Outpatient Anesthesia for Oral Surgery in a Juvenile With Leigh Disease

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We report a case of anesthesia for elective outpatient third molar extraction in a juvenile with Leigh disease, a progressive neurodegenerative disorder related to respiratory chain deficiency. This syndrome usually presents in infancy and is characterized by nervous system dysfunction and respiratory abnormalities. Anesthesia has been reported to aggravate respiratory symptoms and frequently precipitate respiratory failure. Preoperative swallowing difficulty or respiratory symptoms should be carefully diagnosed, because they can be a warning sign of postoperative complications or mortality. Adverse effects of anesthesia may quickly lead into metabolic acidosis. Anesthetics should be carefully chosen that do not interfere with mitochondrial respiration, which can lead to lactic acidosis.

Key Words: Leigh disease; Outpatient anesthesia; Juvenile.

Leigh disease, a subacute necrotizing encephalomyelopathy, is a hereditary neurodegenerative disorder first described in 1951 by Dennis Leigh.¹ The disease usually afflicts children from 3–24 months of age, the incidence of occurrence is approximately 1 of 32,000 births, and the condition progresses to death a few years after diagnosis.^{2–4} Adult-onset and juvenile cases are rare, but these groups benefit from a lower rate of progression.² The disease is transmitted by an autosomal recessive mode of inheritance, possibly maternal, and no genetic basis supports a distinction among groups for differing ages of onset.^{2,5}

Histopathologic findings substantiate diagnosis of Leigh disease. Magnetic resonance imaging or computed tomography often reveals symmetrical necrotic lesions along the brainstem, diencephalon, and basal ganglion.^{6,7} Lesions also occur frequently on the cerebellum and spinal cord but with less definitive histologic features.⁸ The necrosis shows no partiality between gray and white matter, particularly on the brainstem, and the brainstem tegmentum is the structure most frequently damaged.^{5,8} Although certain areas are inclined to suffer lesions, the specific topography of the lesions may vary from case to case.⁸ These incidents may be influenced

by the age of the patient at the onset of the disease.⁹ The lesions may be contemporaneous with optic demyelination and instances of spongiform cavitation.⁷

Leigh disease is thought to be attributable to disorders of energy metabolism, specifically, mitochondrial respiratory chain defects and deficiencies of the pyruvate dehydrogenase complex.¹⁰ These abnormalities elevate pyruvate levels in the serum and cerebrospinal fluid and also instigate lactic acidosis, all of which are defining clinical characteristics of the disease.^{2,10} Recurring focal lesions suggest increasingly insufficient energy supply at these areas as the disease progresses.⁷ A study by Howell et al¹¹ reports that a mutation of mitochondrial DNA may be causatively associated with the presentation of the disease.

Symptoms include dysphagia, regurgitation, and anorexia, as well as blindness, optic atrophy, and nystagmus.⁵ Other symptoms include motor retardation, hypotonia, mental retardation, seizures, tachycardia, and bradycardia.⁵ Respiratory abnormalities are prevalent with Leigh disease. Irregular respiration, apnea, sighing, and stridor are symptoms and often warning signs of impending respiratory failure, the most common cause of death.¹²

Anesthesia for patients with this syndrome requires special precautions in light of potential respiratory complications. Acute intensification of symptoms is a possibility after surgical procedures, and respiratory distress

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is the most frequent source of postoperative morbidity and mortality.^{10,13} General anesthesia has been documented in some instances to precipitate respiratory failure.^{12,13} However, respiratory problems tend to decrease in occurrence with increasing age of disease onset,⁵ diminishing the risk for surgical operations in juvenile cases. We report a case of elective third molar extraction that involved intravenous anesthesia for a patient with Leigh disease.

CASE REPORT

A 16-year-old, 47-kg girl presented for elective extraction of 2 mandibular third molars. Significant medical history included a 9-year history of Leigh disease with secondary spasticity and wheel chair confinement. Her medical history included no known allergies. Current medications included esomeprazole magnesium (Nexium, AstraZeneca Pharmaceuticals LP, Wilmington, Del), 20 mg every day, and baclofen pump. Past hospitalizations included 5 occasions for implantation of a medication pump, most recently 5 years ago. Also, dehydration and surgical correction of a clubfoot required hospitalization 11 and 12 years ago, respectively. The patient's physician was consulted, and he indicated that there were "no neurologic contraindications for Versed/propofol sedation . . . the risk should be considered the same as would be incurred by anyone else." He based his recommendation on the patient's medical history of multiple surgical procedures, all of which were conducted without complication. He also indicated that the patient seemed to have a mild incidence of the syndrome.

The day of operation the patient had nothing to eat or drink 6 hours before surgery but did take 4 mg of diazepam with a small sip of water 1 hour before surgery as prescribed. Pulmonary auscultation showed that her lungs were without rales or rhonchi and she was not in respiratory distress. Cardiovascular auscultation indicated a normal heart rate and rhythm and no murmur. Preoperative vital signs were as follow: blood pressure, 112/75 mm Hg; pulse, 70/min; and pulse oximeter, 99%.

A 22-gauge catheter-over needle was placed in the medial cubital vein with a T-Connector extension set (Baxter Healthcare Corp, Deerfield, Ill) connected to the medication syringe. This would allow emergency drug injection to a medication port connected directly to the intravenous catheter, if needed. The vein remains patent via the intermittent infusion of the attached medication. A total of 1.25 mg of midazolam diluted with 3 mL of saline was slowly administered followed by further titration with 80 mg of propofol using an intermittent bolus technique. A total of 100% oxygen at 4 L by nasal hood

was implemented. The patient was monitored with automatic blood pressure, pulse oximeter, electrocardiogram, and pretracheal stethoscope. Local anesthetic for bilateral mandibular block anesthesia included 3.6 mL of 2% lidocaine with 1 : 100,000 epinephrine and 1.8 mL of 0.5% bupivacaine with 1 : 200,000 epinephrine.

