A Case of Dental Treatment Under General Anesthesia for a Pediatric Patient With Pelizaeus - Merzbacher Disease

Hiroyoshi Kawaai[1], Yumiko Mishina[2], Katsunori Tanaka[1], Norihisa Aizawa[2], Kazuhiro Shimamura[2], Shinya Yamazaki[1]

[1]Department of Dental Anesthesiology, Ohu University School of Dentistry, Japan. [2]Department of Pediatric Dentistry, Ohu University School of Dentistry, Japan

Abstract

Pelizaeus – Merzbacher disease (PMD), one of the progressive and degenerative disorders of the cerebral white matter known as leukodystrophies, is caused by mutations in genes which encode for proteins involved in myelin formation. PMD may present as dysphagia when the clinical state of PMD becomes advanced. On the other hand, General anesthesia for a patient with depressed swallowing function is risky during extubation procedures and post respiratory management.

We had an opportunity to perform dental treatment under general anesthesia for a pediatric patient with PMD. He was four years and three months of age, and diagnosed with PMD when he was four month of age. He went to a private dental clinic, however, safe dental treatment without general anesthesia was not possible because he was uncooperative. He was induced with sevoflurane in 4 L/min nitrous oxide and 2 L/min oxygen. General anesthesia was managed with remifentanil and sevoflurane in 3 L/min air and 1 L/min oxygen. The patient's general anesthesia was managed with the same method in a total of three times of general anesthesia and his respiration and circulatory dynamics were stable during dental treatment under each general anesthesia. Our findings suggest that sevoflurane, fentanyl, remifentanil, rocuronium and midazolam can be safely given in PMD patients, appropriate management with consideration to the degree of developmental disability in the swallowing function should be selected. In addition, we should pay particular attention to prevent airway complications caused by depressed swallowing reflex and pharyngeal muscle activity.

Key Words: Pelizaeus–Merzbacher Disease, Dysphagia, General anesthesia, Pediatric patient, Dental treatment, Leukodystrophy, Central nervous system

Background

Pelizaeus – Merzbacher disease (PMD), one of progressive and degenerative disorders of the cerebral white matter known as the leukodystrophies [1-3], is caused by mutations in genes which encode for proteins involved in myelin formation. Generally, myelin, the major component of cerebral white matter, is composed of lipid membranes that wrap around axonal processes increasing the speed and efficiency of neuronal conduction [4]. Proteolipid protein, one of the protein components involved in myelin formation in the main central nerve, is abnormally synthesized by several hereditary causes according to histological findings of PMD [5].

PMD may present as dysphagia when the clinical state of PMD becomes advanced. General anesthesia for a patient with depressed swallowing function is risky during extubation procedures and post respiratory management [6]. In addition, oral bacteria are more likely to be infecting organisms when aspirated into the lung. Therefore, dental treatment for patients with dysphagia or a depressed swallowing function is important in order to preserve aspiration pneumonitis. Additionally, a PMD patient with dental caries must be treated before his dysphagia or depressed of swallowing function develops. We herein present the case of a PMD patient who was successfully treated for dental caries under general anesthesia.

The present case is very rare, and no previous reports have described general anesthesia for dental treatment in patients with PMD. In our hospital, we experienced an opportunity to safely anesthetize a PMD patient without dysphagia or depressed swallowing function under ambulatory anesthesia.

CaseReport

The patient was four years and three months of age with a height of 98 cm and weight of 15 kg. He was diagnosed with PMD when he was four month of age. He went to a private dental clinic with a chief complain of lower deciduous molar toothache. However, safe dental treatment without general anesthesia was not possible because he was uncooperative. The private dental clinic recommended our hospital, and the patient was introduced to the Department of Pediatric Dentistry. He had rampant caries (all teeth had caries) and mental retardation, and was therefore scheduled for the extraction of deciduous teeth, resin fillings and other procedures for caries under general anesthesia. He took 100mg sodium valproate after each meal.

