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Considerations for general anesthesia combined with epidural anesthesia in a patient with stiff-person syndrome

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Abstract
We report the successful management of anesthesia in a patient with stiff-person syndrome (SPS) undergoing a thymectomy using a volatile anesthetic combined with epidural anesthesia. The anesthetic concern in patients with SPS is the possibility of postoperative hypotonia due to the presence of excessive γ-aminobutyric acid (GABA) resulting from an interaction between the anesthetic agents and preoperatively taken therapeutic drugs. Epidural anesthesia has the advantages of decreasing the required amount of anesthetics with GABAergic action, and relieving the postoperative pain that causes the symptoms of SPS. Epidural anesthesia could be a useful technique in SPS patients.

Key words Bispectral index · GABAergic neurotransmission · Train-of-four ratio

Introduction

Stiff-person syndrome (SPS) is a rare neurologic disease characterized by muscle rigidity and episodic painful spasms. In patients with SPS, stressors such as fear, anxiety, and pain trigger the symptoms. Although the etiology is not well understood, it is postulated that the pathophysiology of SPS is created by antibodies against glutamic acid decarboxylase (GAD), the enzyme essential for γ-aminobutyric acid (GABA) synthesis [1]. The loss of GABAergic input from inhibitory spinal interneurons and impaired supraspinal GABAergic neurons lead to the hyperexcitability of motor neurons and subsequent progressive muscle rigidity [2]. Treatment is based on drugs that facilitate GABA neurotransmission, including diazepam and baclofen. A concern exists that general anesthetics and neuromuscular blocking drugs cause delayed awakening and prolonged muscular weakness in some SPS patients [3-5]. Here, we report successful general anesthesia combined with epidural anesthesia for a patient with SPS undergoing a thymectomy.

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Case report

A 76-year-old man, weighing 32 kg and 157 cm in height, was scheduled for thymectomy. He was diagnosed with SPS based on his symptoms. One year previously, the symptoms had begun as muscle stiffness and painful spasms in his lower extremities. Laboratory findings showed that the plasma anti-GAD antibody level was 7000 to 9000 times higher than the normal limits. Because he had been blind for many years, he was very sensitive to sound. When even a small sound made him nervous, he would panic and exhibit the aforementioned symptoms. He had been treated with baclofen 30 mg, diazepam 5 mg, and clonazepam 1 mg daily. In the course of his examination, computed tomography detected an invasive thymoma, and removal was regarded as potentially therapeutic for SPS. No electrolyte abnormalities were seen preoperatively. For the operation, we planned general anesthesia in combination with epidural anesthesia.

Baclofen, diazepam, and clonazepam were given to the patient as usual in the morning on the day of the surgery. No other premedication was prescribed. In the operating room, bispectral index (BIS) monitoring (model A-2000; Aspect Medical Systems, Newton, MA-USA) was used in addition to standard American Society of Anesthiologists (ASA) monitors. An epidural catheter was placed at the Th 5/6 interspace prior to the induction of general anesthesia. To monitor the depth of neuromuscular blockade, skin electrodes were attached to his wrist before inducing anesthesia. TOF-GUARD (Organon Teknika, Turnhout, Belgium) was used to record the contraction of the adductor pollicis

muscle to train-of-four (TOF) supramaximal stimulation (2 Hz) of the ulnar nerve every 20 s. Anesthesia was induced with fentanyl (50 μg) and propofol (70 mg) administered intravenously. In addition, a short-acting sedative and analgesic available in Japan were chosen. No neuromuscular blocking drug was given. No body movement was observed when his trachea was intubated. His lungs were ventilated mechanically throughout the operation. Anesthesia was maintained with sevoflurane (0.5%–1.7%) and oxygen/air, and supplemental fentanyl (25 μg, twice) was administered as needed. About 20 min before skin incision, an initial dose of 5 ml of 0.25% ropivacaine was given into the epidural space, and 0.25% ropivacaine was administered continuously at a rate of 5 ml·h^{-1}. The sevoflurane concentration was adjusted to keep the BIS below 60. The TOF ratio remained above 90% throughout the anesthesia. His heart rate and blood pressure were stable, and his bladder temperature ranged from 35.9°C to 36.3°C. End-tidal carbon dioxide (CO_2) was maintained at 33 to 40 mmHg throughout the anesthesia. The operation proceeded uneventfully. Soon after discontinuation of the anesthesia, he awoke fully and the BIS returned to 95. His trachea was extubated smoothly. Total anesthetic time was 210 min. He did not feel pain on emergence from the anesthesia. Ropivacaine (0.25%) was administered through the epidural catheter for 48 h postoperatively, at a rate of 5 ml·h^{-1}, and postoperative pain was well controlled. There was no neurological disturbance, such as rigidity and spasm, and no unexpected event was seen in the postoperative course.

