

Electroconvulsive therapy in Neuroleptic malignant syndrome

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Chanpattana W. Electroconvulsive therapy in neuroleptic malignant syndrome. Chula Med J 1993 Apr; 37(4) : 259-262

This report is one case of schizophreniform disorder who upon treatment with haloperidol (30 mg per day), developed neuroleptic malignant syndrome (NMS). All medications were withdrawn, bromocriptine was instituted and gradually increased to 40 mg per day. At this time the patient's condition deteriorated so electroconvulsive therapy (ECT) was started. After the first course of ECT, the temperature went down and blood pressure became stable. Other clinical features of NMS disappeared after the sixth ECT treatment.

Possible mechanisms of ECT's action are discussed together with the pathogenesis of NMS.

Key words : *Electroconvulsive therapy, Neuroleptic malignant syndrome.*

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Received for publication. June 26, 1992.

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วรรณ จันทร์พัฒนา. การรักษาด้วยการช็อคไฟฟ้าในนิวโรเลปติก มาลิกแนนท์ ซินโดรม. จุฬาลงกรณ์เวชสาร 2536 เมษายน; 37(4): 259-262

ผู้ป่วยโรคจิตได้รับการรักษาด้วย haloperidol วันละ 30 มิลลิกรัม เกิดอาการนิวโรเลปติก มาลิกแนนท์ ซินโดรม ขึ้นในวันที่ 13 ของการรักษา ได้หยุดยาทุกชนิด ให้การรักษาประคับประคองและให้ bromocriptine อาการของผู้ป่วยไม่ดีขึ้นแม้ได้รับ bromocriptine ถึง 40 มิลลิกรัมต่อวัน และเกิดมี โรคแทรกซ้อนขึ้น จึงให้การรักษาด้วยการช็อคไฟฟ้า ไข้ลดลงและความดันโลหิตปกติ หลังการรักษาครั้งแรก เมื่อให้การรักษาครบ 6 ครั้ง อาการทั้งหมดหายไป

ได้ทบทวนวารสารกลไกการออกฤทธิ์ของการรักษาด้วยการช็อคไฟฟ้า และพยากรณ์ของนิวโรเลปติก มาลิกแนนท์ ซินโดรม.

Neuroleptic malignant syndrome (NMS) is undoubtedly an underdiagnosed but potentially lethal consequence of neuroleptic treatment. Its cardinal features are hyperthermia, severe extrapyramidal symptoms, altered consciousness and autonomic dysfunction. Delay et al. first described NMS in 1960;⁽¹⁾ since then more than 500 cases have been reported in the literature. From prospective studies, the incidence is between 0.02-0.9 % and retrospectively between 0.5-2.4 % although the true incidence is believed to be higher.⁽²⁾ Conventional treatment consists of immediate withdrawal of neuroleptic medication, supportive measures, and the administration of dopamine agonists and muscle relaxants

This report describes a patient admitted because of catatonia. Upon neuroleptic treatment, the patient developed NMS; standard treatment had failed to improve the clinical conditions so electroconvulsive therapy (ECT) was started.

Case report

Miss A, a 22-year-old woman, was referred to the Psychiatric Department of Vajira Hospital on Dec 6, 1990 following behavioral and mood disturbance suggestive of schizophreniform disorder. There was no history of taking neuroleptic medication. On admission, the patient was mute and inattentive to any relevant stimuli. She demonstrated waxy flexibility and was dehydrated, normotensive, with mild tachycardia. Laboratory investigations, including complete blood count, urine analysis, electrolytes, blood urea nitrogen, creatinine, liver and thyroid function tests, chest x-ray and electroencephalogram, were all normal. Diazepam (20 mg intravenously) could break down all catatonic symptoms hence haloperidol (30 mg per day) and lorazepam (4 mg per day) in divided doses were prescribed. Her psychotic symptoms were markedly improved.

On the thirteenth day of admission her temperature suddenly rose to 39.2 °C, blood pressure swung between 140/60 and 80/60 mmHg, respiration rose to 36 beats/min, and pulse rate varied between 70 and 166 beats/min. She became mute, with lead pipe and cogwheel rigidity, tremulous, hyperreflexia, marked diaphoresis, and incontinence of urine and feces. Abnormal laboratory results included a white cell count of 12,500/mm³ with neutrophilia, creatine kinase (CPK) 1,203 IU/l (normal < 195), serum glutamate transaminase 71 IU/l (normal < 40). Chest x-ray, lumbar puncture and computed tomographic (CT) brain scan were normal; urine and blood cultures were sterile and there was no demonstrable myoglobinuria. Since these clinical features occurred following neuroleptic treatment, NMS was diagnosed.