In the first session of general anesthesia *(Figure 1)*, the patient was induced with sevoflurane in 4 L/min nitrous oxide and 2 L/min oxygen because he could not tolerate an infusion line. After the infusion line was placed, the patient underwent topical nasopharyngeal anesthesia with adrenaline (1:10,000) in 4% lidocaine, and 20 μg fentanyl and 10mg rocuronium bromide were given intravenously. Nasotracheal intubation (#4.5 Nasal RAE Tracheal Tube Uncuffed, Mallinckrodt^{TM}, Covidien, USA) was smoothly performed and general anesthesia was managed with remifentanil and sevoflurane in 3 L/min air and 1 L/min oxygen. The patient's respiration and circulatory dynamics were stable during dental treatment under general anesthesia. Approximately 10 minutes before the end of the operation 10 μg fentanyl was given. Agitation was recognized immediately after the extubation, thus 0.5 mg midazolam was given intravenously and his arousal state improved. The operative duration was 144 minutes and the

Corresponding author: Hiroyoshi Kawaai, DDS, PhD, Department of Dental, Anesthesiology, Ohu University School of Dentistry, 31-1 Misumidou, Tomita, Koriyama, Fukushima 963-8611, Japan; Tel: +81-24-932-9337; Fax: +81-24-932-9337; e-mail: hiroyoshimasumi@gmail.com

general anesthesia duration was 206 minutes. Digital X-rays were taken, then vital pulpotomy with calcium hydroxide (CALVITAL®, Neo Dental Chemical Products Co. Ltd., Japan) was performed in four teeth and forming crowns (Primary Molar Stainless Steel Crowns™, 3M Japan Limited, Japan) were set on the same four teeth during the dental treatment under general anesthesia. He was scheduled for hospital admission before the dental treatment under general anesthesia; therefore, he stayed in his hospital room. He awakened completely from general anesthesia two hours after the completion of the operation and smiled with his family. However, he cried and made a lot of noise at approximately three hours into the post-operative period. At the same time, he was able to consume water without nausea and urinate normally. Therefore, we gave his mother the permission to discharge the patient from our hospital at approximately four hours after the completion of the dental treatment under general anesthesia.

In the second session of general anesthesia *(Figure 2)*, the patient was induced using the same method as in the first session of general anesthesia. Two teeth extractions and six resin fillings (UniFil® Flow and SOLARE, GC, Japan) were performed during the treatment under general anesthesia. The operative duration was 92 minutes and the general anesthesia duration was 140 minutes. The patient was discharged from our hospital at approximately three hours after the completion of the dental treatment under general anesthesia.

In the third session of general anesthesia *(Figure 3)*, the patient was induced using the same method as in the first session of general anesthesia. One tooth extraction and seven resin fillings (UniFil® Flow and SOLARE, GC, Japan) were performed during the dental treatment under general anesthesia. The operative duration was 64 minutes and the general anesthesia duration was 128 minutes. The patient was discharged from our hospital at approximately three hours after the completion of the dental treatment under general anesthesia.

We obtained informed consent from his guardians in regard to reporting to a journal.

