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CLINICAL REPORT

Combined general and epidural anesthesia for major abdominal surgery in a patient with Pompe disease

Won Sung Kim · Ah Reum Cho · Jung Min Hong · Eun Soo Kim · Sung Chun Park · Ji Young Yoon · Tae Kyun Kim

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Abstract We present a case of combined general anesthesia with muscle relaxant and epidural analgesia for hemicolectomy in a 56-year-old woman with Pompe disease. Progressive pulmonary function loss predisposes Pompe disease patients to an increased risk of aspiration pneumonia, atelectasis, and all pulmonary infections. Given the impaired cough resulting from abdominal muscle weakness, patients with Pompe disease who undergo abdominal major surgery are prone to great risks of postoperative pulmonary complications. In our case, to optimize the patient's pulmonary toilet during the postoperative period, epidural block was provided as well as general anesthesia. Although she had a severe scoliotic spine and a worst pulmonary function test, the attempt of epidural block provided excellent pain control and pulmonary toilet care.

Keywords Abdominal surgery · Epidural block · Pompe disease · Pulmonary complications

Introduction

Pompe disease, referred to as acid maltase deficiency or glycogen storage disease type II, is an autosomal recessive disorder with variable penetrance caused by a deficiency of the lysosomal enzyme acid glucosidase [1]. Pompe disease is a single disease that manifests as a clinical spectrum (infantile, juvenile, and adult-onset subtypes) which varies with respect to age at onset, rate of disease progression, and extent of organ involvement. The overall birth prevalence of Pompe disease across the disease spectrum is 1:40,000 births [2, 3].

Late-onset Pompe disease can present at any age and is known as a slowly progressive myopathy with or without respiratory involvement. It is also characterized by a lack of severe cardiac involvement. However, respiratory failure is usually the cause of significant morbidity and mortality in the late form of this disease. Age at death varies from early childhood to late adulthood, depending on rate of disease progression, extent of respiratory muscle involvement, and other comorbidities [4].

As Pompe disease progresses, the muscles weaken, which leads to low lung volumes, an impaired cough, blood gas abnormalities, and sleep-disordered breathing. Patients with Pompe disease are also at an increased risk for aspiration pneumonia. Although disease progression in patients with the infantile form is rapid [5, 6], patients with late-onset Pompe disease have a more gradual onset of similar, but initially less severe, respiratory compromise, which leads to ventilator dependency and eventually death from respiratory failure.

The anesthetic management of the disease in infants and children has been described [7], but there are only a few case reports of adults with the disease. This may be the first case report to describe combined general anesthesia with muscle relaxant and epidural analgesia in a patient with Pompe disease.

Case report

A 56-year-old woman with difficulty of breathing had been diagnosed with Pompe disease by muscle biopsy at

W. S. Kim · A. R. Cho · J. M. Hong · E. S. Kim · S. C. Park · J. Y. Yoon · T. K. Kim (✉)
Department of Anesthesia and Pain Medicine, School of Medicine, Pusan National University, 1-10 Ami-dong, Seo-gu, Busan 602-739, Korea
e-mail: anesktk@pusan.ac.kr

48 years of age. In the patient's family history, her younger brother died of respiratory failure as a result of Pompe disease. Eleven months earlier, orthopnea and respiratory failure had developed gradually, and 2 months later she experienced cardiopulmonary arrest from respiratory failure. She was hardly able to cough enough to clear her airway and discharge heavy secretions. Advanced Pompe disease with superimposed pneumonia was considered as the cause of the cardiopulmonary arrest. Fortunately, she was resuscitated without hypoxic brain injury. She was discharged from the intensive care unit with a tracheostomy and home-based ventilation therapy, which had been used during her sleep. Thereafter, several hospitalizations to the intensive care unit had occurred with the diagnosis of aspiration pneumonia. One month before, she was diagnosed with ascending colon cancer with manifestation of hematochezia and was scheduled to undergo open-abdomen right hemicolectomy.

She was 145 cm tall and weighed 39 kg, with a body mass index of 18.6 kg/m^2. Her exercise tolerance was very poor, and she had some difficulty in sitting up from a supine position. Her Karnofsky scoring was 30–40; the Karnofsky score between 0 and 100 is assigned by a clinician based on observations of a patient's ability to perform common tasks. Thus, 100 signifies normal physical abilities with no evidence of disease. Decreasing numbers indicate reduced ability to perform the activities of daily living [8].

