Case report

Anesthetic management of a patient with stiff-person syndrome and thymoma: a case report

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Stiff-person syndrome (SPS, also called stiff-man syndrome) is a rare neurological disease with autoimmune features. It is characterized by fluctuating and progressive muscle rigidity, and episodic spasm that prominently involve axial and limb musculature.[1,2] Herein we report a case of anesthetic management of a patient with SPS for thymectomy and review several other cases.

CASE REPORT

A 58-year-old man (height 1.70m; weight 67 kg) with SPS was scheduled for resection of a thymoma. The diagnosis of SPS was based on clinical presentation. His symptoms began one month ago with ineffective tongue movement, and sometimes dysphagia. The stiffness and episodic spasm of limbs (left leg, right arm, and then right leg) occurred subsequently, especially when there was sound and other stimulus, which usually made the patient tumble and not to walk. Physical examination revealed extreme hypertonia of the lower extremities, with intercurrent and painful spasms. The laboratory examinations were normal except vitamin B_{12} deficiency. The specific antibodies associated with SPS were not examined because these analyses could not be performed in the laboratory at that time. CT scan of the chest showed a thymic mass in the anterior mediastinum, possibly a thymoma. The symptoms were alleviated with the treatment of diazepam 5 mg b.i.d, baclofen 10 mg t.i.d, vitamine B_{12} 500 μg t.i.d, vitamine B_1 10 mg t.i.d, and folic acid 5 mg t.i.d. Thymectomy was suggested since the patient was considered to be a paraneoplastic SPS case.

No premedication was given to the patient. Electrocardiogram, intra-arterial blood pressure, and SpO_2 were monitored in the operating room. Anesthesia was induced with midazolam (2 mg), propofol (40 mg), and remifentanil (target-controlled infusion at plasma level of 6 ng/ml). After administration of rocuronium (0.6 mg/kg), endotracheal intubation was performed. Anesthesia was maintained with intravenous remifentanil (target-controlled infusion at plasma level of 4 ng/ml) together with inhalational isoflurane (0.2%－0.4%), nitrous oxide (66%) and oxygen. Neuromuscular monitoring showed that, after intubating dose of rocuronium, the onset time (from injection until T_4/T_1 decreased to 25%) was 48 seconds, the 25% recovery time (from injection until T_4/T_1 recovered to 25%) was 51 minutes, and the 100% recovery time (from injection until T_4/T_1 recovered to 100%) was 65 minutes. Muscle relaxation was then maintained with intermittent intravenous injection of rocuronium (10 mg－20 mg) to a total dose of 90 mg. The hemodynamic parameters were stable during the whole procedure. Neuromuscular monitoring showed that the T_4/T_1 ratio had recovered to 100% at the end of operation. The patient waked up quickly after cessation of anesthesia and could raise his head and grasp forcefully. He was extubated and transferred to the surgical intensive care unit. He returned to the general ward on the following day. The pathological examination of the thymic mass confirmed the diagnosis of thymoma.

DISCUSSION

SPS was initially reported and named by Moersch and Woltman as a kind of neurological disease in 1956.[1,2] The pathogenesis of SPS remains unclear. In the 1980s, autoantibodies against glutamic acid decarboxylase (GAD-Ab) were identified in the plasma

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of most SPS patients.[3] Glutamic acid decarboxylase (GAD) is the rate-limiting enzyme for the synthesis of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter in the central nervous system. Conjugation of GAD-Ab and GAD decreases the production of GABA. Moreover, loss of inhibition from higher centers causes over-activity of the gamma motor neuron system and subsequent progressive muscle rigidity. Other autoantibodies, such as antiamphysin antibodies and antigephyrin antibodies, are later identified in the plasma of SPS patients.[4,5] For these reasons, SPS is commonly considered to be an autoimmune disease. Some SPS patients are complicated by non-neurological neoplasms and excisions of these neoplasms alleviate their symptoms. Therefore it is also classified to paraneoplastic neurological syndrome.[6,7] Benzodiazepines are the treatment of choice for SPS patients. They relieve symptoms in most patients and can then be discontinued gradually. Baclofen as an adjunctive therapy is used to improve effectiveness. Other treatments, such as immunodepressant (cyclophosphamide), glucocorticoids, large-dose intravenous immunoglobulin, and plasmapheresis have also been reported helpful.[1,2,6]

