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Lewy Body Dementia: A Case Report.

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ABSTRACT

Lewy Body Disease, though commonly prevalent, has not been given due recognition by clinicians. Clinicians often tend to under-diagnose Lewy Body Disease by confusing it with more familiar presentations of Alzheimer's disease or Parkinson's disease. The absolute diagnosis of DLB is possible only on microscopic examination of brain tissue at autopsy. There is no specific biological test or marker to diagnose DLB. The clinical diagnosis of DLB therefore relies on accurate history-taking, and careful physical and mental status exams. Management issues in DLB include avoidance of neuroleptic sensitivity reactions, achieving optimal level of antiparkinsonian treatment without exacerbating psychiatric symptoms and a beneficial response to cholinesterase inhibitors. Here we describe the case of a 66 year old male with dementia with Lewy bodies.

Keywords: Lewy Body Dementia, Alzheimer's Disease, Parkinson's Disease, neuroleptic sensitivity.

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INTRODUCTION

Lewy Body Disease, though commonly prevalent, has not been given due recognition by clinicians. Clinicians often tend to under-diagnose Lewy Body Disease by confusing it with more familiar presentations of Alzheimer's disease or Parkinson's disease. It has been suggested that almost 36% of patients diagnosed as Alzheimer's Dementia exhibit Lewy Body pathology at autopsy and these autopsy studies have shown that Lewy Body Disease perhaps accounts for almost 15% to 25% of all dementias, the second most common degenerative dementia only surpassed by Alzheimer's Dementia [1].

In scientific literature, various names have been proposed for Lewy Body Disease, 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.

Though clinical presentation of Lewy Body Disease is quite similar to other clinical dementias, its clinical distinction from other dementias is important as it has profound implications management and prognosis. A patient can be benefitted from treatment while being saved from unnecessary treatment complications if Lewy Body Disease is kept in mind while dealing with clinical dementias.

Case Report

A 66 year old man was brought to the Psychiatry OPD by his son with chief complaints of seeing objects without stimulus and muttering to self. The detailed history, as provided by the son, revealed that the patient was a normal functioning farmer till 6 months back when the family members started noticing a gradual slowing of his movements associated with involuntary shaking of both upper and lower limbs. Over the course of couple of months, these complaints further worsened to cause difficulties in his daily routine as well as farming activities and afterwards he completely stopped going to the fields. His family members also started noticing him forgetting where he had kept things or events that had happened in the recent past. As his motor symptoms and memory problems worsened further, he was taken to a physician who prescribed him medications with which, over a period of 15 to 20 days, he showed improvement in his memory but the slowing of movements and involuntary movements of limbs still persisted.

One month back, he reported frequent seeing of objects and persons even without their presence in the house. He would see his villagers sitting next to him and would tell his family members about it. Many times he was noticed talking and smiling to self. On being asked about it he would tell that he was chatting with his village friends.

For these complaints, he was taken to a psychiatrist who prescribed him Tab. Risperidone 1 mg twice a day and Tab. Trihexiphenidyl 1 mg twice a day. After taking these medications, the frequency of his hallucinations increased as well as his movements further slowed down. For his worsened condition, he was brought to our tertiary care hospital psychiatry unit.

His past medical history was not significant and there was no history of psychiatric illness in his family. He had no history of alcohol or other substance abuse.

When examined, patient was an averagely nourished elderly man in no apparent distress. He was afebrile. His pulse was 72 beats per minute, blood pressure was 140/80 mm of Hg and respiratory rate was 16 per minute.

While other systemic examination was unremarkable, his Central Nervous System examination revealed rigidity in all four limbs and tremors in hands and feet. The tremors were coarse, symmetrical and perceptible at rest and on intentional movement. His gait was wide and unsteady. The Glabellar Tap Sign was positive.

On Mental Status Examination, patient was conscious and passively cooperative. His psychomotor activity was significantly decreased. His speech was nonspontaneous with decreased rate and delayed reaction time. Thought revealed poverty of ideation but no delusions were elicited. He reported visual hallucinations of non-threatening nature. On memory testing, his immediate registration score was 2/3 while recall score after

3 minutes was 0/3. His recent memory was impaired but remote memory was intact. On Folstein's Mini Mental Status Examination (MMSE), his score was 21/30 where his particular areas of deficiency were three object recall, following a 3-step command and drawing interlocking pentagons.

He was investigated with standard laboratory workup to rule out medical illness as well as reversible causes of dementia, which were within normal limits. A Computed Tomogram (CT) of head showed age related cortico-cerebellar atrophy.

