwent neurological examination, which showed no worsening of symptoms.
Length of stay was 4 days for the male and 5 days for the female patient, and no complications were observed postoperatively

Discussion

Video-laparoscopic cholecystectomy is the gold standard for the treatment of gallstone disease [8].
In patients with Steinert's DM, both the surgical procedure and anaesthesia are associated with increased risk [9]. Patients with DM have an increased likelihood of developing cardiovascular and respiratory perioperative complications, which occurred at a rate as high as 38% of cases in a retrospective study in a cohort of 219 patients [10]. Anaesthesia may lead to several complications, mainly related to neuromuscular and multi-system abnormalities, as well as to the increased sensitivity to anaesthetics and muscle relaxants.
Administration of anaesthetic drugs such as propofol in DM patients is controversial [11]: some authors have described an increased incidence of respiratory depression and prolonged apnoea associated with lengthening of the awakening phase [12], whereas other have not reported specific issues related to the use of continuous i.v. propofol infusion [13]. In particular, some authors pointed out that, in patients with DM undergoing otorhinolaryngologic surgery, continuous i.v. infusion for 3 hours did not result in any postoperative complications [13].
Use of halogenated anaesthetics in myotonic patients is not recommended, since these agents may trigger malignant hyperthermia in susceptible patients [14].
Extreme caution is required when using muscle relaxants in DM patients, and their use should be limited to carefully selected cases. Depolarizing neuromuscular blocking agents such as succinylcholine may cause the occurrence of malignant hyperthermia and myotonic crises that may complicate both ventilation and intubation of these patients, and are therefore absolutely contraindicated [15]. Use of non-depolarizing muscle relaxants is also associated with delayed recovery of muscular strength and with slower weaning from mechanical ventilation upon completion of surgery[16]. Furthermore, using neostigmine to reverse the neuromuscular blockade induced by non-depolarizing muscle relaxants is not advisable, since DM patients are particularly sensitive to acetylcholine [17].
Based on these assertions, some authors have proposed the use of short-acting non-depolarizing muscle relaxants such as mivacurium [18], atracurium [19] and cisatracurium [20].
Anecdotal use of sugammadex to reverse neuromuscular blockade induced by rocuronium in patients with DM is associated with controversial outcomes [21,22].
In our patients, these issues were dealt with and solved by integrating a "light" general anaesthesia, induced with propofol and remifentanil, with a thoracic peridural anaesthesia, which allowed a muscle relaxation adequate to perform laparoscopic cholecystectomy avoiding the use of curares.
It is likely that, by providing relaxation of abdominal muscles, peridural anaesthesia facilitated the establishment of pneumoperitoneum, which was maintained at an intra-abdominal pressure of less than 10 mmHg throughout the surgical intervention.

Conclusions

Patients with Steinert's Myotonic Dystrophy have a higher operative risk as compared with non-affected individuals. Nevertheless, this does not preclude the possibility of performing safe surgical procedures [2,6]. Minimally invasive surgery with laparoscopic approach, in conjunction with thoracic epidural anaesthesia without using muscle relaxants, allows to reduce perioperative complications and, above all, to decrease hospital stay.

Riassunto

La distrofia miotonica (DM) di Steinert è una malattia autosomica dominante RNA-mediata che ha un'incidenza di 1:8000 nati ed una prevalenza da 2,1 a 14,3 casi ogni 100000 abitanti. L'alterazione genetica responsabile dell'insorgenza della malattia è determinata dalla presenza nei soggetti malati di una proteina alterata, la miotonina, dovuta ad una mutazione nel gene DMPK. Questa mutazione è stata identificata nella presenza di una sequenza instabile di tre basi nucleotidiche (citosina, timida, guanidina o CTG) che è più lunga nei soggetti malati.
Tale patologia ha carattere progressivamente ingravescente ed è caratterizzata da miotonia, distrofia muscolare,

perdita progressiva della forza muscolare e coinvolgimento multisistemico con comparsa di disturbi cardiaci, oculari, gastrointestinali, endocrini e cognitivi.
La sintomatologia gastrointestinale interessa soprattutto la colecisti, con formazione di calcoli che danno luogo a frequenti coliche biliari. L'alterata contrazione della muscolatura liscia della colecisti, la danneggiata motilità e la stasi biliare sono le cause della patogenesi della calcolosi della colecisti nei pazienti affetti da DM di Steinert. L'età di esordio e la gravità della malattia sono molto variabili anche nei soggetti appartenenti alla stessa famiglia. Generalmente i sintomi esordiscono a partire dalla seconda decade. Nella forma congenita la malattia si manifesta alla nascita. In altri casi, può manifestarsi anche verso i 40-50 anni.
In questo lavoro vengono descritti due casi clinici appartenenti allo stesso nucleo familiare, affetti entrambi da DM di Steinert, sottoposti ad intervento chirurgico di colecistectomia video assistita eseguito in regime di anestesia integrata realizzata mediante l'associazione di una anestesia epidurale toracica segmentaria continua ad una anestesia generale endovenosa condotta mediante la somministrazione di propofol e remifentanil, evitando farmaci miorilassanti.

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