

Thymectomy in a cat with myasthenia gravis: a case report focusing on perianaesthetic management

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Summary

An 8 years old male persian cat with a diagnosis of myasthenia gravis was scheduled for transternal thoracotomy. An anterior mediastinal mass, suspected to be a thymoma, had to be resected. Progressive paraparesis and reduced ocular reflexes and menace response were the main clinical features. At the preoperative examination the cat appeared free of significant myocardial or respiratory diseases. The possibility of compromised respiratory function due to muscle weakness was addressed by the choice of a balanced anesthesia protocol without the use of muscle-relaxants. Intravenous induction was followed by intubation, administration of isoflurane in oxygen and ventilatory support. Thorough cardiorespiratory monitoring was performed during anaesthesia. Epidural morphin was given to reduce the amount of inhalation agent required to maintain anaesthesia and supplemental intravenous analgesia was given. At the end of the surgery, intrapleural bupivacaine was administered to help controlling poststernotomy pain, while reducing the need for systemic analgesics. Although rapid returning of swallowing reflex and spontaneous breathing followed the disconnection from the anaesthetic circuit, the cat needed to breath oxygen enriched air to maintain a normal hemoglobin saturation in the early postoperative phase.

Thymektomie bei einer Katze mit Myasthenia gravis: Fallbericht mit Schwerpunkt auf die Durchführung der Anästhesie

Eine achtjährige Perserkatze mit Myasthenia gravis wurde für eine transstemale Thorakotomie überwiesen. Eine mediastinale Masse mit Verdacht auf ein Thymom musste reseziert werden. Klinisch waren eine progressive Paraparese sowie ein reduzierter physiologischer Nystagmus und Drohreflex deutlich. Während der präoperativen Untersuchung war die Katze frei von myokardialen oder respiratorischen Symptomen. Der Möglichkeit einer beeinträchtigten Atmungsfunktion wegen vorliegender muskulärer Schwäche wurde durch die Wahl eines ausgewogenen Anästhesieprotokolls ohne Einsatz von Muskelrelaxantien begegnet. Nach intravenöser Einleitung folgten Intubation, Verabreichung von Isofluran in Sauerstoff und aktive Ventilation. Eine kardio-respiratorische Überwachung erfolgte während der Anästhesie. Morphin wurde epidural appliziert, um den erforderlichen Anteil der Inhalationssubstanz zur Anästhesieaufrechterhaltung zu reduzieren. Ergänzend wurden Analgetika intravenös verabreicht. Am Ende der Operation wurde Bupivacain intrapleural appliziert, um den postoperativen Schmerz zu kontrollieren und den Einsatz systemischer Analgetika zu reduzieren. Obwohl kurz nach der Narkose Schluckreflex und Spontanatmung einsetzten, musste die Katze mit Sauerstoff angereicherte Luft atmen, damit in der frühen postoperativen Phase eine normale Hämoglobinsättigung erreicht werden konnte.

Introduction

Myasthenia gravis is a disease of the neuromuscular junction. It is due to a reduced number of functional nicotinic acetylcholine receptors (nAChR) on the postsynaptic muscle membrane. Two forms, congenital and acquired, are recognized in humans and animals (Layon et al., 1998; Jaffe et al., 1998; Inzana, 2000; Gaschen et al., 2004). The most common is the acquired form, which occurs in adults and has an autoimmune origin. Antibodies

against the nAChR are produced and their binding to the receptors interferes with the action of acetylcholine by blocking the neuromuscular transmission. The onset of clinical signs may be acute, subacute or chronic. Muscular weakness, specially of the ocular, facial and pelvic limb muscles, with progressive ataxia, and variable degrees of laryngeal, pharyngeal and esophageal dysfunction are the typical clinical features.

