〔**Case Report**〕 Matsumoto Shigaku 46：16～22, 2020
key words：Progressive muscular dystrophy (PMD), general anesthesia, dental treatment

General anesthetic management of six cases with progressive muscular dystrophy for dental treatment

Saori OGAWA, Kiichi TANIYAMA,
Keisuke UEDA and Tohru SHIBUTANI

Department of Dental Anesthesiology, School of Dentistry,
Matsumoto Dental University

Summary

Progressive muscular dystrophy (PMD) is a hereditary disease showing degeneration and necrosis of muscle fiber and progressive muscle weakness. PMD includes Duchenne and Becker types, in addition to limb–girdle and Fukuyama types. We report six cases of PMD (two cases of Duchenne type and four cases of Fukuyama type) treated since 2000 to 2019, in which general anesthesia was performed for intensive dental treatment.

The serum level of creatine phosphokinase (CPK) was remarkably higher than normal level in every patients. No remarkable findings in chest x–ray and ECG were pointed. For patients with Duchenne type PMD, anesthesia was induced with propofol and nondepolarizing muscle relaxants, and maintained with nitrous oxide and propofol. For patients with Fukuyama type PMD, anesthesia was induced with sevoflurane in every patients and no muscle relaxant was used. Anesthesia was maintained with nitrous oxide in combination with sevoflurane in three cases, and it was maintained with nitrous oxide and propofol in another case. No remarkable cardiovascular and respiratory dysfunctions were pointed in every patients.

The problems for the management of general anesthesia in patients with PMD are (1) circulatory failure due to myocardial damage, (2) respiratory failure due to respiratory dysfunction, (3) induction of malignant hyperthermia due to agents for general anesthesia, and (4) increased sensitivity and prolonged effects of muscle relaxants. In patients with Duchenne type PMD, volatile inhalation anesthetics were not used, which considered to be a risk factor for malignant hyperthermia. On the other hand, in patients with Fukuyama type PMD, we used sevoflurane since the incidence of malignant hyperthermia by volatile inhalation anesthetic will be low.

Introduction

Progressive muscular dystrophy (PMD) is a hereditary disease showing degeneration and necrosis of muscle fiber and progressive muscle weakness[1,2]. PMD includes Duchenne and Becker

（recieved February 12, 2019 ; accepted March 23, 2020）

types, in addition to limb–girdle and Fukuyama types. Duchenne and Becker types PMD are observed only in male infants through sex–linked recessive inheritance[2]. Duchenne and Becker types PMD are caused by progressive muscle weakness due to dystrophin gene mutations[2]. Limb–girdle type PMD is characterized by proximal muscle weakness or atrophy of the extremities as predominant symptoms[3]. Fukuyama type PMD, which is observed only in Japan, is characterized by developmental disorders with muscle weakness and severe brain deformities due to mutations in fukutin[4].

We report six cases of PMD (two cases of Duchenne type and four cases of Fukuyama type) treated since 2000 to 2019, in which general anesthesia was performed for intensive dental treatment.

Cases

The age, sex, medical history, serum creatine phosphokinase (CPK) level, agents used for general anesthesia, procedures, time of anesthesia and treatment are shown in Table 1.

The patient in case 1 had a history of asthma for which pranlukast hydrate was prophylactically administered. He was able to walk independently in daily life, but had slight limitations when running. The patient in case 2 was unable to walk independently and required support.

The patient in case 3 had no limitations in daily life, whereas the patients in case 4 to 6 were unable to walk independently and used wheelchairs for daily living. The patient in case 5 developed rhabdomyolysis at four years old. The patient in case 6 had a history of asthma, for which tulobuterol was administered upon attack.

Of these six patients, case 1 showed higher serum levels of aspartate aminotransferase (AST), alanine transaminase (ALT), and lactate dehydrogenase (LDH). All patients had remarkable high CPK levels on preoperative blood tests, without abnormal findings on electrocardiogram and chest X–ray. All cases were sporadic.

