

Clinical Case Conference

Psychiatric symptoms in dementia with Lewy Bodies: Diagnostic and management issues

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Abstract

Dementia with lewy bodies is the second most common type of dementia, but may often be misdiagnosed in clinical situations. It commonly presents with visual hallucinations and fluctuating cognition on a background of parkinsonian features and progressive cognitive decline in an elderly patient. A variety of psychiatric symptoms may occur in the course of the illness and often, there is an extreme sensitivity to neuroleptic drugs. In view of several complex and challenging issues, we discuss a case of dementia with lewy bodies from a diagnostic and management perspective.

Keywords: Lewy body dementia, psychiatric symptoms, halucinations

Introduction

Dementia with Lewy Bodies (DLB) has been a subject of great interest as well as debate over the past two decades. Though the disorder did not find a separate mention in the DSM-IV diagnostic criteria (APA, 1994), it has since been recognized as the second most common form of dementia, accounting for up to 25 % of all dementias.¹ Efforts have been made to delineate the characteristic clinical features of DLB to differentiate it from other subtypes of dementias.² The DLB is characterized clinically by a progressive dementia as the central feature along with fluctuations in cognitive functioning (marked variability in alertness over short time), complex visual hallucinations and spontaneous features of parkinsonism.²⁻⁴ Prominent or persistent memory impairment may not necessarily be an early feature, but deficits in

attention, visuospatial ability and executive functions are fairly common early in the course of dementia.⁵ The presence of REM sleep behavior disorders and extreme sensitivity to neuroleptic drugs may often be a suggestive feature towards the diagnosis. Pathologically, DLB is characterized by a diffuse presence of Lewy bodies, which are 15-30 µm, spherical intraneuronal cytoplasmic inclusions (first discovered by Friedrich Lewy in 1912) found throughout the subcortical and cortical areas of the brain.⁶ DLB is also characterized by more severe depletion of neurotransmitters such as acetyl choline and dopamine in the brain especially compared to AD. The diagnosis of DLB can be quite difficult because of the variability in presentation and the overlap of clinical features with other dementias especially Alzheimer's disease (AD) and Parkinson's disease with dementia (PDD).⁷

Psychiatric symptoms may commonly occur in approximately 50-80% of cases of DLB.⁸ These can be in the form of complex hallucinations in visual and other modalities, delusions, depression, anxiety and various other behavioral disturbances e.g. irritability and aggression.^{3,4} The management of DLB requires a careful monitoring as the dopaminergic medication for parkinsonism can worsen the psychosis and behavioral abnormalities, while the antipsychotic treatment may not be tolerated and can worsen the parkinsonian features.

In view of several complex and challenging issues in the diagnosis and management, we present and discuss a case of DLB, which initially presented to the department of neurology and was referred to consultation-liaison services for psychiatric evaluation and treatment.

Case Summary

Mr. A was a 72 years male, widower, belonging to a middle socio-economic status family. He had studied till post graduation and was a retired professor. The information was collected from the patient's son who was residing with him and the patient's sister who visited him frequently. The total duration of illness was six years with an insidious onset and progressive course.

Patient was asymptomatic and functioning well till early 2005, when he starting having difficulty in recalling the daily events and conversations with family members. He would have difficulty in following the routinely watched television shows in home and could not connect the story to previous day's episodes. He would often request the family members to locate his personal belongings e.g. spectacles or prayer beads. Gradually, over next few months he started experiencing difficulty in finding his way back home after the evening walks, especially if he has taken a less familiar and longer route.

Within a year of the onset of initial

symptoms, the family members noticed that the patient had become slower in the routine daily activities. He would have his meals very slowly, taking nearly 30-40 min in contrast to 10-15 min earlier. He would take a long time to bathe and dress himself. His manner of walking had become slow, taking small steps and reduced arm swing. He seemed more unsteady while walking and would use a walking stick while going out of home.

The forgetfulness and slowness increased progressively over next 2-3 years, when patient started having tremor in right hand which was coarse and noticeable at rest. Gradually, the tremors started occurring in the left hand as well as legs over the next year. By this time, his walks outside the home had reduced for fear of falling and difficulty in remembering the directions precisely. Gradually, he started having difficulty in finding a way inside the house e.g. on several occasions, he landed in kitchen while looking for the bathroom in the house. He could no longer help the grandchildren with their studies and would make several mistakes in solving easy problems.