Several cases were reported about anesthetic management of patients with SPS. Johnson and Millar[8] reported a 46-year-old woman with SPS presented to the operating room for repair of an intrathecal baclofen pump. General anesthesia was accomplished with sufentanil, thiopental, isoflurane, and vecuronium. The patient developed prolonged hypotonia and was mechanically ventilated overnight. Five months later, the patient had the same operation under general anesthesia with midazolam and halothane without any muscle relaxant. She did not display any excessive weakness at the time of extubation. The authors recommended to avoid the use of non-depolarizing muscle relaxants in patients with SPS. In another case, a 62-year-old woman with SPS also developed prolonged muscle weakness after resection of a colon carcinoma under general anesthesia. Her preoperative medication included diazepam (7.5 mg, b.i.d) and baclophen (12.5 mg, b.i.d). General anesthetics included propofol, sufentanil, isoflurane (0.6% — 1.0%), morphine, and atracurium. At the end of the procedure, neuromuscular monitoring showed four strong twitches and the patient was responsive. But she could not open her eyes or grasp with either hand. Computer-simulated pharmacokinetic analysis excluded atracurium and opioids as the causes of weakness. The authors presumed that interaction between isoflurane and baclofen was perhaps the cause of prolonged muscle relaxation, since delayed muscle weakness was also described in a non-SPS patient receiving baclofen and undergoing anesthesia with isoflurane (1%).[9] Baclofen therapies (either intrathecal or oral) were administered before operation in the above two SPS cases.

However, prolonged hypotonicity after general anesthesia was not found in other case reports of SPS. A 40-year-old female patient with SPS underwent three times of general anesthesia for thymectomy, emergent appendectomy and endoscopic nasal sinus surgery, respectively. Anesthetics included diazepam, fentanyl, propofol, thiopental, nitrous oxide and isoflurane (0.4% — 1.5%). The patient regained 25% T_1 twitch 30 minutes after the initial dose of vecuronium. During the three procedures, the patient awakened soon after anesthesia without muscle weakness and was extubated successfully.[10] Another patient with SPS was a 60-year-old man, whose respiratory efforts were severely impaired by the rigidity of thoracic and abdominal muscles. He developed respiratory failure secondary to left lung collapse and needed invasive ventilation. General anesthesia (without isoflurane inhalation) was conducted two times to facilitate endotracheal intubation. Atracurium provided good intubating condition each time, but stiffness returned once the muscle relaxant effects had gone off and prolonged muscle weakness did not take place.[11] However, the authors did not mention if baclofen was used preoperatively for the treatment of SPS in these two patients.

In our case, the time of onset and recovery of rocuronium remained in the normal range. The preoperative medication included baclofen (30 mg/d), and isoflurane was inhaled during anesthesia. But the patient was extubated shortly after the operation and did not develop prolonged muscle weakness. This is perhaps because the concentration of inhaled isoflurane was very low (0.2%—0.4%), owing to the combined use of target-controlled infusion of remifentanil and inhalation of nitrous oxide for the maintenance of anesthesia. However, SPS is a

rarely occurring disease. It is still not clear why some patients with SPS developed prolonged hypotonicity after general anesthesia and if the phenomenon was related to the interaction of preoperative medication and intraoperative anesthetics. It is advisable that careful monitoring be carried out during anesthesia to secure the patients with SPS.

REFERENCES

1. Murinson BB. Stiff-person syndrome. Neurologist 2004; 10: 131-137.
2. Meinck HM, Thompson PD. Stiff man syndrome and related conditions. Mov Disord 2002; 17: 853-866.
3. Solimena M, Folli F, Aparisi R, Pozza G, De Camilli P. Autoantibodies to GABA-ergic neurons and pancreatic beta cells in stiff-man syndrome. N Engl J Med 1990; 322: 1555-1560.
4. Folli F, Solimena M, Cofiell R, Austoni M, Tallini G, Fassetta G, et al. Autoantibodies to a 128-kD synaptic protein in three women with the stiff-man syndrome and breast cancer. N Engl J Med 1993; 328: 546-551.
5. Butler MH, Hayashi A, Ohkoshi N, Villmann C, Becker CM, Feng G, et al. Autoimmunity to gephyrin in stiff-man syndrome. Neuron 2000; 26: 307-312.
6. Grisold W, Drlicek M, Liszka-Setinek U, Wondrusch E. Anti-tumour therapy in paraneoplastic disease. Clin Neurol Neurosurg 1995; 97: 106-111.
7. Rosin L, DeCamilli P, Butler M, Solimena M, Schmitt HP, Morgenthaler N, et al. Stiff-man syndrome in a woman with breast cancer: an uncommon central nervous system paraneoplastic syndrome. Neurology 1998; 50: 94-98.
8. Johnson JO, Miller KA. Anesthetic implications in stiff-person syndrome. Anesth Analg 1995; 80: 612-613.
9. Bouw J, Leendertse K, Tijssen MA, Dzoljic M. Stiff person syndrome and anesthesia: case report. Anesth Analg 2003; 97: 486-487.
10. Obara M, Sawamura S, Chinzei M, Komatsu K, Hanaoka K. Anaesthetic management of a patient with stiff-person syndrome. Anaesthesia 2002; 57: 511.
11. Haslam N, Price K. Anaesthesia for stiff-person syndrome. Anaesthesia 2002; 57: 298-299.

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