Course of anesthesia

1. Duchenne type PMD

Anesthesia was rapidly induced using propofol and fentanyl. A non–depolarizing muscle relaxant was administered, followed by tracheal intubation. The anesthesia was maintained by oxygen (1.5–2 L/min), nitrous oxide (2–3 L/min) and propofol (4–6 mg/kg/hr) (Table 1).

2. Fukuyama type PMD

Anesthesia was slowly induced using sevoflurane, followed by tracheal intubation without the use of muscle relaxants. The anesthesia was maintained by oxygen (1–3 L/min), nitrous oxide (2–4 L/min) and sevoflurane (0.6–2%) in cases 3, 4, and 6, and by oxygen (1.5 L/min), nitrous oxide (3 L/min) and propofol (2.5–5 mg/kg/hr) in case 5.

We controlled the dose of propofol according to the change of blood pressure and heart rate in each patient. There were no abnormalities in respiratory and circulatory dynamics throughout the perioperative period in all cases with Duchenne and Fukuyama types PMD, and all patients were discharged on the following day.

Table 1 : The age, sex, medical history, serum creatine phosphokinase level, agents used for general anesthesia, procedures, time of anesthesia and treatment are shown in Table 1. The case 1 and 2 are Duchenne type of PMD and the cases 3 to 6 are Fukuyama type.

	types of PMD	age sex	height weight	ADL	medical history	CPK	agents used for the induction	muscle relaxant	agents used for the maintenance	dental treatment	anesthesia time	treatment time
case 1	Duchenne	4 y male	98.5 cm 14.0 kg	walking independently	asthma	6297 IU/L	propofol fentanyl	vecuronium bromide	O_2 (1.5–2 L/min) N_2O (2–3 L/min) propofol (5–6 mg/kg/hr)	conservative treatment 17 teeth	4 hr40 min	4 hr05 min
case 2	Duchenne	4 y male	109.9 cm 19.8 kg	unable to walk independently	(−)	1777 IU/L	propofol fentanyl	rocuronium bromide	O_2 (1.5 L/min) N_2O (3 L/min) propofol (4–6 mg/kg/hr)	conservative treatment 9 teeth	2 hr15 min	1 hr25 min
case 3	Fukuyama	7 y female	110 cm 12.2 kg	no limitation	febrile convulsion	2775 IU/L	sevoflurane	(−)	O_2 (2–3 L/min) N_2O (3–4 L/min) sevoflrane (1–2%)	conservative treatment 11 teeth extraction 4 teeth	4 hr10 min	3 hr10 min
case 4	Fukuyama	14 y male	146 cm 20.4 kg	unable to walk independently	febrile convulsion	1105 IU/L	sevoflurane	(−)	O_2 (2–3 L/min) N_2O (3–4 L/min) sevoflrane (0.6–1.2%)	conservative treatment 12 teeth	5 hr15 min	4 hr40 min
case 5	Fukuyama	4 y male	95 cm 12.5 kg	unable to walk independently	febrile convulsion rhabdomyolysis	6633 IU/L	sevoflurane	(−)	O_2 (1.5 L/min) N_2O (3 L/min) propofol (2.5–5 mg/kg/hr)	conservative treatment 9 teeth lingual frenectomy	2 hr40 min	2 hr00 min
case 6	Fukuyama	7 y female	110 cm 19.2 kg	unable to walk independently	febrile convulsion asthma	529 IU/L	sevoflurane	(−)	O_2 (1–2 L/min) N_2O (2 L/min) sevoflrane (0.6–1.2%)	conservative treatment 15 teeth	2 hr55 min	2 hr20 min

Discussion

Duchenne type boys will be bone in the ratio of one to 3,500 infants and has the highest frequency among PMD[5]. The mean detective age is 3.5 years old and they will not be able to walk about 10 years old[5]. The prognosis is poor and the mean life span is reported 27.2 years old[5]. Fukuyama type PMD is often seen following Duchenne type PMD and the mean life span is 17.6 years[6]. The main causes of death are heart failure and respiratory failure in both types[7].