Over the past year, patient had started remaining isolated from rest of the family and reduced his interaction with friends and relatives. He would often sit by himself and refused to join the family discussions or common activities such as watching television. Even if they tried to engage him, patient did not follow the conversations and would repeatedly ask questions about the recent events or links to the discussion. He needed some help of family members in carrying out the routine activities. Nearly six months back (Feb 2011), the in-laws of his elder son came to temporarily stay with them to provide help during the grandchild's examinations. Within a few days, the patient started expressing the suspicion to other family members that the elder son and his in-laws were

conspiring against him and planning a strategy to steal his wealth and property. When asked further, he would not provide any evidence and express that their stay at his house was a sufficient proof. The patient's belief was not shared by other family members who would try to assure him by explaining the reasons for their stay and patient would appear convinced for some time. However, he would again express the same belief after some time and would not converse with the in-laws of elder son. This continued for next 1-2 months during which he would often express the feeling of loneliness and isolation in his home. He was reluctant to stay with the elder son and planned to move with the family of the younger son in another city. The younger son observed that the patient would not interact much and often, would answer only in monosyllables or short sentences. On asking, patient would report that he did not feel like speaking and appeared sad most of the time. Family tried to encourage him to participate in the discussions, offer him to take for a walk and tried to keep him occupied in an activity, however patient would not show interest and would confine himself to a room. He continued to carry out his routine activities like bathing, dressing etc himself, however needed a little assistance from family members in view of tremors and slowness.

During the same time, he started experiencing difficulty in the falling asleep and would often wake up early in the morning, sleeping only for nearly four hours in contrast to 6-7 hours earlier. His appetite reduced and he started eating less than one *chappati* per meal. In April 2011, the family decided to consult the family physician for these symptoms. The concerned physician started the patient on Fluoxetine (20 mg) for the sadness and related symptoms, along with a benzodiazepine as required for sleep. Following the initiation of

treatment, the family members perceived some improvement in the low mood, interaction and sleep over the next 3-4 weeks during which fluoxetine was continued.

Thereafter, in May 2011 the patient suddenly appeared confused and unable to comprehend the instructions of family members. His body was stiff, his face appeared expressionless and he continued to stare in one direction for about 30 min. He was taken to a nearby hospital, where he was kept under observation for two days and discharged on L-Dopa (1/2 tab OD), Amantidine (100 mg OD) and Trihexyphenidyl (0.5 mg TDS) for parkinsonian features. Patient showed improvement in tremors following the start of medication but there was no significant improvement in slowness or forgetfulness. He started feeling fatigued even after a minor physical activity e.g. walking inside house or changing clothes and felt lethargic at all the times. He would experience difficulty in standing up from sitting position without support. His forgetfulness continued to progress and often he would not remember having meals or forget about a visitor who came by earlier in the day. Along with increasing dependency on family members, patient would often express that he was of no use to the family and felt like a burden. He would at times make requests to his son to look after the other siblings after his own death. His spontaneous interactions with family members continued to be minimal and his interest in previously pleasurable activities declined further over next 1-2 months.

During the same period, the patient reported seeing things that could not be seen by the family members. He would frequently describe seeing a mouse near his foot and would raise his feet to avoid touching it, however family members sitting near him would be unable to spot a mouse in the room. Patient appeared to be alert and awake to the family members and was able to

recognize his surroundings and time of the day. In another instance, he pointed to the table saying that a small bottle placed on the table is about to fall down, while family members did not see a bottle. He reported seeing a few people on top of the tree outside his window again visible only to him. These phenomenon occurred frequently, almost on a daily basis and during various times of the day. Meanwhile, the episodes in which he appeared blank, expressionless and unresponsive along with profuse sweating became more frequent, each time lasting nearly 30 min. The patient's condition declined further in terms of slowness, forgetfulness and seeing non-existent things.

With above complaints, the family brought him to the neurology out-patient clinic in July 2011, where initially the previous medications were withdrawn gradually in view of its temporal relation with worsening of the condition. Following the stoppage of medications, there was an improvement in lethargy and reduction in the frequency of seeing non-existent things, though other symptoms of the patient continued to show a gradual worsening. Patient was admitted in first week of August 2011 for a thorough evaluation and management.

In the past medical history, patient was successfully operated for the cerebellar hematoma due to an arteriovenous malformation in 1994. There was no family history of neurological illness. His daughter, now 47 years, had been diagnosed with schizophrenia since her twenties and was on regular treatment. Patient had a well-adjusted personality prior to onset of current illness.

There was no remarkable finding on general physical, cardiovascular, respiratory and abdominal examination. The patient had walked in a slow, stooped manner keeping the arms mostly by his side without swinging them. The cranial nerves and sensory system examination

revealed no abnormality. The superficial and deep reflexes were preserved, but cogwheel rigidity and rest tremors were observed in the upper and lower limbs. The cerebellar function tests were impaired as revealed by difficulty in performing rapid alternating movements and tandem walking (possibly due to operative procedure on cerebellum).

