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CASE REPORT

Fabry Disease and General Anesthesia: A Case Report and Literature Review

Tsai-Shan Wu[1], Wei-Cheng Tseng[2], Hou-Chuan Lai[3], Yi-Hsuan Huang[3], Jyh-Cherng Yu[4], Zhi-Fu Wu[5]

[1]School of Medicine, Taipei Medical University, Taipei, [2]Department of Anesthesiology, Tri Service General Hospital and National Defense Medical Center; Department of Surgery, Division of Anesthesiology, Gangshan Branch, Kaohsiung Armed Forces General Hospital, Kaohsiung, [3]Department of Anesthesiology, Tri Service General Hospital and National Defense Medical Center, Taipei, [4]Department of Surgery, Division of General Surgery, Tri Service General Hospital and National Defense Medical Center, Taipei, [5]Department of Anesthesiology, Tri Service General Hospital and National Defense Medical Center, Taipei; Department of Anesthesiology, Chi Mei Medical Center, Yongkang District, Tainan, Taiwan

Fabry disease (FD) is an X-linked lysosomal storage disease. FD presents with a variety of symptoms such as corneal clouding, reduced sweating, abdominal pain, neuropathic pain, angiokeratoma, sleep-disordered breathing, renal failure, cardiovascular diseases, and stroke. Severe organ damage may occur, and its gravity differs between individuals, usually being more serious in males and elders. According to previous reports, possible complications include hypertension, hypotension, bronchospasm, and intubation difficulty. Therefore, identifying FD patients carefully and performing detailed preoperative assessments, such as for cardiovascular, pulmonary, and renal functions, are both critical to increasing the chances of a positive treatment outcome. Advanced hemodynamic monitoring was recommended to prevent severe cardiovascular and respiratory impairment during surgery of advanced FD patients. To the best of our knowledge, there are only four reports on FD treatment, none being from Taiwan. Here, we report on a case of FD treatment undergoing general anesthesia in Taiwan and provide a literature review.

Key words: Fabry disease, general anesthesia, anesthetic events

INTRODUCTION

Fabry disease (FD), also known as Anderson-FD, is a rare, X-linked, lysosomal storage disease, characterized by a deficient lysosomal function. The underlying pathophysiological mechanism is a lack of the enzyme α-galactosidase A, which leads its substrate globotriaosylceramide to accumulate in tissues and thus possibly cause organ damage. Initial symptoms include severe neuropathic or limb pain, corneal opacities, abdominal pain, and angiokeratoma. Severe complications including renal insufficiency or renal failure, cardiomyopathy, and stroke may appear in later adulthood.[1-5]

To the best of our knowledge, general anesthesia (GA) for FD patients is only described in four reports, which together include data on six patients and eight anesthetics.[2,6-8] Furthermore, there are no reports on the use of GA in the treatment of FD patients in Taiwan. In this paper, we report on the treatment of an FD patient receiving breast cancer surgery under GA in Taiwan and review the relevant literature on the topic.

CASE REPORT

A 65-year-old Asian female patient, with a height of 158 cm and weight of 56 kg, was diagnosed with FD through a genetic test last year, influenced by her grandnephew who had also been diagnosed with FD. The patient was admitted to our hospital to undergo quadrantectomy and axillary lymph node dissection to treat a (left) breast cancer. Following our treatment, the patient underwent regular follow-ups at the outpatient's department of another hospital. According to a medical history provided

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Corresponding Author: Dr. Zhi-Fu Wu, Department of Anesthesiology, Chi Mei Medical Center, No. 901, Zhonghua Road, Yongkang District 71004, Tainan, Taiwan, R.O.C. Tel: +886-6-2812811 Ext. 55352. E-mail: aneswu@gmail.com

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both by the patient herself and her medical records, the patient had no symptoms of renal insufficiency (but showed elevated serum creatinine (at 1.03 mg/dL) and decreased estimated glomerular filtration rate (at 69 mL/min)). In addition, her electrocardiography (ECG) was normal and her daily physical activity was >4 metabolic equivalents, and although her records for hypertension, hyperlipidemia, and thyroid nodular goiter were positive, they were under medical control. Finally, other laboratory data were normal. Due to the limited severity of her symptoms, the patient was not undergoing enzyme replacement therapy with α-galactosidase A. Her history was negative for the four pain phenotypes of FD (pain attacks, pain crises, evoked pain/hyperalgesia, and chronic pain) and obstructive sleep apnea.[9,10]