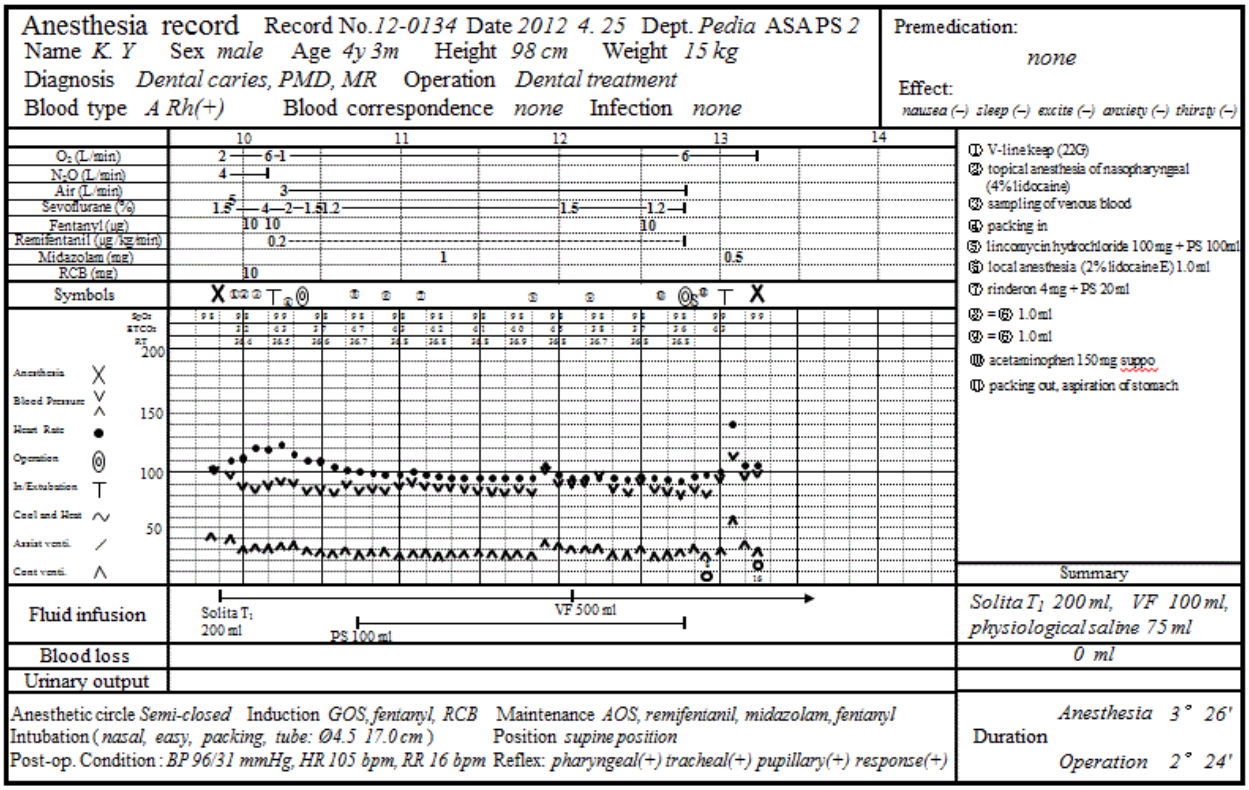

Figure 1. The patient was induced with sevoflurane in 4 L/min nitrous oxide and 2 L/min oxygen. After the infusion line was placed, the patient underwent topical nasopharyngeal anesthesia with adrenaline (1:10,000) in 4% lidocaine, and 20 μg fentanyl and 10 mg rocuronium bromide were given intravenously. Nasotracheal intubation (#4.5 Mallinckrodt tube, USA) was smoothly performed and general anesthesia was managed with remifentanil and sevoflurane in air and oxygen. The patient's respiration and circulatory dynamics were stable during general anesthesia. The operative duration was 144 minutes and the general anesthesia duration was 206 minutes. Digital X-rays were taken, then vital pulpotomy was performed in four teeth and forming crowns were set on the same four teeth.