Myasthenia gravis is often considered a paraneoplastic disorder, being associated with tumors. Reports of thy-

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thymomas in cats confirm their association with myasthenia gravis in this species; concomitant polymyositis, myocarditis and dermatitis have also been described (Carpenter and Holzworth, 1982). Thymoma excision is indicated as the most effective treatment to improve the long-term condition of patients with myasthenia gravis. These neoplasms are commonly benign, well-encapsulated and easy to separate from surrounding tissue (Gores et al., 1994; Urschel and Grewal, 1998).

As many anaesthetics exert a direct or indirect action at the neuromuscular junction, performing general anaesthesia of a myasthenic patient represents a particular challenge. Moreover, depending on the severity of the symptoms and on their progression, the pathologic condition could be unrecognised preoperatively (Prior and Swanston, 1994; Frazer and Chalkiadis, 1995). Specific pathophysiological and therapeutic knowledge is required to provide a safe anaesthesia, while preventing possible drug-related complications (Blobner and Mann, 2001). An example of perianaesthetic management in a cat with acquired myasthenia gravis is the object of this report.

Case history

Anamnesis and clinical diagnosis

An 8 year old male castrated Persian cat was presented at the small animal clinic of the Vetsuisse Faculty of Berne with a four days history of hind legs weakness. Neurological examination revealed reduced palpebral and corneal reflexes, reduced menace responses and a mild tetraparesis with slightly decreased spinal reflexes. Radiographic examination revealed an anterior mediastinal mass (AMM), laying on the sternum, accompanied by caudal displacement of the cardiac silhouette and dorsal deviation of the trachea; pleural effusion and air in the esophagus were also detected. Because lymphoma and thymoma are the most common reasons for AMM in small animals, a neoplasm was suspected. Cytology of the transthoracic fine-needle aspirate however didn't give definitive results. The concomitant presence of AMM and neurological symptoms suggested the complex thymoma-myasthenia gravis as a possible cause for the clinical findings. A positive Tensilon test and a high titre of nAChR antibodies (2.7 nmol/l against normal values of <0.5nmol/l) confirmed the diagnosis of myasthenia gravis. Echocardiographic examination didn't reveal any myocardial abnormality. Surgery for resection of the thymic neoplasm was scheduled.

Anaesthesia

On the day of the surgery, the cat weighed 4.2 Kg. Cardiac rhythm, pulse palpation and thoracic auscultation were normal. Heart rate was 160 beats/min and respiratory rate 45 breaths/min. Capillary filling time was less than

2 seconds, with pink pale mucous membranes, normal blood and electrolytes values, except for an elevated CK (5376 IU).

The cat was premedicated with midazolam (1 mg) and fentanyl (15 µg) IV while oxygen was administered via mask. Five minutes later, propofol was given to effect (total dose 18 mg) until endotracheal intubation could be performed with a cuffed 4 mm-ID tube. The cat was positioned in lateral recumbency, connected to an anaesthetic circle system and immediately ventilated with pressure-controlled intermittent positive pressure ventilation (IPPV). Anaesthesia was maintained with isoflurane in 100% oxygen. An infusion of Ringer lactate was started at 40 ml/hour. Electrocardiography, pulseoxymetry, respiratory gas analysis (including inspiratory and end tidal CO₂, O₂ and isoflurane concentration), oscillometric blood pressure and rectal temperature measurements were continuously performed. A central venous catheter was inserted via the right jugular vein to monitor central venous pressure (CVP). Normothermia was maintained by actively warming the animal. Intermittent positive pressure ventilation was adjusted to keep end-tidal CO₂ around 30 mmHg throughout anaesthesia and suppress spontaneous ventilation. Thirty minutes after anaesthetic induction, morphine (0.8 mg) was injected epidurally in the lumbo-sacral space. Within 10 minutes, a decrease in the mean blood pressure, from 72 to 54 mmHg, was noticed and treated with an IV bolus of 4 ml of hetastarch. The CVP at this time point was 18 cmH₂O. As soon as the mean blood pressure increased to normal values (69 mmHg), the cat was placed in dorsal recumbency. No changes in any of the cardiorespiratory parameters could be observed following repositioning. An infusion of 20 µg/h fentanyl was started. Heart rate and mean blood pressure remained stable during the whole anaesthesia, with mean values of 110 ± 10 (SD) beats/min and 72 ± 12 (SD) mmHg respectively. End-tidal isoflurane concentration ranged between 1.1 and 1.3%. Hemoglobin saturation (SpO₂) was normal and stable during the surgical procedure.

