대한마취과학회지 2008; 54: S 51～4
Korean J Anesthesiol Vol. 54, No. 3, March, 2008

□ 영문논문 □

Anesthetic Management of a Patient with Lafora's Disease

— A case report —

Department of Anesthesiology and Pain Medicine, College of Medicine, Wonkwang University, Iksan;
*Department of Oral and Maxillofacial Surgery, Daejeon Dental Hospital, Wonkwang University, Daejeon;
†Department of Surgery, Wonkwang-Gusan Medical Center, Wonkwang University, Gunsan, Korea

Cheol Lee, M.D., **Seri O,** M.D.*, and **Dong Baek Kang,** M.D.†

Lafora' disease is an autosomal recessive, fatal, generalized polyglucosan storage disorder that occurs in childhood or adolescence with stimulus sensitive epilepsy (resting and action myoclonias, grand mal, and absence), dementia, ataxia and rapid neurological deterioration. We present a 19-year-old, 32 kg woman with lafora's disease was scheduled for tonsillectomy under general anesthesia. Her preanesthetic examination revealed extreme muscle atrophy and dementia. Grand mal, myoclonic seizures, and upper airway obstruction were frequent. General anesthesia and tracheal intubation with sevoflurane and nitrous oxide provided safe anesthesia. The intraoperative course was uneventful and the emergence of anesthesia was smooth. **(Korean J Anesthesiol 2008; 54: S 51～4)**

Key Words: ataxia, epilepsy, dementia, Lafora's diseas.

Lafora's disease (LD) is an autosomal recessive fatal disorder characterized by the presence of polyglucosan inclusions, called Lafora bodies.[1,2] LD typically starts during adolescence in otherwise neurologically normal individuals, usually first seen with generalized or partial epilepsy and myoclonia, followed by rapidly progressive mental decline. The progressive worsening of the neurological disorder usually leads to death within less than a decade.[2-4] Diagnosis is made by polyglucosan inclusions (Lafora bodies) shown in biopsies of the skin, striated muscle, liver, brain, and/or bone.[5]

Clinical features are dementia, severe and drug resistant grand mal, myoclonic seizures temporary blindness and uncertainty about the duration of muscle paralysis, all of which seem to pose a challenge for the anesthesiologist. The mental retardation might create difficulties for the anesthesiologist, both during anesthetic induction and recovery. To our best knowledge, However, there is limited information available on the anesthetic management of a patient with LD. We report the successful management of sevoflurane anesthesia for a patient with LD.

Received : October 1, 2007
Corresponding to : Cheol Lee, Department of Anesthesiology and Pain Medicine, College of Medicine, Wonkwang University, 344-2, Sinyong-dong, Iksan 750-711, Korea. Tel: 82-63-859-1560, Fax: 82-63-857-5472, E-mail: ironyii@wonkwang.ac.kr
This study was supported by the grant 2007 from Wonkwang University.

CASE REPORT

A 19-year-old woman weighting 32 kg and 154 cm in height, diagnosed with LD was scheduled for surgical treatment of chronic tonsillitis. She developed quite normally for the first of 12 years of her life. At the age of 13 years, she began to show sign of myoclonic (jerk-like) seizures. After the first year, generalized convulsions began to occur. By the age of 15 years, she could not ambulation. Meanwhile, mental abilities began a gradual decline. According to guardian, her diagnosis was confirmed in other hospital 3 years ago. On the interview, intellectual disability was present. She responded to painful stimulation but not to verbal command. Because of ataxia and muscle atrophy, she had been bedridden. Although she was taking clonazepam, diazepam and valproic acid, the grand mal and the myoclonic seizures persisted. The frequency of the seizure was about three to five times per day. Her vital signs, chest x-ray, electrocardiography (ECG), and laboratory data were normal. A significant issue in the family's medical history was her brother's death from LD.

The patient took clonazepam 0.25 mg, diazepam 2 mg,

valproic acid 600 mg orally until two hours before the surgery. After atropine 0.5 mg intramuscularly was administerd 30 min before general anesthesia, anesthesia was induced with thiopental 150 mg and fentanyl 50 μg intravenously. After deepening anesthesia with sevoflurane 6−8% and nitrous oxide 50% in oxygen, the trachea was intubated. Anesthesia was maintained with 1−3% sevoflurane and 50% nitrous oxide in oxygen. Reinforced 6.0 mm endotracheal cuffed tube was used in this case. Anesthesia was maintained with nitrous oxide 50% and sevoflurane 1−3% in oxygen. She was ventilated mechanically during surgery. Monitors included ECG, non-invasive automatic arterial manometer, pulse oximeter and capnograph. Inspired and end-tidal concentrations of nitrous oxide and sevoflurane were measured. A peripheral artery was not cannulated since the operation was not a major operation, and without fluid shifts. To avoid hypoglycemia, fluid balance was maintained with a 2.5% dextrose in 0.45% normal saline infusion during operation. Venous blood was sent for plasma glucose concentration measurements. Except for mild hypoglycemia (plasma glucose concentration of 65 mg/dl) at the beginning of the procedure, which was corrected to 110 mg/dl by intravenous administration of glucose, there was no episodes of hypoglycemia. Body temperature was monitored with a rectal thermometer. Her temperature was 36.5−36.8°C throughout the surgery. The surgery was completed within 30 minute. At the end of surgery, anesthetic agents were discontinued. Anesthetic management and recovery presented no complication. Although severe myoclonia was observed, her respiratory and circulatory conditions remained stable in postanesthesia care unit. Myoclonia was controlled using diazepam 2 mg intravenously. Consulting with neurologist on her conditions, we didn't give her special any treatment except administering phenobarbital 5 mg/kg bolus injection and continuous infusion of phenobarbital 2 mg/kg/hr to her. The postoperative course was uneventful, and neurological symptoms were not exacerbated after the operation. The patient was discharged from hospital the following week.