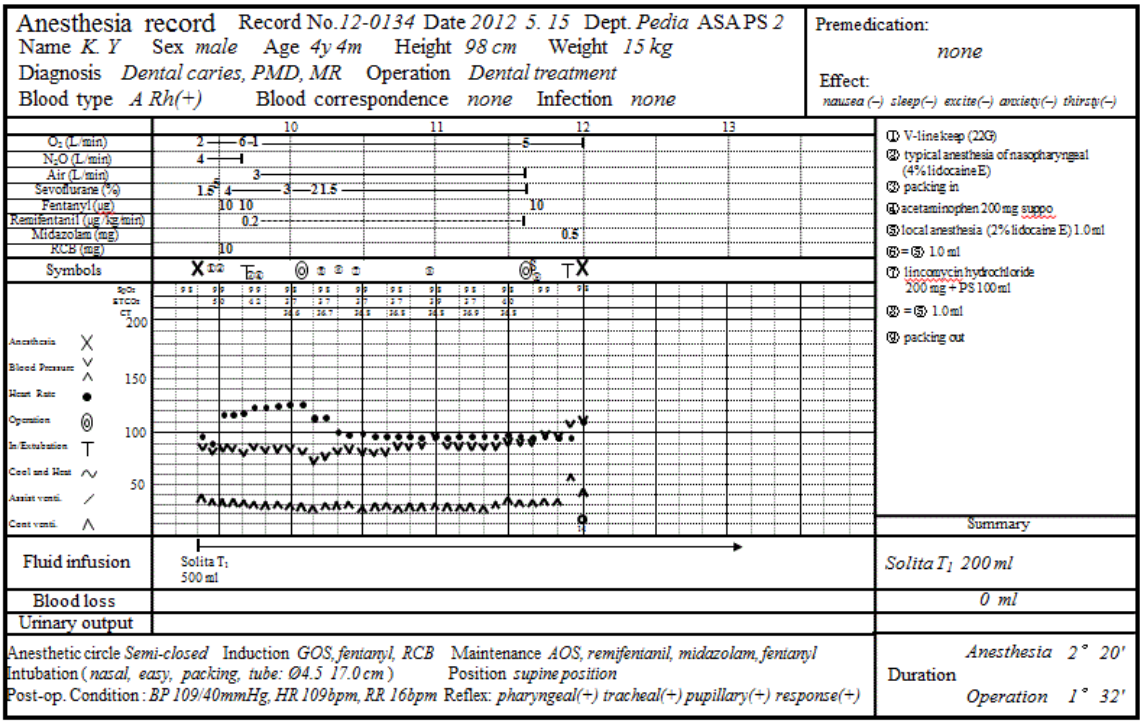

Figure 2. The patient was induced using the same method as in the first session of general anesthesia. Two teeth extractions and six resin fillings were performed during the treatment under general anesthesia. The operative duration was 92 minutes and the general anesthesia duration was 140 minutes. The patient was discharged from our hospital at approximately three hours after the completion of the dental treatment under general anesthesia.