Subjectively, her respiratory function was much impaired. She had nonspecific fiberoptic changes or subsegmental atelectasis in the left lower lobe, and the pulmonary function test showed severe restrictive pattern (Table 1). The patient's spine showed scoliosis with 25.3° by Cobb's method (Fig. 1). An echocardiogram showed normal wall motion, trivial mitral and pulmonary regurgitation, no pulmonary hypertension, and 52% of ejection fraction. Electrocardiography was normal with the exception of sinus tachycardia (105 beats/min). She had no other abnormalities on routine blood tests including arterial blood gas analysis, creatine kinase, alanine transaminase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH). There was no sign or symptom of

Table 1 Results of pulmonary function test

Factor	Reference	Sitting		Supine	
		Measurement	Percentage of reference	Measurement	Percentage of reference
FVC (l)	2.36	0.76	32	0.26	11
FEV1 (l)	1.74	0.69	40	0.26	15
FEV1/FVC (%)	75	90		99	
FEF 25–75% (l/s)	2.29	0.82	36	0.4	17
PEF (l/s)	4.96	1.25	25	0.71	14
MVV (l/min)	95	15	16	9	9
VC (l)	2.36			0.32	13

FVC force vital capacity, *FEV1* forced expiratory volume in 1 s, *FEF* forced midexpiratory flow rate, *PEF* peak expiratory flow, *MVV* minute ventilation volume, *VC* vital capacity

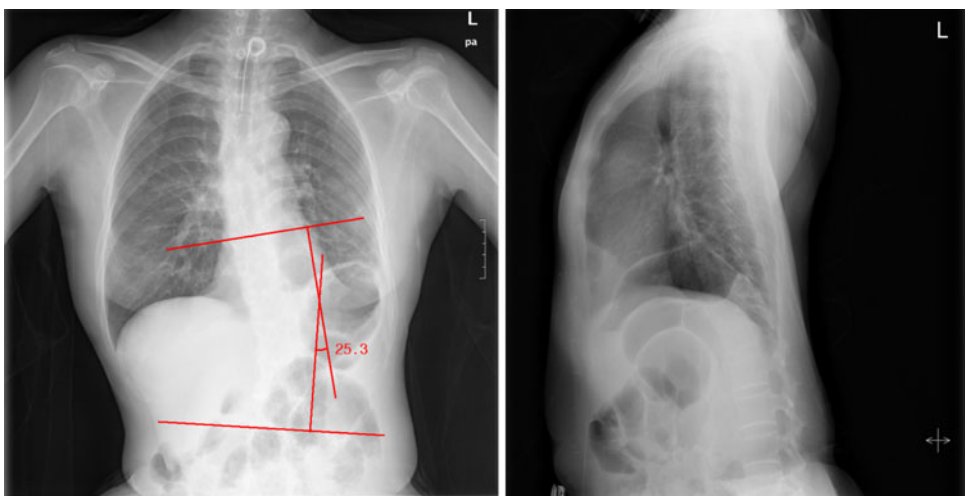

Fig. 1 Chest X-ray: posteroanterior (*left*) and lateral (*right*) views. Chest X-ray shows nonspecific fiberoptic change or subsegmental atelectasis in the left lower lobe. The degree of scoliosis was 25.3° with Cobb's method of measurement

airway infection. Air stacking, deep insufflations, and nocturnal noninvasive assisted ventilation were applied to improve the patient's lung condition.

Continuous arterial monitoring was established with a 20-gauge radial arterial cannula to facilitate titration of vasopressor infusion and close monitoring of blood pressure. No oral sodium citrate was given. Epidural catheter insertion was performed without complication in the right lateral decubitus position at the T9–T10 level with loss of resistance to saline. After an epidural catheter was inserted, leaving 3 cm in the epidural space, 2% of lidocaine 3 ml with epinephrine 15 μg was administered through the epidural catheter to ensure the catheter was not in the intrathecal or intravenous space. The epidural block level was extended with 0.75% ropivacaine 2 ml, saline 2 ml with fentanyl 50 μg. A dense block developed with loss of sensation to cold from T5 to L1.