The problems for the management of general anesthesia in patients with PMD are (1) circulatory failure due to myocardial damage[1,8], (2) respiratory failure due to respiratory dysfunction[8,9], (3) induction of malignant hyperthermia due to agents for general anesthesia[10], and (4) increased sensitivity and prolonged effects of muscle relaxants[11].

Myocardial necrosis and degeneration may progress with age, resulting in heart failure[6]. However, muscle weakness often precludes the detailed preoperative evaluation of cardiac functions in daily life. Therefore, echocardiography should be performed if possible for preoperative evaluation of cardiac functions. In the present cases, no abnormality was found by echocardiography in cases 4 and 5 of Fukuyama type PMD with limited activities of daily living. During the operation, we were careful for circulatory suppression and maintained adequate anesthesia depth to prevent deep anesthesia.

As the respiratory muscles progressively degenerate with age, respiratory depression and ventilatory failure may be caused by the prolonged effects of muscle relaxants and inhalation anesthetics. Caution should also be exercised for respiratory infections, such as aspiration pneumonia, due to decreased cough and swallowing reflexes[12]. Therefore, the recovery of tidal volume and respiratory rate were confirmed before extubation, and we carefully observed even after the operation. The dosage of fentanyl was reduced by combining with nitrous oxide because of the respiratory suppression by fentanyl.

Duchenne type PMD is frequently accompanied by malignant hyperthermia and rhabdomyolysis due to volatile inhalation anesthetics[10]. Therefore, instead of volatile inhalation anesthetics, relatively safe anesthesia management was planned using nitrous oxide, intravenous anesthetics, narcotics and non–depolarizing muscle relaxants. Propofol and fentanyl were administered for anesthesia induction, followed by the maintenance of anesthesia with oxygen, nitrous oxide and propofol.

Few reports have been reported on malignant hyperthermia in Fukuyama type PMD, with only one report on similar symptoms following general anesthesia with halothane and suxamethonium chloride[13]. Therefore, sevoflurane was administered for the induction and maintenance of anesthesia in cases 3, 4 and 6 of Fukuyama type. However, in case 5 with a history of rhabdomyolysis, sevoflurane was used only for the induction, followed by the maintenance of anesthesia with propofol.

Non–depolarizing muscle relaxants are likely to increase the sensitivity to muscle relaxants and prolong their duration of action[11]. Therefore, propofol and fentanyl were administered for the anesthesia induction in Duchenne type PMD at the minimum dosage for muscle relaxants. In some cases, a muscle relaxation monitor was employed to confirm the recovery of muscle strength before extubation. Sugammadex directly encapsulates and inactivates rocuronium bromide and vecuronium bromide. In the present cases, all patients underwent dental treatments, eliminating the use of muscle relaxants during the operation. However, the use of sugammadex should be considered to

antagonize the prolonged action of muscle relaxants.

For tracheal intubation in Fukuyama type PMD, sevoflurane was administered to achieve a sufficient depth of anesthesia without the use of muscle relaxants.

Conclusion

For patients with Duchenne type PMD, anesthesia was induced with propofol and nondepolarizing muscle relaxants, and maintained with nitrous oxide and propofol. For patients with Fukuyama type PMD, anesthesia was induced with sevoflurane in every patients, and no muscle relaxant was used. Anesthesia was maintained with nitrous oxide in combination with sevoflurane in three cases and propofol in another case. No remarkable cardiopulmonary dysfunction was pointed in every patients.

In patients with Duchenne type PMD, volatile inhalation anesthetics were not used, which considered to be a risk factor for malignant hyperthermia. On the other hand, in patients with Fukuyama type PMD, the incidence of malignant hyperthermia by volatile inhalation anesthetic will be low. Therefore, we used sevoflurane.

The authors declare that there are no conflicts of interest associated with the present study.