Considering patient's progressive cognitive decline which started within 6 months of onset of his Parkinsonian features, visual hallucinations and high neuroleptic sensitivity, a probable clinical diagnosis of Diffuse Lewy Body Dementia was made. In initial management, Tab. Risperidone was stopped and he was started on Tab. Quetiapine 25 mg per day and Tab. Donepezil 5 mg per day with which patient showed gradual improvement.

DISCUSSION

The German physician Friedreich Heinrich Lewy, who first described the distinctive spherical, eosinophilic, intracytoplasmic neuronal inclusions on microscopic examination of brain tissue at the beginning of the 20th century in the brainstem of a Parkinson's disease (PD) patient which came to be known as Lewy bodies, eventually lending his name to Lewy body disease (DLB). Okasaki and co-workers in 1961 noted widespread presence of Lewy bodies in the cerebral cortex in two patients with progressive dementia. Dementia with Lewy bodies came into the limelight after a series of reports describing in detail the characteristics and distribution of cortical Lewy bodies by Kosaka in1978. Kosaka and colleagues in 1984 proposed the term Dementia with Lewy Bodies as a designation for a particular type of Lewy body disease [2]. Dementia with Lewy bodies (DLB) was considered to be an uncommon cause of dementia until improved neuropathological staining methods for ubiquitin were developed in the late 1980's. Subsequent recognition that high proportion of dementia cases in older people was associated with Lewy body pathology led to the publication of Consensus clinical and pathological diagnostic criteria for the disorder [3].

The disease is more common in men with a 2:1 sex ratio or higher in some studies. The age of onset of the illness is between 50 to 83 years and the duration of illness has been reported to vary from 1 year to 20 years with a mean of 3.3 to 6 years. The mean age at death reportedly varies from 68.4 to 92 years [4].

Clinically DLB is often misdiagnosed as Alzheimer's Disorder (AD) or Parkinson's Disorder (PD) with dementia. The absolute diagnosis of DLB is possible only on microscopic examination of brain tissue at autopsy. There is no specific biological test or marker to diagnose DLB. The clinical diagnosis of DLB therefore relies on accurate history-taking, and careful physical and mental status exams.

Recurrent visual hallucinations are a core feature of DLB. Hallucinations in other modalities, and systematized delusions are supportive features [5]. Psychosis in DLB may occur even without treatment with dopaminergic therapies or other antiparkinsonian treatments unlike psychosis in Parkinson's dementia. Approximately 75% of DLB patients experience hallucinations and more than 50% have delusions [6].

These patients typically have poor insight, frightening hallucinations. Behavioral changes including "sundowning" and other forms of agitation are common and often require treatment [7].

Visuoperceptual impairment has been reported to be a correlate of, and possible risk factor for, psychosis.[(5)] Increased numbers of Lewy bodies in the temporal lobe and the amygdale are associated with the onset and presence of visual hallucinations [8]. Brain perfusion imaging has demonstrated reduced occipital uptake in areas of the visual cortex [5].

Preliminary attempts to determine whether particular clinical symptoms are associated with DLB were based on retrospective autopsy-proven case note reviews [2]. These early operationalised criteria proposed that the key symptoms suggestive of DLB rather than AD are fluctuating cognitive impairment with episodic delirium, prominent psychiatric symptoms, especially visual hallucinations, a parkinsonian syndrome

occurring spontaneously often as part of an abnormal sensitivity to neuroleptic medication [9]. To improve diagnostic reliability and validity, consensus criteria for clinical diagnosis of DLB were outlined [3].

A recent re-evaluation of the Consensus criteria has confirmed many aspects of the original recommendations, supplementing these with suggestions for improved pathological characterisation, clinical detection and management [3]. Table 1 shows Revised Criteria for the Clinical Diagnosis of DLBD (2005) [10].

