Severe Catatonia and Neuroleptic Malignant Syndrome: Report of 3 Cases

DUANGJAI KASANTIKUL, M.D.*,
PHACHARAWUT KANCHANANAKHIN, M.D.*

Abstract

Catatonia is a syndrome characterized by motor rigidity or stupor, negativism, mutism and inappropriate or bizarre posture. Without proper management, patients may have significant morbidity and mortality from stupor, coma and death (lethal or malignant catatonia).

Neuroleptic malignant syndrome (NMS) is characterized by a sudden appearance of motor rigidity, fever, autonomic effect, increased white blood cell count, serum creatinine phosphokinase, liver enzymes, and myoglobin. The mortality rate is 15 per cent to 25 per cent or even higher when depot form of neuroleptic is used. We report a patient with severe catatonia and two cases of NMS. Death was encountered with one of the latter.

Key word : Catatonia, Neuroleptic Malignant Syndrome

Catatonia is a syndrome characterized by motor rigidity or stupor, negativism, mutism and inappropriate or bizarre posture. Two of these symptoms are sufficient for the diagnosis of this syndrome[1,2]. Nakane found only 1.9 per cent among Japanese patients with schizophrenia, whereas, the hebephrenic type contributes to 48.5 per cent[3]. Psychiatric and medical catatonia are frequently indistinguishable at clinical presentation. Patients with catatonia often improve with immediate and adequate treatment. Without proper management, patients may have significant morbidity and mortality from stupor, coma and death (lethal or malignant catatonia)[1,2,4,5].

In the diagnostic and statistical manual of mental disorders -4 (DSM-IV)[6], catatonia is defined as a subtype of schizophrenia, nevertheless, it is often seen in mania, depression, and various medical and neurological conditions which include neuroleptic (antipsychotic)-induced catatonia, akinetic mutism (lesion at the anterior cingulate prefrontal cortex, large frontal lobe injuries), stroke, encephalitis, SLE, drug toxicity and withdrawal, degenerative diseases, and metabolic disorders such

*Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

as hyponatremia[4,5,7]. These conditions must be treated aggressively and properly.

Neuroleptic malignant syndrome (NMS) should be considered in the differential diagnosis of any case of acute catatonia[8-11]. It is characterized by sudden appearance of motor rigidity, fever and autonomic effects such as increased pulse and blood pressure. Laboratory findings include increased white blood cell count, serum creatinine phosphokinase, liver enzymes, and myoglobin. Symptoms usually evolve over 1 to 3 days, with the untreated syndrome lasting for 10 to 14 days. The mortality rate is 15 per cent to 25 per cent or even higher when a depot form of neuroleptic drug is used. NMS has become the most serious and life threatening complication of antipsychotic treatment. Many experts believe it to be a drug-induced variant of catatonia[12-14]. We wish to report a patient with severe catatonia and two cases of NMS. Death was encountered with one of the latter.

Case 1.

A 39-year-old, married, Thai housewife was brought to the emergency room (ER) after having remained immobile in her bed for 10 days. Two weeks prior to admission she had become very upset and agitated after having a fight with her husband about his affair. Then she became manic i.e., hyperactive, talkative and spending her money extravagantly. She refused to sleep or eat and was irritable and aggressive. She also made several inappropriate phone calls late at night and sometimes walked around the house naked. Her manic episodes lasted for a week and remitted after haloperidol, 10 mg/d orally, was prescribed for only one day. It was discontinued as she started to calm down. Then she became quiet, lying still in bed and refused to eat. A few days later her condition became worse, she did not even utter a word or show any emotion when she was brought to the ER. The history revealed that she had had bipolar disorders since, giving birth 14 years ago. She always had similar manic symptoms every year, however, she refused to take any medication during her symptom-free period. She had never had any catatonic or depressive episodes before. She had always been healthy with no history of chronic medical illness. Examination on admission revealed a body temperature of 38°C, blood pressure of 100/70 mmHg and pulse rate of 120/minute, regular. She was cachectic, with poor skin turgor. There was a 6 cm x 2 cm deep infected sacral bedsore covered with pus. Neurological examination was normal. She showed restricted affect, lying still with staring eyes. She was mute and did not respond to command. Poor hygienic care was obvious. She exhibited no rigidity or resitance to movement. Laboratory data including CBC, UA, BUN/Cr, serum electrolytes, thyroid function test, liver function test, EEG, computerized scan of the brain, lumbar puncture and urine drug screen were unremarkable. The diagnosis was bipolar disorder, and severe catatonia. The catatonic symptom subsided gradually within two weeks with monitered multiple electroconvulsive therapy (MMECT) for 9 sessions as well as correction of her dehydration and deep bed sore. She also received lithium carbonate, 900 mg/day, risperidone, 2 mg/day, lorazepam, 1 mg tid, and was discharged after 4 weeks hospitalization. She was doing well when seen one year later and was maintained only on lithium carbonate, 900 mg/day.