The ward course showed a fluctuating level of consciousness and mental state examinations were conducted separately for cooperative and uncooperative patient. The first mental state examination conducted on second day of admission showed an awake patient, oriented to time, place and person. The psychomotor activity was decreased. Speech was relevant, coherent and goal-directed, but rate and volume was decreased with increased reaction time. The affect of the patient was depressed. Thought content revealed ideas of worthlessness, hopelessness and preoccupation with the physical illness. In the perceptual abnormality, he reported seeing some religious persons and Gods (Lord Krishna and Lord Indra Dev) clearly, in full form and pointed towards an empty space in front of him. The higher mental functions revealed an impairment in concentration, immediate memory, recent memory, verbal fluency, complex paired associate learning and complex calculations. The comprehension, repetition, reading, naming and word finding and remote memory were largely intact. The mini mental state examination was 23/30.

The mental state examination on the next evening revealed an uncooperative patient who appeared apathetic to the surrounding persons and kept on staring in one direction. He kept on lying in bed with minimal voluntary movements and drooling of saliva was present. He responded to his name by turning his head and vocalized on pain stimuli. There was spontaneous crying on

one occasion. Eyes were mostly open with decreased blinks and fixed gaze. He followed the simple instructions to show tongue or move limbs. Rigidity of limbs and tremors were present. The speech was found to be irrelevant on few occasions during the interview. He mentioned seeing Gods approaching him, but could not elaborate further. He was unable to write clearly due to tremors.

An ICD-10 F02.8 diagnosis of Dementia in other diseases classified elsewhere predominantly depressive (ICD 10 CM G31.83 dementia with lewy bodies) and a DSM- IV TR diagnosis of Dementia with Lewy Bodies 331.82 was made.^{9,10} The hemogram and biochemistry investigations were within normal limits. The thyroid function tests and Vit B 12 levels were also normal. MRI brain revealed no abnormality besides the gliosis in cerebellum (due to old operative procedure). Formal neuropsychological tests was planned for a later date when the patient's general condition improved and he was more amenable to assessment. Patient was kept off-medication for observation and evaluation in the first week of admission. His consciousness kept on fluctuating from alert and awake to delirious-like state. Even in the alert and awake state, he reported that he can see the Gods (Lord Krishna and Lord Indra Dev) clearly and in full form. He would offer prayers and sing religious songs praising them. His family members could not see any one as described by patient, however patient would insist that they should also offer the prayers to the Gods who have come to meet him. Patient recognized the family members and relatives accurately during this time, but at times he insisted that the place was heaven instead of a hospital since so many Gods are seen around him. He had intermittent worsenings when he appeared confused and would keep on staring in one direction.

After observation, he was started on 25 mg/day of Quetiapine for these symptoms, however there was a marked increase in sedation and consequent risk of falls. As a result, it was subsequently reduced to 12.5 mg/day. The patient was monitored regularly and provided supportive treatment. Family members were explained about the non-pharmacological measures for symptom management and help the patient maintain contact with surroundings. The visual hallucinations would remit only temporarily for a couple of days and thereafter would re-emerge and persist in a clear and conscious state for most of the time. The visual hallucinations did not cause significant behavioral disturbances and an aggressive treatment was not considered. The patient remained in a clear conscious state and was able to recognize the persons around him. In the second week of admission, he was initiated on Rivastigmine 3 mg BD for cognitive and neuropsychiatric symptoms. Trihexyphenidyl (2 mg) ½ BD was added for motor symptoms of parkinsonism. The supportive treatment continued and effort was made to maintain adequate nutrition and hydration. PEG tube had to be inserted for maintaining proper nutrition. Patient was discharged on above treatment with a partial improvement in neuropsychiatric symptoms and advice to follow up in out-patient clinic. Family members were explained about the likely course and symptom progression of DLB, management of the common problems which can be encountered in dementia care and educated for the care-related issues at home.

Discussion

The diagnosis of DLB often requires a careful probing and delineation of symptoms as it could easily be misdiagnosed as AD or PDD due to overlapping features. In this case, the elderly patient initially presented to out-patient

clinic with prominent parkinsonism and some evidence of cognitive decline. The history of fluctuating nature of cognitive symptoms was not available at that time and the onset of visual hallucinations was temporally related to dopaminergic agonist medications. Therefore, a differential diagnosis of PDD was initially entertained in addition to a possible DLB. Subsequently, with more information and observation of the patient, it became clear that there are marked fluctuations in the patient's cognition over short periods of time and complex visual hallucinations were found to be persist even after discontinuing the medications. It was also ascertained from multiple informants that the cognitive impairments preceded the parkinsonian features by nearly a year. Therefore, a probable diagnosis of Dementia with Lewy Bodies as per criteria (provided in table 1) could be established.²

The patient had persistent visual hallucinations for a few months before presentation. There was no obvious distress associated with visualizations of religious persons and Gods, rather the patient appeared to enjoy and would ask others to join him in offering prayers. The presence of visual hallucinations is one of the core features of DLB. The hallucinations in DLB are typically recurrent, well formed, detailed and complex in nature. Studies suggest that visual hallucinations are present in nearly 75% of patients with DLB, followed next in frequency by delusions (commonly paranoid and phantom boarder) in over half of patients and less commonly, hallucinations in other modalities. Depression is common in DLB occurring in nearly 25% of all cases. The patient with DLB described above had ideas of persecution which lasted for several weeks followed by spontaneous disappearance and there were significant depressive symptoms which remitted only after treatment with SSRI.

