―**Reports on Experiments and Clinical Cases**―

Repeated propofol anesthesia for a patient with
a history of neuroleptic malignant syndrome

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Abstract

Neuroleptic malignant syndrome （NMS） is the most serious side effect produced by the administration of antipsychotic drugs. NMS shares many clinical similarities with malignant hyperthermia （MH）, but the etiology of NMS and the relation between NMS and MH remain unknown. Anesthetic regimens for patients with NMS are not well established.

We gave repeated anesthesia to a patient with a history of NMS undergoing electroconvulsive therapy for the treatment of depression. Propofol and vecuronium were used in twelve consecutive ECT sessions without complications. In this case report, we describe the safe and satisfactory repeated use of propofol in a patient with a history of NMS, and outline NMS and its questionable relation to MH. （J Nippon Med Sch 1999; 66: 262―265）

Key words: propofol, neuroleptic malignant syndrome, malignant hyperthermia

Introduction

Neuroleptic malignant syndrome （NMS） is uncommon, but it is the most serious of the acute neurological side effects CAN BE OMITTED！ of antipsychotic drugs. It has been reported in association with every commercial by available standard neuroleptic, and is believed to occur in 0.1～1.8%[1] of patients exposed to neuroleptics. The syndrome is characterized by hyperthermia, muscle rigidity, altered consciousness and autonomic instability, and many reports suggest common pathogenic mechanisms for NMS and malignant hyperthermia （MH）. Against this, several authors have recommended that known triggering agents of MH be avoided when anesthetizing a patient with or recovering from NMS[2]. For the present, the pathophysiology of NMS has not been fully elucidated, and anesthetic regimens for patients with this poorly understood NMS are not well established. This case report describes the repeated use of propofol in a patient with a history of NMS undergoing electroconvulsive therapy （ECT） for the treatment of depression.

Case report

A 57-yr-old man with a 6-yr history of involution melancholia with psychotic features was admitted through the outpatient clinic of neuropsychiatry with increasing depression, psychomotor retardation, and repeated suicide attempts of four weeks' duration. His medication on admission included clomipramine （75 mg daily）, amoxapine（75mg daily）, levomepromazine （25 mg daily） and alprazoram （2.4 mg daily）. His past medical history showed one significant previous hospitalization due to acute psychosis, which responded to various antipsychotic medications. He had never undergone general anesthesia, and had no personal or family history of malignant hyperthermia（MH）or other anesthetic-related problems.

On physical examination, the patient weighed 51.5 kg, had normal blood pressure and sinus tachycardia at 110 beats/min, and was afebrile at 36.0℃. Serum concentration of electrolytes, liver function tests, thyroid function test, serum glucose level and complete

blood count were all within normal limits. His chest radiograph was unremarkable. His electrocardiogram showed incomplete right branch bundle block, left axis deviation and sinus tachycardia.

After admission to the psychiatric ward, his dose of amoxapine, which had proved to be the most effective drug during his previous hospitalization, was increased to 150 mg/kg daily. On his 7th day of hospitalization, the patient's mental status deteriorated and he experienced increasing confusion and disorientation and showed extrapyramidal symptoms. He developed a fever of 39.3℃ with increased muscle tone on that night. Neuroleptic malignant syndrome（NMS） was suspected, and all psychotropic medications were discontinued. Over the next three days, his serum concentration of creatine phosphokinase（CPK）increased to 31,915 units/*l*. A diagnosis of NMS was made based on the patient's fever, rigidity, altered mental state, and elevated CPK. The onset of these signs and symptoms was temporally related to the use of neuroleptics and there was no organic pathology to explain his condition. Medical therapy for NMS was begun, including recommended doses of dantrolene（80～250 mg daily）and bromocriptine（5.0～12.5 mg daily）. There was an improvement in his condition and the CPK level returned to normal over the next 40 days. However, because of persistent psychosis and lack of suitable psychotropic medication, electroconvulsive therapy was scheduled.