The patient underwent routine monitoring that includes ECG (lead II), noninvasive blood pressure, pulse oximetry, and end-tidal carbon dioxide pressure ($EtCO_2$) and was administered with intravenous fentanyl (at 2 μg/kg and 2% lidocaine 1.5 mg/kg). Subsequently, a continuous infusion of propofol (Fresofol 1%) was delivered using the Schneider's kinetic model of TCI (Fresenius Orchestra Primea; Fresenius Kabi AG, Bad Homburg, Germany) with the effect-site concentration (Ce) of 4.0 μg/mL. When the patient lost consciousness, 0.6 mg/kg of rocuronium was administered, followed by endotracheal tube intubation. Anesthesia was maintained using TCI with a propofol Ce of 3–4 μg/mL and was adjusted to 0.2 μg/mL according to the hemodynamics under oxygen (0.3 mL/min) and air (0.4 mL/min) flow. The ventilation rate and maximum airway pressure were adjusted to maintain the $EtCO_2$ pressure at 35–45 mmHg, according to the pressure control model. Rocuronium (5 mg) was administered as required to antagonize the return of neuromuscular function.[11,12] The surgery took place without complications and lasted 60 min. Reversal of neuromuscular function was achieved by administrating sugammadex (100 mg) to prevent residual paralysis. Once the patient regained consciousness with spontaneous and smooth respiration, the endotracheal tube was removed. Then, the patient was transferred to the postanesthesia care unit for further care.

DISCUSSION

FD is a pan-ethnic disease, with a reported incidence of 1:476,000–1:117,000 worldwide. However, such incidence values are likely underestimated since newborn screening initiatives have revealed a prevalence of 1:3,100 (approximately) in Italy. In Taiwan, the prevalence of FD is about 1:1500 for newborn males, higher than other countries.[13]

FD presents with a variety of symptoms such as corneal clouding, reduced sweating, hearing loss, abdominal pain, diarrhea, neuropathic pain, angiokeratoma, sleep-disordered breathing, renal failure, cardiomyopathy, arrhythmia, cochleovestibular, and stroke, especially in males, the symptoms in females may range from mild to severe.[9,13,14] Among these symptoms, early-onset renal insufficiency is now the most common early sign, leading to the diagnosis.[2]

Due to the various symptomatic manifestations of FD, differences in organs involved, sex, and age, preoperative assessments must be performed carefully to identify the specific set of symptoms present in each patient and avoid serious complications. Of special importance, severe damage to the heart, brain, lung, and kidney must be avoided either by optimized preoperative assessments or through careful control of the patient's health status during anesthesia with an appropriate monitoring system.[2]

In four publications, we identified six patients who, among them, had experienced eight anesthetics [Table 1]. Of these patients, one had hypertension during cholecystectomy,[8] one had bronchospasm during renal transplantation,[6] two had unresponsive hypertension or unexpected difficult intubation during renal transplantation,[7] and one had hypotension during orthopedic surgery.[2] In the other two cases, the patients did not suffer from any perioperative anesthetic events [Table 1].

Cardiovascular responses such as hypertension and hypotension might result from the accumulation of the globotriaosylceramide substrate, which causes cellular dysfunction within the cardiovascular system. Dysfunctions of the cardiovascular system such as hypertension, concentric left ventricular hypertrophy without obstruction, and coronary artery disease result from injuries to the endothelial cells of vascular smooth muscles.[2] It is recommended that noninvasive cardiac stress tests are done in FD patients who are >30 years of age and have relevant symptoms.[6] Moreover, the titration of anesthetics and adequate monitoring are needed during anesthesia.