Anesthesia was induced and maintained with sevoflurane 0.8–2 vol% followed by a bolus infusion of propofol 30 mg and rocuronium 20 mg. The trachea was intubated with a 6.0-mm-ID endotracheal tube via the tracheostomy site. There was no additional administration of rocuronium, but continuous neuromuscular monitoring was applied. Lactated Ringer solution was administered at 400 ml/h with further 100-ml boluses. Dopamine was infused at a dosage of 3–6 μg/min/kg. The changes of mean arterial pressure, heart rate, BIS, and partial pressure of end-tidal carbon dioxide during the operation are presented in Fig. 2. Hemodynamic instability (increased heart rate and decreased blood pressure) was seen after anesthesia induction, the reason for which was believed to be relative hypovolemia from sympathetic block caused by the epidural anesthesia and superimposed general anesthesia.

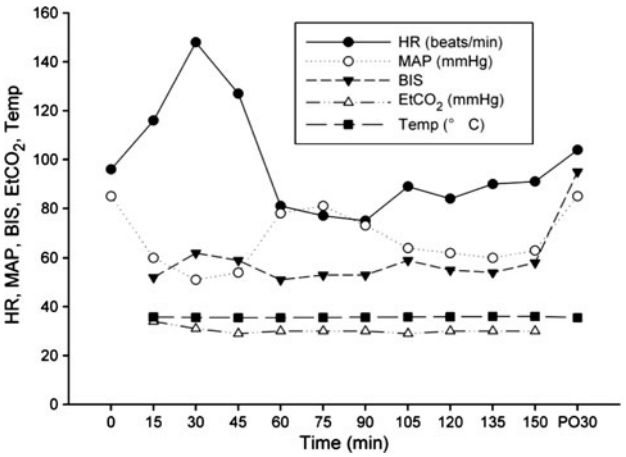

Fig. 2 Changes of vital signs, BIS, and temperature during the surgery. *HR* heart rate, *MAP* mean arterial pressure, *BIS* bispectral index, *$EtCO_2$* end-tidal carbon dioxide, *Temp* temperature, *PO30* postoperative 30 min. Hemodynamic instability between 15 and 45 min is considered as relative hypovolemia from sympathetic block caused by epidural anesthesia and superimposed general anesthesia

Dopamine infusion and fluid loading failed to prevent hemodynamic instability initially. Later, hypotension and tachycardia recovered readily.

At the end of the operation, dopamine was stopped, and she was transferred to the intensive care unit. Operation time was 120 min and total anesthetic time was 150 min. Arterial blood gas analysis and blood sugar were checked pre-, post-, and intraoperatively (Table 2). Estimated total blood loss throughout the operation was approximately 250 ml. The train of four ratio for the monitoring of muscle relaxation in the emergence period was 85%, increasing to 94% in the first 30 min postoperatively. No postoperative nausea or vomiting occurred.

Throughout her intensive care course, the patient experienced no transient oxygen desaturation episodes but remained ventilator dependent on synchronized intermittent mandatory ventilation with pressure support. In the intensive care unit, we focused on noninvasive pulmonary toilet care. Intermittent, not routine, bronchial suctions were applied to avoid obstruction by mucous plugging. Patient assessment, including auscultation and visual inspection, and finding a sawtooth pattern in the expiratory flow signal, were used to determine the need for suctioning every half-hour. Shallow suctioning with a minimally invasive catheter was performed. Five episodes of bronchial suctioning were carried out to remove mucous plugging. Chest percussion and chest wall vibration were done three times per day without postural drainage. Saline instillation was not used, but heating and humidifying of the breath circuit was used to prevent drying of secretions. Manual hyperinflation was applied to simulate a cough, but violent cough was avoided. The patient was encouraged to take deep breaths with functional cough only. Because of her abdominal surgery, manual-assisted coughing was not applied in the perioperative period. After 1 day of intensive care, she was weaned from the ventilator and discharged to the general ward.

The patient-controlled analgesic (PCA) pump (Aim*plus*; Abbott, Chicago, IL, USA) was set to deliver a epidural continuous infusion of 0.2% ropivacaine 1.5 ml with 5 μg fentanyl, a lockout time of 15 min, and a maximum cumulative dose of 30 ml every 4 h with a bolus dose of

Table 2 Arterial blood gas analysis and blood sugar

Factor	Preoperative	Intraoperative	Postoperative
ABGA			
pH	7.389	7.425	7.375
$PaCO_2$ (mmHg)	39.2	33.4	41.4
PaO_2 (mmHg)	88.4	245.6	273.4
SaO_2 (%)	96.80	99.90	99.90
FiO_2		0.5	0.5
Blood sugar (mg/dl)	101	140	137

0.2% ropivacaine 3 ml with 10 μg fentanyl. She breathed comfortably without interruption by pain from the operation site. The visual analogue pain score was 0–20 mm. However, when the epidural PCA device was removed after 2 days of engagement, the operation site pain became aggravated, although the pain was not so much as could disturb her respiration. The patient was recommended to use PCA again to prevent atelectasis and promote respiratory toilet. However, she refused, and tried to overcome the pain and breathing difficulty with the help of a home ventilator. After 1 week of hospitalization, she was able to be discharged without any respiratory problem.