References

1) Deconinck N and Bernard D (2007) Pathophysiology of Duchenne muscular dystrophy: Current hypotheses. Pediatric Neurology **36** : 1–7.
2) Ishihara T (2015) Duchenne muscular dystrophy. Japanese journal of Clinical medicine **35** : 14–7.
3) Oishi R, Obara S, Takahashi S, Akatsu M, Isosu T and Murakawa M (2009) Anesthetic management of a patient with Limb–Girdle–Type muscular dystrophy. Journal of Clinical Anesthesia **33** : 837–9.
4) Kanagawa M and Toda T (2011) Pathomechanism of Fukuyama congenital muscular dystrophy and related disorders. Medical science **62** : 91–4.
5) Konno H (2006) Duchenne /Becker muscular dystrophy. Japanese Journal of Pediatrie Medicine **38** : 768–9.
6) Osawa M and Hino N (2015) Fukuyama type congenital muscular dystrophy. journal of Clinical medicine **35** : 97–102.
7) Oda H, Himeno K, Taniyama K, Sumida S, Ogasawara T and Shibutani T (2008) General anesthesia for dental treatment of a child with Duchenne muscular dystrophy. Journal of Japanese dental society of anesthesiology **37** : 42–3.
8) Matsumura T, Saito T, Fujimura H, Shinno S and Sakoda S (2011) A longitudinal cause–of–death analysis of patients with Duchenne muscular dystrophy. Clinical Neurology **51** : 743–50.
9) Smith C L and Bush G H (1985) Anaesthesia and progressive muscular dystrophy. British Journal of Anaesthesia **57** : 1113–8.
10) Takahashi H, Shimokawa M, Sha K, Sakamoto T, Kawaguchi M, Kitaguchi K and Furuya H (2002) Sevoflurane can induce rhabdomyolysis in Duchenne's muscular dystrophy. The Japanese Journal of Anesthesiology **51** : 190–2.
11) Narimatsu E and Niiya T (2008) Neuromuscular disorders affecting the action of rocuronium. The Journal of Japan Society for Clinical Anesthesia **28** : 865–72.
12) Gotoh K and Fukushima K (2003) The Pathophysiology and its Anesthetic management of neuromuscular disease –especially on Progressive Muscular Dystrophy–. Journal of Clinical Anesthesia **27** : 7–14.
13) Nakazato A, Shime H, Morooka K, Nonaka I and Takagi A (1984) Anesthesia–induced rhabdomyolysis

in a patient with Fukuyama–type congenital muscular dystrophy. Brain and Development **16**：386–92.

抄録：進行性筋ジストロフィー患者 6 症例の歯科治療のための全身麻酔管理

小川さおり，谷山貴一，上田敬介，澁谷　徹
（松本歯大・歯科麻酔）

進行性筋ジストロフィーとは，筋線維の変性，壊死を主病変とし，進行性に筋力低下を示す遺伝性疾患である．進行性筋ジストロフィーには，Duchenne 型，Becker 型の他に，肢帯型，福山型がある．われわれは，2000年から2019年までに進行性筋ジストロフィー患者の集中的歯科治療時に対する全身麻酔を 6 例経験したので報告する．

術前血液検査では，全例で CPK が高値であった．全ての症例で，胸部エックス線写真と心電図検査で異常はなかった．

Duchenne 型筋ジストロフィーの 2 症例では，導入は，プロポフォールによる急速導入を行い，非脱分極性筋弛緩薬を使用した．麻酔維持は，酸素・亜酸化窒素・プロポフォールで行った．

福山型筋ジストロフィーの 4 症例では，導入は，全例がセボフルランによる緩徐導入で行い，筋弛緩薬は使用しなかった．麻酔は，3 例では酸素・亜酸化窒素・セボフルランで，もう 1 例はプロポフォールで維持した．

すべての症例において，周術期を通じて，呼吸，循環動態ともに大きな変動は認められなかった．

麻酔管理上の問題点として，①心筋障害による循環不全，②呼吸機能障害による呼吸不全，③悪性高熱症の可能性，④筋弛緩薬に対する感受性の亢進や効果の遷延が挙げられる．Duchenne 型筋ジストロフィーでは，悪性高熱症の危険因子と考えられる揮発性吸入麻酔薬は使用しなかった．一方，福山型筋ジストロフィーでは，揮発性吸入麻酔薬による悪性高熱症の発症頻度は低いとされているため，セボフルランを使用した．