

Dementia with Lewy Bodies : A Case Report

Chien-Chi Hsu, Yi-Wen Sun, and Shih-Jung Cheng*

Department of Psychiatry, *Neurology Mackay Memorial Hospital, Taipei

Abstract

Current clinical classifications do not contain diagnostic categories for patients with dementia with Lewy bodies (DLB), and Taiwan lacks research of similar cases. We report a classic case of DLB, discuss its symptoms, diagnosis, clinical course and treatment, and review the literature.

A 78-year-old female suffered from memory impairment since one year ago. The impression at that time was Alzheimer's disease (AD). Six months later, she began to have psychotic symptoms. She exhibited severe neuroleptic sensitivity along with cognitive deteriorations despite trials with different atypical antipsychotics and her psychosis persisted. She had no history of stroke or psychosis, and her laboratory exams did not explain her clinical symptoms. However, her clinical symptoms fulfill the consensus criteria for clinical diagnosis of DLB.

DLB is often misdiagnosed as AD. They have early neuropsychiatric symptoms leading to evaluation and treatment at medical facilities. When presented with such cases, we must consider the possible diagnosis of DLB, and the danger of using antipsychotics , in order to provide safer treatment strategies to them. (J Intern Med Taiwan 2003;14: 42-46)

Key Words : Dementia with Lewy bodies (DLB), Alzheimer's disease(AD), Neuroleptic sensitivity

Introduction

Lewy bodies (LBs), are spherical, eosinophilic, intracytoplasmic neuronal inclusions that were first discovered between 1910 and 1912 by German neuropathologist Friedrich Lewy in the brainstem of a Parkinson's disease (PD) patient. LBs were understood to be limited to the neuropathological change seen in PD, until a report indicating possible link between LBs and dementia appeared in 1961¹. Although numerous similar cases were reported over the next 20 years, there were no significant findings. This was because cortical LBs do not exhibit the classic characteristics of

brainstem LBs when traditional pathological staining methods were used, therefore the association between cortical LBs and dementia was not noted. Towards the end of the 1980's, following improvement of pathological staining methods, the relationship between cortical LBs and dementia was once again taken into attention. Various names were proposed, including dementia with Lewy bodies (DLB), Lewy body dementia, diffuse Lewy body disease, senile dementia of Lewy body type, and Lewy body variant of Alzheimer's disease. These studies indicate that such cases account for 15% to 25% of clinical dementia, thus making it the second most common degenerative dementia after Alzheimer's disease(AD) 2. Currently, however, its diagnosis has not yet to be formally classified (DSM-IV & ICD-10), and Taiwan lacks research of similar cases. We report a classic case of DLB, discuss its symptoms, diagnosis, clinical course and treatment, and review the literature.

Case Report

The patient is a 78-year-old female who was physically able to work as a farmer 2 years ago. She was healthy and did not have any significant family psychiatric history. One year ago, she began to suffer episodes of memory loss and insomnia, and sought medical treatment at our neurological clinic. Laboratory data included normal serum chemistry levels, electroencephalography (EEG) study with steady and generalized theta wave, and brain computed tomography (CT) scan with mild brain atrophy. The single photon emission computed tomography with technetium-99m-d,l-hexamethylpropyleneamine oxime(99m TC-HMPAO SPECT) scan showed evidence of hypoperfusion within the bila-teral dorsolateral frontal, temporal, inferior parietal and left superior parietal cortices. The medical impression at that time was AD. She was treated with dihydroergotamine mesylate & donepezil but did not return regularly for follow-up visits. Six months la-ter, she began to have persecutory delusions, visual hallucinations (appeared obviously frightened from seeing non-existent snakes), incidents of delusional misidentification with television characters and her family members, and acts of violence. She was brought to the psychiatric clinic for evaluation, diagnosed with senile dementia with psychotic feature, and prescribed with low dose antipsychotic agents, including risperidone(0.5 mg/day), which was later changed to haloperidol(0.5mg/day). However, the psychosis did not improve and she exhibited evidence of acute dystonia, akathisia, bradykinesia, syncope and repeated falls. The patient was therefore admitted to the hospital for further treatment.

Upon admission, mental status exams revealed that she had limited speech and was not well oriented. Neurological exam only revealed signs of apparent Parkinsonism but no other neurological signs. Biochemical blood tests were within normal limits,

and EEG, Brain CT and 99m TC-HMPAO SPECT results were unchanged. The possibility that drug-induced Parkinsonism was causing the patient's condition to worsen was considered; she was therefore treated with amantadine (200mg/day), and switched to another antipsychotic drug olanzapine (5 mg/day). However, her psychosis and Parkinsonism persisted. It was not until olanzapine was replaced with quetiapine (25mg /day) that she showed slight improvement of her Parkinsonism, with increased speech and activity level, and better mental orientation. Since her behavioral problems improved, the patient was discharged and followed by outpatient treatment.

After her discharge from the hospital, she had no apparent behavioral problems. She was able to tend to her own living, although at a slower pace. She still experienced apparent visual hallucinations and had a tendency to fall spontaneously. Several weeks later, she exhibited severe Parkinsonism, could not feed or take care of herself, and was readmitted to the hospital. Her clinical symptoms and exams were similar to those of her previous admission. She was mainly treated with quetiapine (25mg /day) and amantadine (300mg/day). Her clinical course, inpatient observations and exams, and neurological consultation were consistent with the diagnosis of DLB. However the patient did not show any apparent reaction to drug therapy, and she did not return to the hospital for re-regular follow-up.