Discussion

In general, regional anesthesia is recommended as the best option for the patient who suffers from a muscular disease. However, the anesthesiologist can be faced with complicated cases in which one has no choice but to deliver general anesthesia with a muscle relaxant. This case confidently reported a successful outcome of scheduled general anesthesia and planned administration of muscle relaxant to a Pompe disease patient.

The circumstances in which we have to deliver general anesthesia with muscle relaxant include the following: (1) the patient's wish for complete deep sedation, (2) the surgeon's indication of possible prolongation of the operation, (3) the fear of postoperative fatigue from self-respiration in a supine position in which the patient had troublesome breathing because of scoliosis, (4) the possibility of noncoordination with mechanical ventilation under sedation without muscle relaxation and subsequent respiratory muscle fatigue, and (5) the risk of patchy epidural block. Additionally, investigation of the effect and safety of pyridostigmine for the reversal of a neuromuscular block in patients with Duchenne muscular dystrophy provided some allowance for the use of rocuronium [9].

The operation team made a maximal effort to seek any other options to avoid the potential risk associated with general anesthesia. There was, however, no option but general anesthesia. Palliative surgery was not an appropriate choice. The patient's colon cancer was stage T2N0M0, causing intermittent hematochezia. In this case, even though the amount of hematochezia was not large, surgical control, that is, tumor resection, was needed. Tumor resection was worth attempting in consideration of her life expectancy. Surgeon, anesthesiologist, and patient were willing to take the risk of therapeutic surgery. Combined spinal and epidural anesthesia also was worthy of consideration; however, the patient did not want regional anesthesia without sedation. We thought that simple sedation could increase the risk of respiratory holding and aspiration intraoperatively.

Because of their underlying muscle weakness, Pompe patients may be more sensitive to neuromuscular blockade. Rocuronium increases the risk of postoperative continuous mechanical ventilation. Rocuronium is regarded to act by reducing metabolic demands and preventing ventilator asynchrony. Agents such as suxamethonium chloride should be avoided in Pompe disease as in all myopathic patients because of the potential risk of rhabdomyolysis and hyperkalemia. Malignant hyperthermia precautions should be taken. A study reported a higher risk of pulmonary complications among patients receiving the long-acting neuromuscular blocker pancuronium than among those receiving the shorter-acting atracurium or vecuronium [10].

Preassessment is primarily aimed at determining the extent of respiratory compromise, which is shown by pulmonary function testing (Table 3). The usual findings are reduced lung volumes. Diaphragmatic weakness, manifested as a difference between pulmonary function in sitting and supine position of more than 20%, is an important feature in Pompe disease [11, 12]. This finding can be used to detect whether there is a need for nightly ventilation. In this case, the need of home ventilation therapy during her sleep had already revealed the diaphragmatic weakness. Although carbon dioxide retention and hypoxia usually are seen with advanced disease, she showed normal arterial blood gas analysis. The cough, gag, and swallow reflexes may be weakened by abdominal muscle dysfunction, which increases the risk of postoperative atelectasis, aspiration, and pneumonia. Without epidural pain control, abdominal surgery might have worsened those risks.

Routine blood tests usually show increased levels of creatine kinase, ALT, AST, and LDH in Pompe disease [5]; this finding may reflect the presence of ongoing muscle damage, although the levels measured are not indicative of the severity of the disease. In this case, no abnormal laboratory findings were found; however, this could be interpreted as meaning the far-advanced disease progression may reflect that no more muscles remain to be destroyed.

In early-onset Pompe disease, the common form of pathology is cardiac issues include cardiomyopathy, heart failure, and arrhythmia. There is also a component of cardiac dysfunction that contributes to respiratory failure. True Wolf-Parkinson-White syndrome has been reported to occur in Pompe disease [13]. These conduction abnormalities could place these patients at high risk of tachyarrhythmia and sudden death, especially in situations of stress such as infection, fever, dehydration, and anesthesia [14, 15]. In patients with late-onset Pompe disease there is generally no clinically identifiable heart disease. Electrocardiography and an echocardiogram can assure safety from cardiac involvement. Although this patient's cardiac function was well preserved, her history of arrest and resuscitation was also a burden for us.