Besides, the globotriaosylceramide substrate may accumulate in the respiratory system; hence, patients with FD may have obstructive airway disease[9] and bronchospasm, and difficult intubation has been reported.[6,7] According to Woolley and Pichel,[6] respiratory functions should be evaluated in patients who smoke. For obstructive pulmonary disease patients, preoperative hydrocortisone treatment should be taken into consideration. Bronchodilators may be used, but treatments or drugs associated with histamine release are best avoided when possible. In addition, it is necessary to perform airway evaluations and to have alternative strategies available for airway management in difficult cases.[7]

The globotriaosylceramide substrate may also accumulate in the kidney, and renal failure causes the death of FD patients the most often.[7] According to Sorbello *et al*.,[7] FD patients undergoing renal transplantation need a detailed preoperative

Table 1: Literature review of reported cases of Fabry disease undergoing general anesthesia

Source	Age, years/sex	Presentation	Surgery	Medications during anesthesia	Anesthetic events
Watanabe *et al*., 1995[8]	45/female	ESRD under HD, hyperglycemia, ischemic heart, and hypertension	Cholecystectomy	Thiopental, vecuronium, nitrous oxide, isoflurane, nicardipine, and nitroglycerin	Hypertension
Woolley and Pichel 2008[6]	Nil/male	ESRD, angiokeratomas, acroparaesthesia, ophthalmic signs, stroke, and moderate concentric left ventricular hypertrophy	Renal transplantation	Fentanyl, propofol, atracurium, and sevoflurane	Bronchospasm
Sorbello *et al*., 2008[7] Case 1	42/male	Hypertension, left ventricular hypertrophy, incomplete right bundle block, moderate mitralic and aortic insufficiency, ESRD under HD, and angiokeratomas	Renal transplantation	Propofol, cisatracurium, fentanyl, sevoflurane, fenoldopam, nitroglycerine, and morphine	Hypertension, unexpected difficult intubation Both patients received intraoperative transdermal nitroglycerine during surgery
Sorbello *et al*., 2008[7] Case 2	53/male	Myocardial infarction, hypertension, chronic obstructive lung disease and ESRD under HD, and angiokeratomas	Renal transplantation		
Krüger *et al*., 2017[2] Case 1-1	37/female	Hypertension, renal insufficiency	Diagnostic laparoscopy	Propofol, fentanyl, rocuronium, remifentanil, paracetamol, metamizole, (lidocaine added in second surgery), dexamethasone, ondansetron, neostigmine, and glycopyrrolate	Nil
Krüger *et al*., 2017[2] Case 1-2			Laparoscopic resection for endometriosis		
Krüger *et al*., 2017[2] Case 2-1	67/F	Angiokeratomas, chronic neuropathic and myofascial pain, cardiomyopathy, hypertension, and renal insufficiency	Osteosynthesis of the left ankle	Propofol, fentanyl, rocuronium, desflurane, remifentanil, paracetamol, metamizole, dexamethasone, ondansetron, norepinephrine, ephedrine, and desflurane changed to propofol for second surgery	Hypotension
Krüger *et al*., 2017[2] Case 2-2			Removal of osteosynthetic hardware		

ESRD=End-stage renal disease; HD=Hemodialysis

evaluation of cardiovascular and pulmonary function, including ECG and spirometry. Advanced hemodynamic monitoring during renal transplantation to prevent severe cardiovascular and respiratory impairment was recommended. Moreover, the authors suggested that a standard anesthetic protocol could be applied, while special care should be taken in the treatment of concomitant pathologies, which may significantly affect the early postoperative outcome. In addition, a renal protective strategy should be devised and applied to all treatment recipients to improve the long-term outcome of renal transplanted FD patients.

Since patients may suffer from autonomic dysfunction symptoms such as reduced sweating, gastrointestinal pain, and changes in gastrointestinal motility and cardiac rhythm,[14] anesthesiologists should be cautious with the use of neostigmine, glycopyrrolate, and atropine for reversal of muscle relaxation.[8] In addition, for reversal of rocuronium, sugammadex should also be used with care on renal hemodialysis patients because it is not recommended for use in renal impaired patients.

Fortunately, our patient had no symptoms of FD and underwent electric breast cancer surgery without suffering from an anesthetic event.

In conclusion, patients with FD, a disease characterized by a variety of symptoms that differ between sex, age, and its severity, require careful assessment before GA if a good treatment outcome is to be expected.[2]

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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