Table 1: Revised criteria for the clinical diagnosis of DLB (2005) [10]

1	**Central feature (essential for a diagnosis of possible or probable DLB)**
	Dementia defined as progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function.
2	**Core features (two core features are sufficient for a diagnosis of probable DLB, and one for possible DLB)**
	Fluctuating cognition with pronounced variations in attention and alertness
	Recurrent visual hallucinations that are typically well formed and detailed
	Spontaneous features of parkinsonism
3	**Suggestive features**
	REM sleep behaviour disorder
	Severe neuroleptic sensitivity
	Low dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET imaging.
4	**Supportive features**
	Repeated falls and syncope
	Transient, unexplained loss of consciousness
	Severe autonomic dysfunction, e.g., orthostatic hypotension, urinary incontinence
	Hallucinations in other modalities
	Systematised delusions
	Depression
	Relative preservation of medial temporal lobe structures on CT/MRI scan
	Generalised low uptake on SPECT/PET perfusion scan with reduced occipital activity
	Abnormal (low uptake) MIBG myocardial scintigraphy
	Prominent slow wave activity on EEG with temporal lobe transient sharp waves
5	**A diagnosis of DLB is less likely**
	In the presence of cerebrovascular disease evident as focal neurologic signs or on brain imaging
	In the presence of any other physical illness or brain disorder sufficient to account in part or in total for the clinical picture
	If parkinsonism only appears for the first time at a stage of severe dementia
6	**Temporal sequence of symptoms**
	DLB should be diagnosed when dementia occurs concurrently or within one year of parkinsonism (if it is present).

Management issues in DLB include avoidance of neuroleptic sensitivity reactions, achieving optimal level of antiparkinsonian treatment without exacerbating psychiatric symptoms and a beneficial response to cholinesterase inhibitors [2]. Table 2 shows therapeutic guidelines in patients with DLBD. Adverse reactions to antipsychotic and tricyclic antidepressant agents are common. A retrospective study showed 81% of DLBD patients had adverse reactions compared with only 7 % of AD patients [9].

Cholinesterase inhibitors are the only class of psychiatric medications that have been evaluated in RCTs for the treatment of DLBD. They appear to be effective on cognition as well as neuropsychiatric symptoms, including psychosis. One prospective randomized study for showed Rivastigmine led to significant improvement on a composite neuropsychiatric score that included delusions, hallucinations, depression, and apathy [7].

Given the possibility of sensitivity reactions, antipsychotic medications should be considered only after a thorough discussion of the risk-benefit ratio with both the patient and an informed other, and with close clinical monitoring for adverse effects. Other strategies for managing these symptoms should be exhausted before resorting to medications. When neuroleptics are necessary it might be wise to consider admission to the hospital for dose titration. Antipsychotics like quetiapine and clozapine are safer options if antipsychotics are necessary after careful weighing of the risk-benefit ratio [7].

Table 2: Therapeutic guidelines in patients with DLB [2]

1.	In most cases the symptoms of the parkinsonian syndrome (akinesia, rigidity, tremor) can be improved by levodopa. In most cases 300 mg/d is the maximal dosage because of psychiatric side effects.
2.	Psychotic symptoms occur spontaneously but can be triggered or exacerbated by levodopa therapy.
3.	Therapy with dopamine agonists cannot be recommended because of higher prevalence of psychiatric side effects.
4.	In case of wearing-off phenomena therapy with a COMT inhibitor can be performed at a decreased dose of levodopa.
5.	Visual hallucinations and delusions can be improved by therapy with atypical neuroleptics (clozapine, risperidone, quetiapine). Clozapine seems to be the drug of first choice. Doses of 3 x 12.5 up to 3 x 50 mg/d can be used. Rarely atypical neuroleptics worsen parkinsonian symptoms and state of consciousness.
6.	Fluctuating cognitive deficits can be improved by treatment with cholinesterase inhibitors (donepezil, rivastigmine, galantamine).
7.	Orthostatic hypotension can be treated with sympathico-mimetics, bladder dysfunctions with alpha-receptor blockers or with anticholinergics.

In a placebo-controlled study of the treatment of psychosis in Alzheimer's disease with olanzapine, a post hoc analysis of a subgroup of patients who were retrospectively diagnosed with DLB showed that olanzapine led to a decrease in positive symptoms of psychosis without worsening either Parkinsonism or cognition.[11] A negative impact of Cholinesterase inhibitors on parkinsonian motor scores might be predicted because of their procholinergic effect on the normal balance with dopamine in the basal ganglia.

CONCLUSION

We have discussed the case of a 66 year old male who presented initially with symptoms of Parkinsonism with memory disturbances beginning within a few months of the onset of motor symptoms. He was initially treated with anti-parkinsonian drugs which were followed by development of florid hallucinations. Treatment with antipsychotic medications lead to severe neuroleptic reaction with worsening of both motor and cognitive symptoms. The case illustrates the need to have a high index of suspicion for Lewy body disease in patients presenting with parkinsonian symptoms and cognitive, psychotic, or behavioural symptoms to be able to choose appropriate management strategies and avoid neuroleptic induced adverse reactions.

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