Case 2

A 25-year-old, single, Thai man who had a 5 – year history of thyrotoxicosis with irregular treatment. On November 7th, 1998 he was brought to a mental hospital because of "psychosis" and received haloperidol 5 mg I.M, fluphenazine decanoate (depot), 50 mg I.M, and was sent home the same day with chropromazine, 200 mg h.s, and artane (trihexyphenidyl), 2 mg tid. A week later he was admitted to the medical unit of Chulalongkorn Hospital due to fatigue, restlessness, muscle rigidity, exopthalmos and moist skin. Grave's disease was the diagnosis (T4 = 24/μg/dl, T3 = 787/ng/dl, TSH = 0.05/μ/u/ml, Wbc 8100/mm^3 with N 47,% L32%). Thus, I 131 15 mci and PTU were given to him. A few days later, the patient developed extrapyramidal symptoms (EPS) i.e. occulogyric crisis, slurred speech and dystonia, then cogentin –benztropine (1 mg) was administered. However, he was readmitted on December 8th with high fever (39°C) muscle rigidity and drowsiness. He appeared restless, with tachypnea, tachycardia and moist skin. His blood pressure fluctuated from 130/80 mmHg to 180/105 mmHg and his pulse rate was 100 beats/minute. Laboratory data revealed a white cell count of 19,900/mm^3 with 90 per cent neutrophiles, serum creatinine phosphokinase (CPK) was 3350 IU/L and 5420 IU/L a week later. Urine tests for phenothiazine and amphetamine were negative. The diagnosis was felt to be radiation thyroiditis superimposed by

NMS and infection. Thus atenolol 50 mg/d, dexamethazone, clonazepam bromocriptine and antibiotics were administered. The patient, however, continued to have autonomic instability, muscle rigidity and confusion. After psychiatric evaluation, the clinical diagnosis of NMS was rendered. Cogentin and lorazepam were administered in addition to an increased dosage of bromocriptine. The muscle rigidity improved on the next day. He did well and was sent home a week later.

Case 3

A 56-year-old, obese, single, Thai woman, living alone, had been diagnosed with bipolar disorder for the past 15 years. She had had several psychiatric hospitalizations due to her poor drug compliance. Her recent admission was for her wandering behavior and grandiose delusions. She received haldoperidol decanoate, 100 mg 1.M monthly, twice during this hospitalization. Other medications were haldol, 10 mg 1.M, clopixol acuphase, 100 mg 1.M, and lithium carbonate, 900 mg/d (blood level = 0.8 mEg/L), artane, 6 mg/day, haldol, 20 mg/d. She also received glibenclamide (daonil) 10 mg/day and gemfibrozil (lopid), 1200 mg/day for her well controlled diabetes and dyslipidemia which she had been suffering from for 2 years. She was discharged in good condition. Her home medications were lithium, 1200 mg/day, artane, 6 mg/day, and haldol, 10 mg/d. Six days later she was brought back to the ER with high fever (38.5°C), muscle rigidity and semiconsciousness. Her heart rate was 120 beats/minute, blood pressure of 160/100 mmHg, respiratory rate 28/minute. Her skin was warm and moist. Marked muscle fasciculations were noted in all extremities. There were no neurological deficits except for hyperreflexia (3+) of both knees.

Laboratory investigations including CT scan of the brain, EKG, thyroid function test were unremarkable. Her blood parameters were Hb 13.8 g/dL, Hct 39.8 per cent, Wbc 9700/mm^3, FBS 240 mg/dL, BUN 31 mg/dL, Cr 1.0 mg/dL, alkaline phosphatase 536 U/L, SGOT 60 U/L, SGOT 59 U/L, cholesterol 195 mg/dL, triglycerides 315 mg/dL. Urine analysis showed protein 2+. Blood lithium level was 2.45 mEq/L (normal = 8.0 – 1.5 mEq/L). The patient was diagnosed with NMS superimposed on lithium toxicity and diabetes. Diazepam, 10 mg 1.V q 6 hours, bromocriptine, 5 mg QID, benztropine, 2 mg QID, and baclofen, 2.5 mg tid per NG tube feeding were given to her, as well as correction of dehydration and lithium toxicity. Nevertheless, the patient progressed towards urinary tract infection, pneumonia, and worsening of renal function with subsequent septic shock. She died 12 days after hospitalization. The autopsy was not permitted.

DISCUSSION

Functional catatonia, if left untreated, may progress to turn malignant or lethal, in which case electro-convulsive therapy (ECT) should be considered as the first-line treatment. Lorazepam, clonazepam and diazepam induce temporary remission of catatonic symptoms. Benzodiazepine (BDP) is usually considered diagnostic because catatonic symptoms will return when the drug's therapeutic effects wane[5]. However, Rosebush et al[15] reported five elderly patients who became catatonic when tapering off BDP (2 to 7 days) after having taken it for 6 months to 15 years. All patients were acutely immobile, mute, rigid and refused or were unable to eat or drink. Thus, life threatening catatonia can develop after BDP withdrawal, particularly in older individuals. It is possible that at least some of the cases of catatonia reported in association with various medical conditions may have been secondary to unrecognized BDP withdrawal which was precipitated by hospital admission. Approximately 80 per cent of patients with catatonia respond dramatically to lorazepam, 2-6 mg/day, within a few hours.