Table 1: Diagnostic criteria for Dementia with Lewy bodies

Central feature:

Progressive dementia - deficits in attention and executive function are typical.

Prominent memory impairment may not be evident in the early stages.

Core features:

Fluctuating cognition with pronounced variations in attention and alertness.

Recurrent complex visual hallucinations.

Spontaneous features of Parkinsonism.

Suggestive features:

REM sleep behaviour disorder (RBD), which can appear years before the onset of dementia and Parkinsonism.

Severe sensitivity to neuroleptics occurs in up to 50% of LBD patients who take them.

Low dopamine transporter uptake in the brain's basal ganglia as seen on SPECT and PET imaging scans.

Supportive features:

Repeated falls and syncope (fainting).

Transient, unexplained loss of consciousness.

Autonomic dysfunction.

Hallucinations of other modalities.

Visuospatial abnormalities like depth perception, object orientation, directional sense and illusions.

Other psychiatric disturbances like systematized delusions, aggression and depression.

A probable LBD diagnosis requires either:

Dementia plus two or more core features, or

Dementia plus one core feature and one or more suggestive features.

A possible LBD diagnosis requires:

Dementia plus one core feature, or

Dementia plus one or more suggestive features.

The presence of marked alterations of attention and cognitive functions along with psychiatric symptoms e.g. visual hallucinations as described in this patient may easily be confused with a clinical picture of delirium.¹³ This peculiar state in DLB has been described as a variable attention, incoherent speech, hypersomnolence, impaired awareness of surroundings, staring into space, or suddenly appearing 'glazed' or 'switched off' at one time and 'alert' at another time.^{8,13} The cognitive fluctuations

and delirium-like state in DLB is reported to occur in the periods of relative lucidity and may be present relatively early in the course of dementia. Furthermore, it has been suggested that this type of fluctuation is not restricted to cognitive functioning, but may generalize to other mental, physical and behavioral capacities.⁸

The management of psychiatric symptoms often proves to be a daunting task in DLB. Nearly 50% patients may have extreme neuroleptic sensitivity with risk of developing severe extrapyramidal symptoms and confusion with traditional and some atypical neuroleptics.^{13,14} The lower density of dopamine D2 receptors in the corpus striatum seen may be responsible for the proneness to extrapyramidal adverse effects. Specifically, the antipsychotic agents with D2 antagonism and anticholinergic properties can precipitate and/or exacerbate extrapyramidal signs and cognitive impairment respectively. Quetiapine has a relatively better profile of safety in DLB¹⁵ and therefore, was used in this patient at very low dosages. The aggressive management of psychiatric symptoms is not warranted especially if there are no associated behavioral disturbances.

The cholinesterase inhibitors (rivastigmine, galantamine, donepezil) have been found to be useful in the treatment of neuropsychiatric symptoms in DLB.¹⁶ It could be due to the fact that the cholinergic deficit in DLB is more severe compared to a dopaminergic deficit, particularly in patients who have hallucinations.¹⁷ Double blind RCTs have shown that rivastigmine may decrease the psychiatric symptoms associated with DLB, particularly apathy, anxiety, hallucinations, and delusions.¹⁸ Similar to AD, the cholinesterase inhibitors may also be useful in the control of dementia progression. This patient was also initiated and discharged on Rivastigmine 6 mg/day with a plan to continue it over long-term. Trihexyphenidyl was added to

control the motor symptoms of parkinsonism, and will require a careful monitoring for its side-effects, including delirium. The use of levodopa for motor symptoms of parkinsonism in DLB is limited particularly in view of doubtful efficacy and propensity to cause psychosis.^{3,4}

The nonpharmacological management in this patient comprised of education of the carers to deal with specific symptoms of the illness as well as general issues of caring for a patient with dementia. Various interventions including structuring of environment, teaching behavioral skills and improving sensory impairment have been found useful in dementias and might also be useful in patients suffering from DLB.¹⁹

To conclude, the case highlights the need to keep a diagnostic possibility of DLB while evaluating cognitive decline in an elderly patient. Psychiatrists need to be aware of the unique clinical characteristics and treatment implications associated with the diagnosis of DLB.

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Source of funding : Nil

Conflict of Interest: None declared

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