The first and all subsequent ECT treatments were given in the recovery room with equipment and drugs to treat MH immediately available. An ECG, oscillometric blood pressure cuff, end-tidal CO_2 monitor, muscle relaxation monitor and rectal temperature probe were applied. Anesthesia was induced with 1.5 mg/kg propofol iv, followed by vecuronium bromide 5 mg and continuous infusion of propofol（2～4 mg/kg/hr for 30 min）. Before the administration of vecuronium bromide, a tourniquet applied to the upper arm was inflated to isolate the circulation to the arm and permit an accurate assessment of the motor seizure. After the intubation, the patient was ventilated with 50% oxygen and maintained normocapnea. A 7-second direct current electrical stimulation was delivered via bipolar electrodes placed bilaterally over the frontal regions, producing a 50-sec. motor seizure,

which was evaluated by the time from the ECT stimulus to cessation of tonic-clonic motor activity in the "isolated" arm. Spontaneous respiration resumed 25 min after the induction of anesthesia, and the patient was awake in 40 min. and extubated in 60 min. Reversal agents were not administered as the mechanographic train-of-four ratio exceeded 0.8 and a 50-Hz tetanus for five seconds induced a sustained contraction of the adductor pollicis muscle. There was a slight increase in arterial blood pressure with the ECT stimulus which returned to baseline after 5 min. There was no change in body temperature, arterial blood gases, serum potassium, or CPK during the perianesthetic period. The patient received ECT on ten subsequent occasions over the following 3 weeks. Propofol and vecuronium bromide were administered for each treatment without complications. The patient was discharged 4 weeks after ECT treatments with normal vital signs and improved mental status.

Discussion

ECT is an effective treatment for severe depression in patients who have not responded to pharmacotherapy[3], and is now used in patients who have chronic pain complicated by affective symptoms[4]. The advantages of administerting general anesthesia for electroconvulsive therapy are to provide the patient with a lack of awareness, to modify the motor effects of the seizure in order to prevent injury, and to produce rapid induction and recovery with minimal side effects. Among the many intravenous anesthetics, propofol is now widely used because of its characteristics of rapid emergence from anesthesia, minimal postoperative confusion[5], and a lower incidence of hypertension during the procedure of ECT[6]. However, there have been few reports about propofol anesthesia for patiens with NMS[7]. In our NMS patient, propofol anesthesia was selected for ECT treatment, because propofol is unlikely to trigger an episode of MH[8] and can be safely used in MH patients[9].

One more thing we have to consider in ECT procedurs is the use of muscle relaxants. In our case, succinylcholine was avoided as a muscle relaxant because it may increase the risk of triggering a MH crisis. Succinylcholine has traditionally been used as part of the

anesthetics for ECT because of the short nature of the procedure and the lack of a suitable non-depolarizing relaxant. There have been many reports of patients with NMS treated with ECT using succinylcholine who have shown no signs or symptoms of MH[10]. However, some succinylcholine-induced side effects have been reported, such as hyperkalemia[11] or cardiac arrest[12]. At present, it is still unknown whether succinylcholine increases the risk of triggering an MH crisis in NMS patients.

The etiology of NMS and the relation between NMS and MH remain unknown. In addition, the diagnostic criteria of NMS have not been standardized. Our patient was diagnosed as having NMS because he clearly met the criteria published by Levenson[13]. He demonstrated three of the major manifestations (fever, rigidity, elevated CPK level) plus six minor manifestations (tachycardia, abnormal blood pressure, tachypnea, altered consciousness, diaphoresis, leukocytosis). However, certain aspects of the definition of NMS remain controversial, and different diagnostic criteria have been suggested by different authors[14,15]. NMS shares many clinical similarities with MH, such as, fever, muscle rigidity, hypermetabolism, rhabdomyolysis, elevated serum CPK levels, and therapeutic response to dantrolene. Muscle biopsy specimens from several patients with a diagnosis of NMS have exhibited an abnormal response to halothane[16], but not from all[17]. Recently, Keck et al. reviewed the literature concerning NMS over the 14 years from 1980[18]. They proposed two primary hypotheses to explain the pathophysiology of NMS. The first suggests that NMS is produced by abrupt and extensive central dopamine receptor blockade by neuroleptics in the striatal and hypothalamic dopaminergic pathway. The second proposes that NMS, like MH, is the result of a preexisting defect in the skeletal muscle metabolism that is unmasked or provoked by neuroleptic exposure. Few recent reports have supported the second proposal, and Keck et al.[18] concluded that although NMS and MH are clinically similar, they are pharmacologically distinct, implying that cross-reactivity between triggering agents is unlikely to occur. In addition, a recent report which investigated the MH-susceptible skeletal muscle rayanodine receptor gene mutations in unrelated NMS patients, does not support the association between NMS and gene mutation associated with MH[19]. Clinically, however, many kinds of anesthetics have been used for NMS patients, and some symptoms including fever and an increase in CPK are still reported[20]. More clinical and laboratory investigations will be necessary to resolve this issue.

Anesthetic regimens for patients with the poorly understood NMS are not well established. In this case report, NMS and its questionable relation to MH are discussed. The safe and satisfactory repeated use of propofol in a patient with NMS is presented.

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