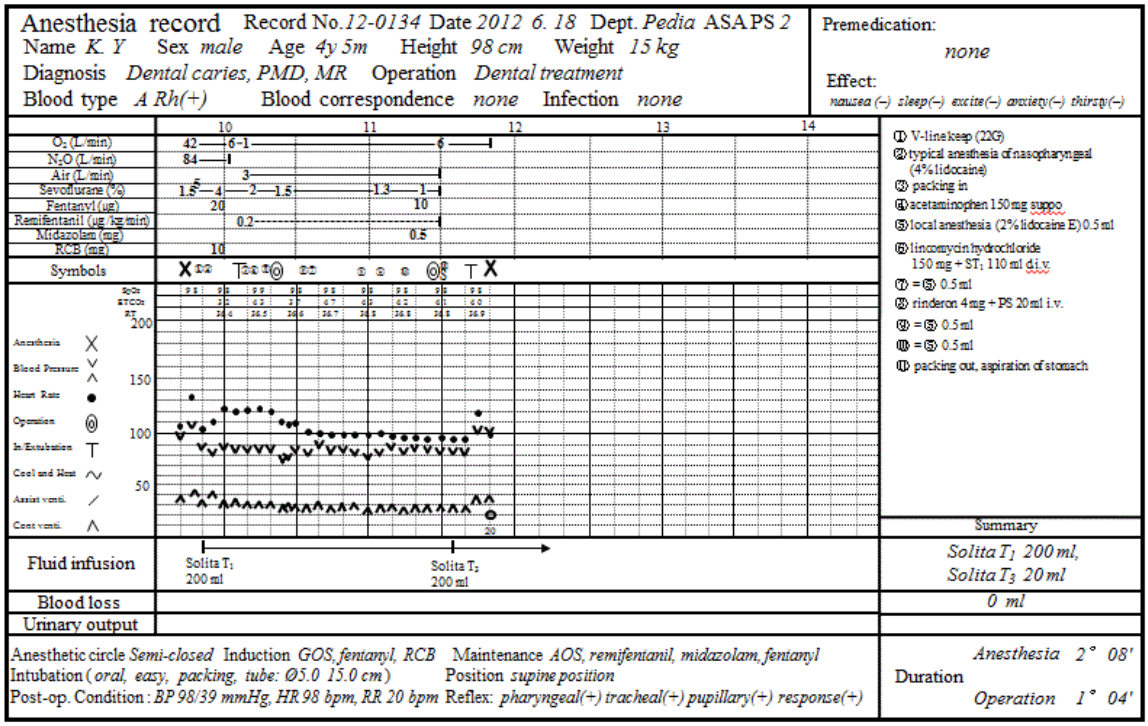

Figure 3. The patient was induced using the same method as in the first session of general anesthesia. One tooth extraction and seven resin fillings were performed during the dental treatment under general anesthesia. The operative duration was 64 minutes and the general anesthesia duration was 128 minutes. The patient was discharged from our hospital at approximately three hours after the completion of the dental treatment under general anesthesia.

Discussion

According to the latest epidemiological survey, the prevalence of PMD is estimated to be approximately 1.45 in 100,000 live births in Japan [7,8]. The incidence of PMD in Japan is relatively higher compared with Germany (0.13 in 100,000 live births) [9]. Additionally, PMD is categorized into some classical types [10]. When patients with PMD develop a depressed swallowing reflex and pharyngeal muscle activity, dental treatment becomes difficult not only during consciousness but also general anesthesia. Following dental treatment under general anesthesia for a case such as a PMD patient, complications may arise during the post-operative period due to the depressed swallowing reflex. From the point of view of preventing aspiration pneumonitis, an appropriate opportunity to perform general anesthesia for PMD patient is before they develop a depressed swallowing reflex and pharyngeal muscle activity or after they undergo laryngo-tracheal separation due to a depressed swallowing reflex and pharyngeal muscle activity. In the present case, depressed swallowing reflex and pharyngeal muscle activity were not recognized and he had no previous history of aspiration pneumonia. In addition, he could not cooperate during dental treatment due to mental retardation and all his teeth required treatment. Therefore, we chose dental treatment under general anesthesia.

PMD patients are not typically susceptible to malignant hyperthermia because abnormal conformations are not observed in the muscle structures. However, a previous report [6] suggested that hyperkalemia may occur in patients with PMD given intravenous depolarizing relaxant due to muscle atrophy [11]. The present case was not given intravenous depolarizing relaxants for this reason. Regarding non-depolarizing relaxants and anesthetics, another case report [12] indicated that no complications occurred in a patient with PMD, who was given isoflurane by inhalation and intravenous fentanyl and vecuronium. For these reasons, we gave our patient sevoflurane by inhalation, and intravenous fentanyl, remifentanil, rocuronium and midazolam. Hypercapnia, hyperthermia and a prolonged effect of the relaxant were not recognized during or following the operation in the present case. Therefore, this case demonstrates that sevoflurane, fentanyl, remifentanil, rocuronium and midazolam can be safely used in patients with PMD.