Sternal thoracotomy was performed from the manubrium to the middle thorax. At the moment of incision, an increase in the heart rate (from basal 100 beats/min to 150 beats/min) and blood pressure (mean values from 70 to 120 mmHg) were noticed. An intravenous bolus of 2 mg ketamine was given. Within five minutes a return to previous values of heart rate and respiratory rate was observed. A soft, 6×3 cm, lobulated, well limited mediastinal mass was identified and resected. The CVP decreased to 13 cmH₂O and then remained stable until the end of surgery. Once the mass was removed, the lungs could be directly visualized and, as expected, appeared partially atelectatic. A positive end-expiratory pressure (PEEP) of 3 cmH₂O was applied and this caused a visible progressive pulmonary reexpansion. In absence of intrathoracic bleeding, the sternum was closed with metallic sutures and a thorax drain, connected to a feeding tube, was placed.

Fentanyl infusion was stopped. After control radiographs, 190 minutes after anaesthetic induction, the isoflurane vaporizer and the ventilator were turned off and IPPV was continued manually.

Postoperative management

Intrathoracic bupivacaine 0.25% (6 mg) was administered through the thorax drain and the cat was subsequently left for 5 minutes in a prone position. By adjusting IPPV the end-tidal CO₂ was allowed to increase to 45 mmHg. A progressive return of palpebral reflexes accompanied the return of spontaneous breathing. The cat was disconnected from the anaesthetic system and maintained under pulseoxymetric and capnographic monitoring. Despite regular spontaneous ventilation, haemoglobin saturation (SpO₂) decreased progressively (from 99% to 85%), while end tidal CO₂ was kept in an acceptable range (45–55 mmHg). The cat was then placed in an oxygen cage to provide an inspiratory O₂ fraction of 60%: SpO₂ rapidly rose to 99%. The trachea was left intubated as long as possible even after the returning of the swallowing reflex. Ringer lactate was infused at 12 ml/h for the first 12 postoperative hours, during which the cat remained in the oxygen cage. Temperature, respiratory rate and pulse were measured every 15 minutes and remained stable. Antibiotic medication (cefalexin, IV, 80 mg) and intrathoracic bupivacaine, 0.25% (6 mg) were repeated QID. During the first night, the cat appeared to be comfortable and remained quiet. In absence of pleural effusion, the thoracic drain could be removed 24 hours after the surgery.

General conditions and neurological symptoms improved rapidly and one week later the cat was given to the owner with almost normal postural and motoric functions. On the basis of histopathology, the resected mediastinal mass could be identified as a cystic thymoma.

Discussion

The cat was presented for elective excision of an AMM with a diagnosis of myasthenia gravis. The temporary increase in the rear limbs muscle strength after the administration of the ultrashort-acting anticholinesterase edrophonium chloride, at the dose of 0.1 mg/kg, (Tensilon test), strongly suggested the diagnosis. Definitive evidence came from the demonstration of a high titre of serum antibodies against nAChR (Shelton, 1992).

The surgical approach was scheduled before any symptomatic therapy with long-acting cholinesterase inhibitors or immunosuppressive agents could be started. Therefore, considerations about early postsurgical increase in ACh sensitivity and possible drug-related cholinergic crisis were not necessary. Recent experience in humans would suggest to maintain this therapy unchanged until the anaesthetic induction and then to adjust the postoperative

dosage to the patient requirements (Blobner and Mann, 2001), on the basis of neuromuscular monitoring.