DISCUSSION

LD is an autosomal recessive inherited disorder, characterized by generalized seizures, myoclonias, and cognitive decline, that is eventually fatal. In their first decade of life, LD patients experience a normal development that cannot be distinguished from those of their unaffected siblings. In the majority of patients, the onset of the progressively worsening seizure disorder is between 12−17 years of age.[2-5] LD is caused by a mutation in the EPM2A gene, which encodes 2 isoforms of the laforin protein tyrosine phosphatase, and this mutation is shown in 80% of the patients.[2,3,6,7]

Pathognomonic hallmark of LD are Lafora bodies, intracytoplasmic, basophilic, periodic acid-Schiff-positive, 0.5−30 μm diameter, polyglyglucosan inclusions, found in neurons and in other sites, including heart, skeletal muscle, liver, and sweat gland duct cells. Skin biopsy is the least invasive method of pathologic diagnosis even if a negative biopsy specimen in patients with progressive myoclonic epilepsy is not sufficient to exclude diagnosis of LD.[2] Lafora bodies are also similar to the polyglucosan bodies found in adult polyglucosan body disease (APBD). APBD is characterized by adult-onset progressive sensory and upper and lower motor neuron disease, dementia, but no seizure, or myoclonias.[8]

There is limited information available on the anesthetic management of a patient with LD. We practiced anesthetic management of LD with reference to those of adult polygucosan body disease (APBD)[9] and myoclonic epilepsy with ragged fibers syndrome similar to symptoms or pathophysiologic mechanisms.[10]

Clinical features are dementia, severe and drug resistant grand mal, myoclonic seizures and temporary blindness, all of which seem to pose a challenge for the anesthesiologist. Anesthetic management should begin with careful investigation of the medical history and a complete physical examination to exclude possible associated comorbidity. Since there are no reports of anesthesia of patients with LD and it is uncertain how intravenous anesthetic agents affect the nervous system in such progressive diseases, induction, and maintenance of anesthesia should be simple to avoid abnormal reactions. We tried to limit anesthetic drug doses to minimum, necessary for airway instrumentation and surgery. The possibility of increased sensitivity to volatile and intravenous induction agents in these case makes careful titration and monitoring essential. The concentration of intravenous agents cannot be monitored clinically, whereas inspired and end-tidal concentrations of inhaled anesthetics can be easily measured. Intraoperative and postoperative course were uneventful except for myoclonia during emergence from general anesthesia. Thus, we anticipated possible problems during the management of anesthesia in our patient.

First, the risk of exacerbating neurological symptoms was a

consideration that oriented our choice of anesthetic agents. The patient had taken several types of anticonvulsants. The mechanisms of action of these anticonvulsants may involve drug-induced increases in the activity of inhibitory neurotransmitters such as GABA.[11] We used titrated doses of thiopental for induction, because thiopental is known to share the same mechanism of action of these anticonvulsants. Sevoflurane was selected because of its low blood gas partition coefficient and anticonvulsive action at low concentration, and because of its pleasant, nonirritating odor and lack of pungency.[12,13] Although sevoflurane has been implicated in causing seizure-like activity, other inhalation anesthetics, including isoflurane, can also trigger spike wave activity in the electroencephlogram and convulsion.[14,15] Interestingly, these inhalational anesthetics have also anticonvulsive action at low concentration.

Second, in a patient with progressive neurological disease, there is a concern about the risk of exacerbating co-existing neurological symptom. In patients with neurological disorders involving motor deficits, succinylcholine is contraindicated[16] and nondepolarizing muscle relaxants must be used cautiously because of uncertainty about the duration of muscle paralysis. We did not use muscle relaxants for endotracheal intubation to prevent any associated problems, including prolonged effect of the drugs. Moreover, sevoflurane can provide sufficient muscle relaxation to facilitate tracheal intubation[17] and the surgical procedure did not require further muscle relaxation in this case.