Discussion

To our knowledge, no previous report has described epidural anesthesia in SPS patients, in whom the clinical effects of general anesthetics, including intravenous and inhalation anesthetics, and neuromuscular blocking drugs remain to be determined [3,5]. In some SPS patients, no adverse postoperative events were observed [6,7]. Johnson and Miller [3] reported postoperative weakness despite the appropriate reversal of muscle relaxation, and the need for postoperative mechanical ventilation for 48 h. Bouw et al. [4] postulated that prolonged neuromuscular blockade was explained by the synergistic effect of volatile anesthetics via the $GABA_B$ receptor in SPS patients receiving baclofen preoperatively. We did not use a neuromuscular blocking drug in our patient. Autoantibodies against GAD, the enzyme essential for GABA production, are detected in 90% of SPS patients [8]. Although the etiology of this disease remains unclear, an autoimmune pathogenesis is suspected. In fact, after thymomectomy in our patient, the plasma anti-GAD antibody level was 30 to 50 times less than the preoperative level. Some recent reports suggest the potential benefits of plasma exchange and intravenous immunoglobulin therapies for SPS symptoms [9, 10]. At present, these are not fully established treatments for SPS, but they may be considered in patients who are refractory to drugs and surgery.

In addition to general anesthesia, we planned to perform epidural anesthesia in our patient. The anticipated advantages of epidural anesthesia in our patient were that it would relieve the painful postoperative stress that might have induced symptoms, especially for surgery with severe postoperative pain; decrease the requirement for volatile anesthetics that could enhance the effects of therapeutic drugs with GABAergic action; and avoid the use or overdose of neuromuscular blocking drugs and opioids with unknown interaction in SPS patients. Particular attention should be paid to the patient so as not to induce SPS symptoms during a procedure in which a needle is inserted into the patient's back. In our patient, an adequate preoperative explanation of the anesthetic technique settled him down and minimized his stressors such as fear, anxiety, and pain.

As reported previously, the TOF ratio suggested to us that the neuromuscular junction was unlikely to be affected in SPS [6, 7]. It is possible that neuromuscular blocking drugs could be used in SPS patients with an evaluation of the neuromuscular junction. In our patient, the BIS was monitored during anesthesia to assess the hypnotic effect of the anesthetics used. Monitoring the BIS had the advantage of allowing us to maintain the minimum necessary concentration of volatile anesthetic and reduce the possibility of postoperative hypotonia.

Recently, Elkassabany et al. [11] reported that somatic paravertebral blockade was beneficial for avoiding postoperative hypotonia in SPS patients. This finding combined with our findings, suggests that regional anesthesia using a peripheral nerve block is likely to be safe for SPS patients. Furthermore, successful anesthetic management using total intravenous anesthesia (TIVA) has been reported for ear, nose, and throat (ENT) surgery in SPS patients [12]. TIVA is also a valuable technique for surgery when neuraxial anesthesia cannot be applied.

General anesthesia and epidural anesthesia were performed successfully in our patient. Epidural anesthesia is effective for reducing the risk of postoperative hypotonia due to excessive use of general anesthetics and neuromuscular blocking drugs, and to alleviate postoperative pain in SPS patients. Regional anesthesia that includes epidural anesthesia and spinal anesthesia should be considered for surgery in patients with this disease.

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