In order to minimize anaesthetic-related risks for the myasthenic patient, a careful and specific preoperative assessment should be performed. The actual degree of muscular function impairment has to be established, and the level of serum electrolytes (calcium, phosphorus, magnesium) has to be measured for their possible effects on the neuromuscular excitability. Examination of the pulmonary function should be directed to rule out a beginning of aspiration pneumonia or a clinically relevant reduction of the vital capacity. This last condition would indicate possible postoperative need for prolonged assisted ventilation. Considering the reported concomitance of the diseases (Carpenter and Holzworth, 1982; Blobner and Mann, 2001), possible presence of myocarditis or other forms of myocardial impairment need to be investigated by electrocardiography and echocardiography.

Generally, for the choice of the anaesthetic agents, their effects at the neuromuscular end-plate and interactions with altered physiological functions have to be considered. Whenever possible, local anaesthetic techniques should be preferred. Having to perform general anaesthesia, we decided to premedicate the cat intravenously, with a combination of midazolam and fentanyl. Although benzodiazepines are known to have a myotonolytic effect, their intravenous application assures a quick effect and the possibility to rapidly intubate the patient (Blobner and Mann, 2001). Opioids have no direct effects on the NMJ, and their use allows to reduce the amount of inhalation agent required. It is necessary however to use correct doses to avoid undesired depression of the respiratory function as its muscular component is basically weak in myasthenic patients (Florence, 1984; Lorimer and Hall, 1998).

Propofol is the agent of choice for the anaesthetic induction, with no specific effects on the NMJ and easy to administer to effect (Lorimer and Hall, 1998). Once intubated, the cat received isoflurane, which, as every other inhalation anaesthetic, inhibits the neuromuscular transmission in an unspecific way. Non-depolarizing muscle relaxants were not used, but a proper NM monitoring would allow their application (Jaffe et al., 1998; Blobner and Mann, 2001). A balanced anaesthetic technique was obtained by the use of preoperative epidural morphine combined with intravenous fentanyl as a continuous infusion. When it was necessary to deepen the anaesthetic plane, a small dose of ketamine was injected intravenously (0.3–0.5 mg/kg). In general, these analgesic supplements allowed to keep the end-tidal isoflurane concentration low, decreasing the risk of dose-related cardiocirculatory depression (Akpolat et al., 1997; Hubler et al., 2000). Light hyperventilation of the cat rapidly eliminated spontaneous breathing and allowed easy control of ventilation throughout the surgical procedure.

As a sternal thoracotomic approach was chosen for thymectomy, it was necessary to position the cat in dorsal

recumbency. In presence of a mediastinal mass and specially during IPPV, dorsal recumbency can possibly lead to life-threatening acute compression of vital structures like major airways, pulmonary artery, superior vena cava or heart. A thorough monitoring of cardiorespiratory function, including CVP measurement, allows an early detection of such a sudden impairment and a rapid intervention to re-establish physiologic conditions. Epidural morphine was administered before surgery to provide long lasting postoperative analgesia (Troncy et al., 2002; Robertson and Taylor, 2004). Additionally, intrathoracic bupivacaine was administered during recovery and at regular intervals thereafter to control poststernotomy pain. The aim was to diminish the need for systemic drugs and favour an adequate respiratory function. Despite the fact that spontaneous, regular breathing re-

turned soon after disconnection from the anaesthetic circuit, a normal SpO₂ could not be maintained when the cat breathed room air. This was probably due to residual respiratory depression, provoked by isoflurane and by the opioids in the presence of weak muscle function due to myasthenia. Epidural morphine is known to have delayed onset of action and prolonged effect that might have worsened the respiratory depression caused by fentanyl (Tung and Yaksh, 1982; Lalley, 2003). Advantages and drawbacks of each drug should be carefully weighed when planning the anaesthetic procedure. During the recovery phase pulseoxymetry and capnography were performed as long as possible to monitor the adequacy of tissue oxygenation and ventilation. For a complete assessment of the postoperative respiratory function, arterial blood gas analysis could have been performed in addition.

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