Third, in the perioperative management, it is crucial to ensure normoglycemia, normothermia, normotension and optimal oxygenation. Preoperative fasting should be as brief as possible and glucose containing fluids should be intravenously administered perioperatively. Blood glucose concentrations must be carefully monitored since hypoglycemia can be severe. Moreover, intraoperative hypoglycemia can mask its clinical signs and symptoms. In our case, the mild hypoglycemia detected in the beginning of the procedure was treated by an intravenous infusion of a glucose containing solution. Meticulous attention to the prevention of hypoglycemia is important issues in the perianesthetic management of these patients. But Administering fluids that provide free water (i.e., fluids that do not have sufficient non-glucose-containing solutes to render them isoosmololar with respect to blood) will lower serum osmolarity if the amount of free water administered is in excess of that required to maintain ongoing free water loss. Half-normal saline is probably a reasonable choice for the traditional maintenance fluid allowance.[18] In our case, fluid balance was maintained with a 2.5% dextrose in 0.45% normal saline and 0.9% normal saline infusion during operation to prevent reduction of serum osmolarity which may be induced by fluid administered to avoid hypoglycemia.

In conclusion, a safe perioperative management of a patients with LD can be achieved by careful attention to the derangements that occur with the disease. General anesthesia using thiopental, nitrous oxide and sevoflurane provided satisfactory anesthetic and operative conditions in a patients with LD.

REFERENCES

1. Lohi H, Turnbull J, Zhao XC, Pullenayegum S, Ianzano L, Yahyaoui M, et al: Genetic diagnosis in Lafora disease: genotype-phenotype correlations and diagnostic pitfalls. Neurology 2007; 68: 996-1001.
2. Minassian BA: Lafora's disease: towards a clinical, pathologic, and molecular synthesis. Pediatr Neurol 2001; 25: 21-9.
3. Franceschetti S, Gambardella A, Canafoglia L, Striano P, Lohi H, Gennaro E, et al: Clinical and genetic findings in 26 Italian patients with Lafora disease. Epilepsia 2006; 47: 640-3.
4. Berkovic SF, Cochius J, Andermann E, Andermann F: Progressive myoclonus epilepsies: clinical and genetic aspects. Epilepsia 1993; 34(Suppl 3): 19-30.
5. Chan EM, Omer S, Ahmed M, Bridges LR, Bennett C, Scherer SW, et al: Progressive myoclonus epilepsy with polyglucosans (Lafora disease): evidence for a third locus. Neurology 2004; 63: 565-7.
6. Serratosa JM, Delgado-Escueta AV, Posada I, Shih S, Drury I, Berciano J, et al: The gene for progressive myoclonus epilepsy of the Lafora type maps to chromosome 6q. Hum Mol Genet 1995; 4: 1657-63.
7. Ganesh S, Delgado-Escueta AV, Suzuki T, Francheschetti S, Riggio C, Avanzini G, et al: Genotype-phenotype correlations for EPM2A mutations in Lafora's progressive myoclonus epilepsy: exon 1 mutations associate with an early-onset cognitive deficit subphenotype. Hum Mol Genet 2002; 11: 1263-71.
8. Robitaille Y, Carpenter S, Karpati G, DiMauro SD: A distinct form of adult polyglucosan body disease with massive involvement of central and peripheral neuronal processes and astrocytes: a report of four cases and a review of the occurrence of polyglucosan bodies in other conditions such as Lafora's disease and normal ageing. Brain 1980; 103: 315-36.
9. Inoue S, Ishii R, Fukuda H, Saitoh K, Shimizu R: Sevoflurane anaesthesia for a patient with adult polyglucosan body disease. Can J Anaesth 1996; 43: 1257-9.
10. Vilela H, Garcia-Fernandez J, Parodi E, Reinoso-Barbero F, Duran P, Gilsanz FL: Anesthetic management of a patient with MERRF

syndrome. Paediatr Anaesth 2005; 15: 77-9.
11. Kalviainen R, Eriksson K, Parviainen I: Refractory generalized convulsive status epilepticus : a guide to treatment. CNS Drugs 2005; 19: 759-68.
12. Eger EI 2nd: New inhaled anesthetics. Anesthesiology 1994; 80: 906-22.
13. Hilty CA, Drummond JC: Seizure-like activity on emergence from sevoflurane anesthesia. Anesthesiology 2000; 93: 1357-9.
14. Poulton TJ, Ellingson RJ: Seizure associated with induction of anesthesia with isoflurane. Anesthesiology 1984; 61: 471-6.
15. Yogendran S, Prabhu A, Hendy A, McGuire G, Imarengiaye C, Wong J, et al: Vital capacity and patient controlled sevoflurane inhalation result in similar induction characteristics. Can J Anaesth 2005; 52: 45-9.
16. Gronert GA, Theye RA: Pathophysiology of hyperkalemia induced by succinylcholine. Anesthesiology 1975; 43: 89-99.
17. Kimura T, Watanabe S, Asakura N, Inomata S, Okada M, Taguchi M: Determination of end-tidal sevoflurane concentration for tracheal intubation and minimum alveolar anesthetic concentration in adults. Anesth Analg 1994; 79: 378-81.
18. Drummond JC, Patel PM: Neurosurgical anesthesia. In: Miller's Anesthesia. 6th ed. Edited by Miller RD: New York, Churchill Livingstone. 2005, pp 2143-4.