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Neuroleptic Malignant Syndrome Following a Withdrawal of Levodopa

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Neuroleptic malignant syndrome is a serious complication of levodopa withdrawal in patients with Parkinson's disease. We report a patient with advanced parkinsonism who developed neuroleptic malignant syndrome in setting of withdrawal of levodopa intake.

Key Words: Neuroleptic malignant syndrome, Levodopa

Neuroleptic malignant syndrome(NMS) is potentially fatal disorder characterized by hyperthermia, rigidity, altered mentation and autonomic instability.[1] Recognition of this condition is essential because its complications are potentially leathal, leading to death in 20% of patients.[6] Often associated with the use of high-potency neuroleptics, it can also occur with the newer atypical neuroleptics. NMS has also been reported to occur in the setting of antiparkinsonian medication withdrawal in patients with parkinsonism who have not been exposed to neuroleptics.

We report a patient with advanced parkinsonism who developed NMS during in setting of medication withdrawal.

Case report

A 67-year-old man was hospitalized for the insomnia and confused mentality for several days. He has been followed at our hospital with a 15-year history of Parkinson's disease and his medications were 600mg of levodopa, 15mg of bromocriptine, 600mg of entacapone and 6mg of biperiden per day for parkinsonism, 20mg of paroxetine for depression. He did not take any other medication, and there had been no changes in medication for 8 months. He was slightly dependent in most daily activity, but require constant supervision to confusion and memory loss. Physical examination on admission revealed a body temperature of 37.8℃ and blood pressure and pulse rate is within normal ranges. He suffered from insomnia for 1 weeks, and he revealed confused mentality and intermittent visual hallucinations.

After admission, we prescribed 1mg of risperidone per day for control of delirium.

He did not eat well because of the delirious mentality, and did not take his medication constantly. On the fifth day of hospitalization, he was noted to be perspiring profusely, tachypneic and extremely stiff, and he became drowsy. The body temperature is 39℃, and there were fluctuation in blood pressure. The white blood cell count was 13,000 and myoglobin was 335 ng/ml and CK-MB was 14.20 IU/L. He was treated with bromocriptine and dantrolene, intravenous hydration, empiric antibiotics, but extreme stiff-

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ness and perspiration were not improved. The day after his symptom onset, we started the 300mg per day of levodopa. On day 7 of his admission, he was more alert, less rigid and followed simple demand. Repeat myoglobin and CK-MB on day 8 were normalized. The levodopa was increased at the previous dosage, the generalized hypertonia was gradually subsided and he became more mobile over the next day.

Discussion

Neuroleptic malignant syndrome (NMS) is a fatal, uncommom condition characterized by hyperthermia, rigidity, altered mentation and autonomic instability.[1]

No definition is universally accepted for diagnosis of NMS and rest on clinical criteria, supportive laboratory test, and the exclusion of other potential diagnosis.

Research criteria for diagnosing NMS from the fourth edition of the Diagnotic and Statistical Manual of Mental Disorders require severe rigidity and fever accompanied by 2 of 10 minor features including diaphoresis, dysphagia, tremor, incontinence, altered mentation, mutism, tachycardia, elevated or labile blood pressure, leukocytosis, and elevated creatine phosphokinase.[2] The diagnosis of NMS requires exposure to a dopamine receptor blocking drug, however, this syndrome has been reported in Parkinson's disease patients, never exposure to neuroleptics, whose levodopa medication have been abruptly withdrawan, but reduction in any parkinson disease medication was also belived to be causal.[3,4] In Parkinson's disease patients, the most common sign was fever followed by altered mental state, and then worsening of motor function.

Initially, we considered the possibility of risperidone induced NMS, and so that medication was stopped. Caroff et al reviewed NMS associated with atypical antipsychotics. They concluded that NMS associated with the use of atypical antipsychotics may present with less dramatic elevations of temperature, rigidity, or tremors than cases associated with typical agents.[5] In our patient, the elevation of temperature and rigidity were prominent, and symptoms did not improved by stopping this agent.

We also considered the possibility of serotonin syndrome, but this syndrome typically develops within hours or days of the addition of new serotomimetic agent or changes in dose.[6,7] Our patient had symptoms similar to those reported for serotonin syndrome, but he was taking paroxetine for several years, and its dose had not been changed recently. While we cannot exclude risperidone induced NMS or serotonin syndrome as a cause for our patient's symptoms, his clinical presentation was not classical for either, and the rapid response and sensitivity to levodopa makes NMS from levodopa withdrawal more likely.

The pathogensis of NMS is unknown but it is thought to be related to dysregulation of the dopaminergic system.[6] It is assumed to be due to a functional dopamine deficiency state, and may occur due to dopamine receptor blockade or dopamin withdrawal. When levodopa is used in parkinsonism, there is an iatrogenic increase in dopaminergic transmission. In this setting, NMS may occur following a sudden decrease in the dosage of levodopa.[6]

The treatment of NMS includes removal of the offending agents, close observation, and supportive care with hydration and fever control. Drug treatment of NMS is controversial. Several reports describe the benefit of dantrolene, bromocriptine, dantrolene and bromocriptine together, lisuride, and electroconvulsive therapy. In Parkinson's disease patients, recommends that the medication reduction which cause the malignant syndrome be restored, and that bromocriptine or levodopa, and that intravenous dantrolene considered.

The timely diagnosis and appropriate treatment of NMS can be life-saving. Therefore, it is critical that the entire spectrum of causes of this syndrome be appreciated, including withdrawal, reduction, or alteration of dopaminergic therapy.

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