Orally or intra-muscularly administered neuroleptic drugs, especially high-potency ones, may also cause a syndrome strikingly similar to catatonic stupor. Symptoms include withdrawal, mutism, and a variety of neuromuscular and extrapyramidal symptoms (e.g., bizarre posturing, rigidity, immobility, and catalepsy). Catatonia as a side effect of neuroleptics is now seen more often than catatonic schizophrenia because the latter is relatively uncommon. Moreover, neuroleptic-induced catatonia may be life-threatening. The drug should be presumed responsible for catatonic symptoms that appear or worsen shortly after initiation of neuroleptic therapy. The neuroleptics should be discontinued immediately. Although catatonic symptoms may persist because of the long elimination half-life of neuroleptics, symptoms usually resolve within several days to a few weeks. However, progressive medical complications may develop that may be irreversible or fatal despite intensive treatment as seen in our patient (cases 3).

Neuroleptic malignant syndrome (NMS) should also be considered as a differential diagnosis of any patient suffering from acute catatonia. Wae-Alee and Tanchaiswad, reported 12 cases of NMS (4 women, 8 men, age range 15-69 years) found in Songklanagarind Hospital during 1987-1994[16]. All cases exhibited fever, muscle rigidity, autonomic disturbances and alterations of consciousness with high CPK levels. Ten patients developed NMS after starting or changing the dosage of antipsychotics, two after antidepressants. The complications were acute renal failure (2 cases), pneumonia (3 cases) and urinary tract infection in 1 case. However, all patients recovered without any serious sequelae with only supportive treatment. Bromocriptine was administered to only 4 cases and diazepam to the other two. Atypical neuroleptic drugs, such as clozapine, risperidone are not expected to cause dystonia or NMS. Since its introduction, nevertheless, there have been more cases of risperidone or clozapine – associated NMS[17,18] including one occurring in the absence of muscular rigidity, the other with a normal CPK level.

In this study our patient (case 2) with NMS had underlying radiation thyroiditis. Another patient (case 3) suffered from DM, dyslipidemia and lithium toxicity which is believed to have enhanced dopamine metabolism and aggravate the NMS in this elderly woman. The mechanism of NMS is presumed to be a striatal dopamine receptor blockade resulting in a severe hypodopaminergic state[19]. Therefore, the most appropiate treatment is to reverse the disease by discontinuation of antipsychotic drugs and administration of bromocriptine (dopamine agonist) 5.0 to 7.5 mg tid daily, or dantrolene sodium (peripheral skeletal muscle relaxant-unavailable in Thailand), as well as supportive measures. The course of treatment usually persists for 5-10 days. Anticholinergic drugs such as cogentin (benztropine) or artane (trihexyphenidyl) may relieve muscle rigidity, nevertheless, they infrequently aggravate the associated hyperthermia and tachycardia. BDP i.e. lorazepam is also recommended in order to control "agitated" patients with NMS.

ACKNOWLEDGEMENT

The authors wish to thank Miss. Araya Suwannarit, Miss. Ratiya Buthranasiri and Ms. Petra Hirsch for preparing the manuscript.

(Received for publication on March 31, 1999)

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คาทาโทเนียรุนแรงและกลุ่มอาการนิวโรเล็พติค มาลิกแนนท์ : รายงานผู้ป่วย 3 ราย

ดวงใจ กสานติกุล, พ.บ., พัชรวุฒิ กาญจนนาคินทร์**

คาทาโทเนียเป็นกลุ่มอาการที่ผู้ป่วยมีอาการเกร็งตัวอยู่ท่าเดียวนาน ๆ เหมือนไม่รู้สึกตัว ไม่พูดไม่ตอบสนองต่อสิ่งเร้า ขัดขืนการเคลื่อนไหว อาจอยู่ในท่าแปลก ๆ นาน ๆ ไม่รับประทานอาหาร พบได้ในโรคทางกายต่าง ๆ และโรคทางจิตเวช เช่น เมเนีย ซึมเศร้า และจิตเภท รายที่รุนแรงอาจจำเป็นต้องรักษาด้วยไฟฟ้า

NMS เป็นกลุ่มอาการที่คล้าย ๆ คาทาโทเนียแต่จะมีไข้สูง กล้ามเนื้อแข็งเกร็ง ซึมหรือกระวนกระวาย ประสาทอัตโนมัติแปรปรวน ตรวจทางห้องปฏิบัติการจะมีการเพิ่มขึ้นของจำนวนเม็ดเลือดขาว serum creatinine phosphokinase และ myoglobin หลายท่านเชื่อว่าเป็นคาทาโทเนียที่มีสาเหตุจากยาด้านโรคจิต โดยเฉพาะยาฉีดฤทธิ์ยาว มีอัตราการตายสูงถึง 15–20%

ได้รายงานผู้ป่วยคาทาโทเนียรุนแรง 1 ราย และ NMS 2 ราย ซึ่ง 1 ราย เสียชีวิต

คำสำคัญ : คาทาโทเนีย, กลุ่มอาการนิวโรเล็พติค มาลิกแนนท์

* ภาควิชาจิตเวชศาสตร์, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330