Discussion

In studies with confirmed pathological diagnosis, the following clinical features of DLB were noted: (1) apparent Parkinsonian features or neuroleptics-induced Parkinsonism; (2) fluctuating cognitive symptoms (mostly from day to days or weeks, not fluctuations within 24 hours); (3) psychotic symptoms of delusional misidentification, delusion and hallucinations; (4) recurrent falls and syncope 3-7. Consensus guidelines for the clinical and pathologic diagnosis of DLB were then proposed by the International Workshop of the Consortium on DLB in 1996 and 1999 2, 8. When studies focused on the diagnostic accuracy of the consensus clinical criteria in cases with autopsy confirmed diagnosis were reviewed, we found the specificity to be 0.9~1.0, and sensitivity to be 0.22~0.83 9-12. The consensus clinical criteria, as McKeith et al indicated, could be used for the diagnoses and confirmation, but not for the screening, of DLB 8, 12-13.

Based on the consensus guidelines for clinical diagnosis of DLB, this patient's apparent memory loss, with progressive cognitive decline that interfered with her daily living functions, already conforms to the clinical representation of dementia. Furthermore, she had persistent visual hallucinations and often displayed marked fluctuations in her cognition with pronounced variation in alertness. She also had

unusual reaction to low-dose neuroleptics that lead to severe Parkinsonism, with repetitive falls and syncope episodes with loss of consciousness. The patient had no history of stroke or other psychosis, and the results of laboratory investigation did not explain her clinical symptoms. However the combination of her clinical symptoms and features fulfills the consensus criteria for clinical diagnosis of probable DLB. Although there is now greater understanding about DLB, its clinical presentation and neuropathological findings share many similarities with AD and PD. The neuropathological findings of PD involve neuron loss and the formation of LBs mainly within the brainstem nuclei, especially the substantia nigra, thus producing manifestations of motor disorder. In DLB, most LBs are located within the paralimbic and neocortical structures, which together cause depletion of acetylcholine neurotransmission in neocortical areas. 'Lewy neuritis' can also be found in the substantia nigra. These extensive pathological alterations could account for the characteristic neuropsychiatric features of DLB 14. Although AD-type pathological changes such as senile plaques could also be seen in most reported cases of DLB, neurofibrillary tangles are relatively less commonly observed. Because the strict pathological diagnosis of AD require that the number of neocortical neurofibrillary tangles must reach a particular level, Mckeith et al felt that most DLB should be classified as 'Spectrum of LB-related disorders' which include DLB,PD and PD with dementia , and not as a subtype or variant of AD 15.

Clinical DLB is often misdiagnosed as AD. The accurate diagnosis of DLB still relies on accurate history-taking, and careful physical and mental status exams. There is currently no specific premortem biological test or marker to diagnose DLB. Nevertheless, initial data shows that 123 I-FP-CIT SPECT could be used to differentiate AD from DLB. This technique uses a fluoroalkyl analogue of cocaine to bind the presynaptic dopaminergic terminals of nigrostriatal pathway. In DLB and PD, the binding of the nigrostriatal pathway appear decreased; however, no such nigrostriatal degeneration is appreciated in AD 16.

In the past, antipsychotic agents have been the main stay of therapy for the treatment of behavioral and psychological symptoms in dementia. But in DLB, usage of antipsychotic agents could not only cause irreversible Parkinsonism and further cognitive impairment in 40-50% of reported cases, but also a 2-3 fold increase in the mortality rate 17. Although some studies report fewer side effects and even some improvement of psychosis when atypical antipsychotic agents are used 18, the risk for neuroleptic sensitivity reaction still remains 19. Such is the case with our patient, who exhibited severe neuroleptic sensitivity reaction along with cognitive deterioration despite trials with different atypical antipsychotic agents. We therefore do not recommend the use of any antipsychotic agent for the treatment of DLB. As for

other pharmacologic treatments, there are already studies reporting that usage of cholinesterase inhibitors could improve the cognitive function, psychosis and behavioral problems of DLB. This could mean that cholinesterase inhibitors may be considered as a first line treatment for DLB sometime in the future 20.

In conclusion, there are available consensus criteria for clinical diagnosis of DLB now. Nevertheless, many studies also indicate a rather low sensitivity about DLB from the clinicians' part. What is of major concern is the fact that not only is DLB the second leading cause of degenerative dementia in foreign literature, but also patients with DLB often have early neuropsychiatric symptoms leading to evaluation and treatment at medical facilities. And so when presented with such cases, we must take into consideration the possible diagnosis of DLB, and the danger of using antipsychotic agents, in order to provide safer and more treatment strategies to the patient and family members.

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路易氏癡呆症：一例報告

徐堅棋 孫藝文 鄭世榮*

馬偕紀念醫院 精神科 *神經內科

摘要

路易氏癡呆症並未被列入目前正式的診斷系統，台灣也缺少此類個案之研究。我們提出一位典型個案，討論其症狀、診斷、臨床病程及治療，並做文獻回顧。78

歲女性，一年前起出現記憶缺失、失眠，當時診斷為阿滋海默病；半年後，出現精神症狀。雖然嘗試使用數種非典型抗精神病藥物，但精神症狀未見改善，還出現嚴重的抗精神病藥物敏感反應。個案未曾有中風或精神病史，實驗室檢查無法解釋其臨床症狀。此表現符合路易氏癡呆症之臨床診斷。路易氏癡呆症常誤診為阿滋海默病。前者因早期之神經精神症狀就醫；面對這類個案時，必須考慮可能是路易氏癡呆症及使用抗精神病劑之危險性，才能對患者提供安全有效的治療策略。