All medications were withdrawn and nasogastric bromocriptine (7.5 mg/day) was started in addition to cooling and rehydration. Bromocriptine dosage was in-

creased to 20 mg and 40 mg during the second and third day, respectively. Despite these medical interventions, her condition deteriorated further and was complicated by urinary tract infection and unexplained diarrhoea. In view of her progressive catatonia and medical complications, electroconvulsive therapy (ECT) was administered every other day under general anesthesia using thiopentone and succinyl choline on the twenty-fourth hospital day. After the first course of ECT, temperature went down to 37.3 °C, blood pressure became stable (110/70-120/80 mmHg). There was gradual improvement in rigidity and mutism, CPK levels dropped to normal by the fifth treatment. After receiving six ECTs, she was afebrile, ambulatory and communicable; she was able to resume oral feeding. Bromocriptine was tapered off and there was no recurrence of NMS.

Thioridazine (200 mg) was reinstated on the forty-sixth day in hospital in order to control her residual psychotic symptoms. Her behaviour gradually improved and she was discharged from the hospital on the sixtieth day. She could go back to work and, at one-year follow up she still appeared normal; she was taking thioridazine (200 mg/day).

Discussion

There are many medications that could stop the catatonic symptoms including intravenous diazepam⁽³⁾ and oral lorazepam⁽⁴⁾ as in this case. The possible mechanism of the medications might be potentiation of the gamma-aminobutyric acid (GABA) system.⁽⁵⁾ The characteristic features of NMS include the sudden development of symptoms on the thirteenth day following neuroleptic administration, which accounts for 66 % of cases⁽⁶⁾ of NMS. Although the bromocriptine dosage could be increased to 60 mg,⁽⁷⁾ her medical condition deteriorated further so that ECT was introduced on the eleventh day of treating NMS. This is the twentieth case report in the English-language literature concerning the successful use of ECT in NMS.

There is limited knowledge about the use of ECT in the treatment of NMS; in major reviews of NMS, it is ignored as a potential therapy. In order to understand the mechanism of the therapeutic action of ECT, it is necessary to know the pathogenesis of NMS thoroughly.

All neuroleptics block dopamine receptors in the central nervous system (CNS). Blockade of dopamine in the preoptic anterior hypothalamus could result in disruption of core temperature regulation and fever.⁽⁸⁾ Blockade of striatal dopamine receptor is a well-known cause of rigidity. Blockade in the thoracolumbar sympathetic trunk could cause autonomic dysfunction.⁽⁹⁾ Blockade of the mesocortical and mesolimbic pathway could account for mental status changes.⁽¹⁰⁾ Neurotransmitters other than dopamine have been implicated in the pathophysiology of NMS, particularly

GABA⁽¹¹⁾ and serotonin.⁽¹²⁾

Electroconvulsive therapy has been reported to result in increased dopaminergic function in CNS,⁽¹³⁾ possibly via increased postsynaptic dopamine receptor sensitivity⁽¹⁴⁾ or decreased presynaptic dopamine receptor density.⁽¹⁵⁾ ECT could produce a functional increase in GABA ergic activity⁽¹⁶⁾ so that imbalance in the dopamine-GABA system, that is postulated in the pathogenesis of NMS, would then be alleviated. There is some evidence that ECT results in increased 5-hydroxytryptamine-2 (5HT₂) receptor numbers;⁽¹⁶⁾ therefore, it is fairly certain that ECT produces increased serotonergic function which could counteract the condition of serotonergic hypoactivity in NMS.

In this case, ECT was introduced because of the clinical deterioration which resulted from prolonged immobility and high fever, and after conventional treatment had failed to improve the condition. A dramatic reduction of fever and stable blood pressure were observed after the first ECT treatment. This clinical improvement occurred in the same fashion as the previous case reports.^(13,17,18) ECT should be considered as an alternative treatment for NMS, especially in cases of prolonged and refractory NMS.

Summary

A patient with schizophreniform disorder who developed neuroleptic malignant syndrome on the thirteenth day of neuroleptic treatment is reported. Because conventional treatment failed to improve her clinical condition, electroconvulsive therapy was introduced: it resulted in an excellent clinical response. The pathogenesis of NMS and possible mechanism of ECT's action are discussed.

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