Previous reports [6,12] regarding the use of general anesthesia in patients of PMD included laryngotracheal separation; however, no studies regarding dental treatment under general anesthesia have yet been reported. This may be because PMD develops earlier in childhood and dental treatment is not performed because the clinical state of PMD advances early. On the other hand, the more caries a patient has, the more bacteria present in the patient's mouth. If a patient with PMD has significant caries and depressed swallowing reflex and pharyngeal muscle activity, then he is more likely to develop aspiration pneumonia. The best method of preventing would be for patients to have no caries before the development of depressed swallowing reflex and pharyngeal muscle activity. The present case suggests that a patient with PMD should be completely treated for dental caries under general anesthesia before the depressed swallowing reflex and pharyngeal muscle activity develops. If PMD patients are unable to be treated under general anesthesia due to depressed swallowing reflex and pharyngeal muscle activity, then they should attempt to prevent dental caries development until after the early postnatal period. Otherwise, dental treatment should be promptly performed in these patients following laryngotracheal separation.

In summary, dental treatment under general anesthesia for patients with PMD may be safely managed using sevoflurane, fentanyl, remifentanil, rocuronium and midazolam. Careful attention is necessary to prevent airway complications caused by depressed swallowing reflex and pharyngeal muscle activity. In addition, appropriate management for dental treatment should be carefully chosen with consideration for degree of developmental disability in the swallowing function.

References

1. Menkes JH. Heredodegenerative diseases. In: Menkes JH (Ed.). Textbook of Child Neurology. 2nd ed. Lea & Febiger, Philadelphia, 1980, 110-147.

2. Hodes ME, Pratt VM, Dlouhy SR. Genetics of Pelizaeus-Merzbacher disease. *Developmental Neuroscience*. 1993; **15**: 383-394.

3. Woodward K, Malcolm S. Proteolipid protein gene: Pelizaeus-Merzbacher disease in humans and neurodegeneration in mice. *Trends in Genetics*. 1999; **15**: 125-128.

4. Pizzini F, Fatemi AS, Barker PB, Nagae-Poetscher LM, Horská A, et al. Proton MR spectroscopic imaging in Pelizaeus - Merzbacher disease. *AJNR American Journal of Neuroradiology*. 2003; **24**: 1683-1689.

5. Anderson TJ, Schneider A, Barrie JA, Klugmann M, McCulloch MC, et al. Late-onset neurodegeneration in mice with increased dosage of the proteolipid protein gene. *Journal of Comparative Neurology*. 1998; **394**: 506-519.

6. Tobias JD. Anaesthetic considerations for the child with leukodystrophy. *Canadian Journal of Anesthesia*. 1992; **39**: 394-397.

7. Torii T, Miyamoto Y, Yamauchi J, Tanoue A. Pelizaeus–Merzbacher disease: Cellular pathogenesis and pharmacologic therapy. *Pediatrics International*. 2014; **56**: 659-666.

8. Numata Y, Gotoh L, Iwaki A, Kurosawa K, Takanashi J, et al. Epidemiological, clinical, and genetic landscapes of hypomyelinating leukodystrophies. *Journal of Neurology*. 2014; **261**: 752-758.

9. Hobson GM, Garbern JY. Pelizaeus-Merzbacher disease, Pelizaeus-Merzbacher- like disease 1, and related hypomyelinating disorders. *Seminars in Neurology*. 2012; **32**: 62-67.

10. Gencic S, Abuelo D, Ambler M, Hudson LD. Pelizaeus-Merzbacher Disease: An X-linked Neurologic Disorder of Myelin Metabolism with a Novel Mutation in the Gene Encoding Proteolipid Protein. *American Journal of Human Genetics*. 1989; **45**: 435-442.

11. Cooperman LH, Strobel GE Jr, Kennel EM. Massive hyperkalemia after administration of succinylcholine. *Anesthesiology*. 1970; **32**: 161-164.

12. Astle WF, Papp A, Huang PT, Ingram A. Refractive laser surgery in children with coexisting medical and ocular pathology. *Journal of Cataract & Refractive Surgery*. 2006; **32**: 103-108.