Table 3 Checklist for anesthetic care for Pompe disease

Preoperative test	Respiratory compromise	Respiratory muscle dysfunction	Pulmonary function test
			Arterial blood gas analysis
			Subjectively respiratory function
			History of respiratory failure
		Other exercise tolerance	Karnofsky scoring
			Decreased tendon reflexes
	Cardiac compromise	Cardiomyopathy, heart failure	Echocardiogram
		Conduction abnormalities (True Wolf-Parkinson–White syndrome)	Electrocardiography
	Other compromise	Lordosis and/or scoliosis	Cobb's method
		Oropharyngeal involvement	Cough, gag and swallow reflexes
		Ongoing muscle damage	Creatine kinase, ALT, AST, and LDH
		Other blood tests	Blood sugar test
Anesthetic plan	Surgery	Surgery type	Therapeutic surgery vs. palliative surgery
		Operation site	Abdomen, chest, and other site
		Other	Operation time, etc.
	Anesthesia technique	Local or regional anesthesia	Site and duration of regional blockade, block technique
		General anesthesia	Consider neuromuscular blockade, method of keeping airway, macroglossia
	Preoperative management	Improve patient lung condition	Air stacking, deep insufflations, nocturnal noninvasive assisted ventilation
		Airway infection	Chest film, auscultation, other sign and symptom
	Monitoring	Muscle relaxation	Train of four, etc.
		Anesthetic depth	BIS, entropy
	Postoperative complication	Continuous mechanical ventilation	Avoid muscle relaxant
		Aspiration pneumonia	Prevent nausea and vomiting: preoperative oral sodium citrate
		Postoperative analgesia	Patient-controlled analgesia, opioid and other analgesics
		Other respiratory problem	Atelectasis, pneumonia

Table 4 Secretion management in mechanical ventilation

	Methods	Details
Routine management	Mobilization heating and humidifying	"Up and out of bed"
Maintaining the endotracheal tube lumen	Suctioning	Open/closed suctioning
		Bronchial suctioning
		Minimally invasive suctioning (shallow suctioning)
		No saline instillation
	Novel methods	The mucus slurper
		The mucus shaver
Enhance secretion removal	Simulate a cough	Manual hyperinflation
		Insufflation–exsufflation
	External application of force to loosen secretions	Percussion and postural drainage, high-frequency chest wall vibration
	Manual ribcage compression	Kinetic therapy
	Intrapulmonary percussive ventilation	

Chest physiotherapy consists of varying amounts of percussion, chest wall vibration, postural drainage, and suctioning (Table 4). These stressful procedures may have significant metabolic and hemodynamic effects [16], that is, increase in heart rate, systolic and mean blood pressures, and cardiac output. Consequently, harmful results may occur in critically ill patients. There are only a few reports of efforts to reduce these stresses induced by physiotherapy [16, 17]. In this case, the epidural analgesia played a great role not only in intraoperative adjuvant analgesia but also in postoperative analgesia for chest physiotherapy. Postoperative epidural analgesia reduces the rate of pulmonary complications in patients at high risk [18]. With the help of epidural anesthesia, the patient could receive the whole course of chest physiotherapy more effectively and comfortably.

There have been a few laparoscopic surgery cases in muscular disease. The fact that pulmonary function deteriorates significantly less in laparoscopic surgery compared with the open procedure contributes to the smooth postoperative course [19]. However, we were under the need of open abdomen, so epidural analgesia and pulmonary toilet care were necessary indeed. Even with repetitive aspiration pneumonia, one should avoid long surgical procedures, such as a Nissen fundoplication, because of the high anesthesia risk. The surgical site is the most important predictor of pulmonary risk. Risk increases as the incision approaches the diaphragm [20, 21].

This case report described major abdominal surgery in a patient with Pompe disease. A few reports of late-onset subtypes strongly recommend using regional anesthesia technique and avoiding using a muscle relaxant. However, if regional anesthesia is impossible, it might be considered that this planned and scheduled administration of muscle relaxant will be a substantive help to physicians who must use a muscle relaxant for anesthesia of adult Pompe disease patients.

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