During the 25-minute surgical procedure the patient had some nonpurposeful movement that was managed with 5- to 10-mg boluses of propofol. Intraoperative vital signs remained stable and within normal limits. Postoperative observation revealed no sign of complication, and 20 minutes after surgery the patient was alert and oriented. She was discharged with postoperative vital signs as follows: blood pressure, 129/75 mm Hg; pulse, 101/min; and pulse oximeter, 99%. Discharge medications included hydrocodone, 5 mg, with acetaminophen, 500 mg, $\frac{1}{2}$ or 1 tablet by mouth every 4 hours as needed; and promethazine, 12.5 mg, $\frac{1}{2}$ or 1 tablet by mouth every 4 hours as needed for nausea or vomiting or with pain medication. The patient was advised to take ibuprofen, 400 mg, immediately after surgery and then every 4 hours as needed. She was instructed to take the narcotic and/or antiemetic medication for breakthrough pain or nausea, respectively. Postoperative recovery was uneventful, and at 1 week she was discharged from further treatment.

DISCUSSION

Respiratory abnormalities often indicate the beginning of the final bout with Leigh disease.¹² The most common problems are irregular respiration, apnea, sighing, sobbing, gasping, stridor, and episodes of hyperventilation.^{5,10} A patient with respiratory symptoms before surgery that involved general anesthesia is likely to encounter postoperative respiratory complications or respiratory failure.¹⁰ Grattan-Smith et al¹² described 3 young patients who developed respiratory failure after general anesthesia for diagnostic radiography. All 3 had preoperative respiratory abnormalities, such as asthma, stridor, choking fits, and sighing respiration.¹² One of the patients under general anesthesia for muscle biopsy developed excessive depression of muscle tone and had to be intubated. The patient improved and seemed to recover after surgery, but 12 hours later he developed stridor and intermittent respiration and required reintubation.¹² Cooper and Fox¹³ describe a 21-year-old woman, diagnosed as having Leigh disease as an infant, who failed to wean from respiratory support after corrective spinal surgery. She did not have typical symptoms associated with postoperative respiratory failure, but she did have poor cough, poor bulbar function, and poor cooperation with physiotherapy, all of which the au-

thors suggest placed her into a category of high risk. Postoperative imaging revealed rapid necrosis of the patient's brainstem, which indicated a reactivation of the disease, likely the causative agent of her failure to wean from respiratory support, and her ultimate respiratory mortality. In contrast to these cases, Grattan-Smith et al¹² mention 8 patients without preoperative respiratory symptoms, who were involved in 14 total surgical procedures, all of which were performed with uneventful anesthetics.

Third molar extraction for our patient was recommended for orthodontic purposes. Based on the available research, the outpatient procedure was thought to be of acceptable risk. The patient showed no signs of respiratory abnormality before the operation. Neither did she have a history of respiratory symptoms associated with the disease. Preoperative evaluation revealed no contraindications for the procedure.

The patient's tolerance for ambulatory surgery versus hospital care could have been further evaluated with medical testing of the patient's exercise tolerance. The ability to note a marked increase in heart rate and respiratory rate would be difficult to assess with an electric wheelchair-bound patient, but her ability to blow out a match held several inches in front of an open mouth and possibly the use of a simple Volumeter to test the vital capacity could be considered. Pulmonary function testing that included an arterial blood gas would have been helpful as a baseline. Careful preoperative management may prevent catastrophic intraoperative events and could determine if there was a correctable pulmonary condition present.

Anesthesia was administered intravenously with propofol, which was chosen for its propensity for rapid recovery. Intraoperative monitoring with an electrocardiograph, noninvasive automatic blood pressure monitor, pretracheal stethoscope, and pulse oximeter was meticulously observed. Maintaining normal ventilation is needed.¹⁰ End-tidal capnography with a visual waveform would have increased the accuracy of respiratory monitoring if it had been available. Postoperative pain management using nonsteroidal anti-inflammatory medication was encouraged versus narcotic analgesics to reduce any chance of postoperative sedation.

Anesthesia experience for this disease has been rarely reported.^{10,12,13} Primary dangers include the possibility of lactic acidosis and unfavorable metabolic manifestations of some common anesthetics, such as halothane and barbiturates.¹⁰ Acid-base status and normoventilation should be monitored throughout the procedure, and because lactic acidosis is a frequent manifestation of the syndrome, use of lactate-containing fluids, such as lactated Ringer solution, are discouraged.¹⁰ Before surgery, lactic acid concentration and blood pH may be

normalized by treatment with dichloroacetate, riboflavin, and thiamine.¹⁰ Only brief exposure to inhalational anesthetics has been recommended, because these agents interfere with mitochondrial respiration and there is a tendency to cause metabolic acidosis.¹⁰

Operations performed with the patient under general anesthesia pose a considerable threat of mortality in a patient with severe respiratory deficits secondary to Leigh disease. The third molar extraction under deep sedation was performed only after the patient presented with no indications of respiratory abnormality. Anesthesia and recovery were uneventful with midazolam and propofol. Particular attention was given to the selection of anesthetic agents and the patient's respiratory status before, during, and after the operation. No postoperative complications arose, and at 1 week the patient was discharged from further treatment. Anesthesia can be safely preformed on a juvenile with Leigh disease, but extreme caution is required if the patient presents with respiratory manifestations of the syndrome.

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