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Probable dementia with Lewy body

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ABSTRACT

V.A. female, 67 years, old admitted in our clinic for neurological assessment because of a Parkinson syndrome, in association with neurocognitive disorder established in a psychiatric service. Motor disturbances and cognitive disorders are frequently associated in Dementia with Lewy body (DLB) and in Parkinson Disease (PD). Psychiatric symptoms are diffi cult to manage as antipsychotics have frequently motor side effects. Criteria for possible and probable diagnosis of DLB according McKeith criteria and Diagnostic and Statistical Manual of Mental Disorders (DSM 5) are discussed.

Keywords: Dementia with Lewy body (DLB), diagnosis criteria, probable and possible disease

DLB has an overall incidence of 7 per 1,000 individuals among people over 65 years (1) Prevalence is estimated between 0.1%-5% in general elderly population and from 1.7-30.5% of all dementia cases. It is considered that almost 20% of institutionalized elderly suffer of DLB (2). Diagnosis is often hard to be established, as motor features can lead to a diagnosis of neurocognitive disorder due to Parkinson disease. Both diseases are synucleinopathies and exhibit motor and cognitive symptomatology (3), as in both we found deficits in dopaminergic and cholinergic pathways (4) and presence of Lewy body, neuronal inclusions formed of neurofilaments of abnormal phosphorylated proteins, and aggregates of ubiquitin and alphasynuclein. DLB can be differentiated from neurocognitive disorder (NCD) due to PD based on the chronological onset of symptoms. Individuals with NCD and LB will exhibit cognitive symptoms before the onset of motor symptoms (it is accepted a period of maximum one year before appearance of dementia after motor signs) and in PD the sequence is reversed. Anyway there is a broad variation in clinical spectrum in these patients, who always associate different combination of parkinsonism, dementia, tremor.

According McKeith criteria revised in 2005 (5,6) which are considered most reliable for diagnosis, DLB is characterized by progressive cognitive decline, **core features** of the disease being:

- fluctuating cognition with variations in attention and alertness,
- recurrent well formed visual hallucinations, and
- spontaneous motor signs of parkinsonism.

Suggestive clinical features include:

- rapid eye movement (REM) sleep behaviour disorder,
- severe neuroleptic sensitivity,
- low dopamine transporter uptake in basal ganglia demonstrated by Single-photon emission computed tomography (SPECT)/positron emission tomography (PET) imaging.

Diagnosis in DLB is mainly clinical, **probable disease** being demonstrated when at least two of three core features are present in presence of dementia or when one core feature is present along with a suggestive one; a **possible** form of DLB is sustained when dementia is accompanied of a core or a suggestive feature of those announced above.

Supportive features may be (commonly present but no diagnostic specificity):

- repeated falls and syncope,
- transient loss of consciousness, without explanation,

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- severe autonomic dysfunction (orthostatic hypotension, urinary incontinence),
- sensitivity to neuroleptics,
- delusions and hallucinations in other modalities,
- mood disorders (depression),
- relative preservation of medial temporal lobe structures on (computed tomography) CT/ magnetic resonance imaging (MRI),
- generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity
- proeminent slow wave activity on electroencephalography (EEG) with temporal lobe transient sharp waves.

There is less likely to have a diagnosis of DLB in presence of stroke with focal signs or brain imaging or evidence of other illness or brain disorder sufficient to account for clinical picture.

According DSM 5(7) criteria diagnosis for major/mild neurocognitive disorder with Lewy body presume an insidious onset and gradual progression. Disturbance is not better explained by other pathology as cerebrovascular disease, neurodegenerative one, or effects of various substances or other systemic diseases.

Core diagnosis features are:

- fluctuating cognition with variations in attention and alertness,
- recurrent visual hallucinations well formed and detailed,
- spontaneous features of parkinsonism with onset subsequent to the development of cognitive disorder.

Suggestive diagnosis features are:

- rapid eye movement sleep disorder,
- severe neuroleptic sensitivity.

CASE PRESENTATION

Beginning of the disease was in February 2014 with an acute psychotic episode with auditory hallucinations with religious content; since then she was treated with different typical and atypical antipsychotics (amilsulpride, risperidone, olanzapine, clozapine, paliperidone) with no improvement. Imaging exploration was not performed. In January 2016, she developed a parkinsonian syndrome so, the outpatient psychiatrist initiated treatment with trihexiphenidyl, but no improvement was obtained. She was admitted again in psychiatric clinic, in February 2016, where assessment showed neurocognitive major disorder (Mini Mental State Examination-MMSE=16/30, Sunderland clock Test 2/10) and movement disturbances, so clinical aspect was considered an organic catatonic disorder. A CT scan was performed and showed global cerebral and cerebellar atrophy, without other pathological features. She was discharged with indication of therapy with rivastigmine, combination Levodopa/carbidopa and amilsulpride, and she was referred to our department for neurological assessment.

When admitted, general examination showed a patient with low weight (body mass index BMI=17) and orthostatic hypotension (110/60 mm Hg in clinostatism and 70/60 mm Hg in orthostatism).

Neurological examination revealed: anterior flexion of the trunk, possible walk with unilateral support, with small steps, without balance of arms, bilateral resting and postural tremor in upper limbs, hypomimia, slight dysphagia for solids and liquids, general bradykinesia, generalized rigidity with bilateral cogwheel sign, absence of pathological reflexes and exaggerated postural reflexes.

Psychiatric examination showed a patient in a neat hospital outfit, with fixed gaze, hypomimia and bradykinetic gestures; mentally and visually contact relatively easy to maintain; partially oriented allo and autopsychic; bradykinesia; auditory hallucinations, with mystical and mandatory content; spontaneous and voluntary hypoprosexia; fixation and evocation hypomnesia; bradypsychia, reduced capacity of associations and abstracting; depleted spontaneous language; depressed mood; hypobulia; no instinctual disorders; without any sleep disorders; reduced output performance; partial insight.

A detailed medical history revealed that patient also had visual hallucinations, well formed and detailed, although auditory hallucinations were predominant.

We tried to perform cerebral MRI, but because of persistent auditory and visual hallucinations, it was impossible, investigation should have been done with sedation.

Considering all data we established that there were met criteria for diagnosis of Probable Dementia with Lewy body, as two core features for diagnosis were fulfilled according DSM 5 and McKeith criteria.

We decided to initiate antipsychotic therapy with atypical antipsychotic without affinity for D2 receptors (quetiapine) (8), considering that in fact this one hasn't been tried before, even thought it was for first intention and we realized the switch, with a good outcome. It was also initiated a treatment with mineralocorticoids (fludrocortisones) for orthostatic hypotension, with great improvement of

balance and gait. For cognitive disturbance it was continued treatment with rivastigmine (6).

After six months patient came in clinic for revaluation of neurological and psychiatric status and examination showed a good evolution with stationary parkinsonism, but persistent hallucinations.

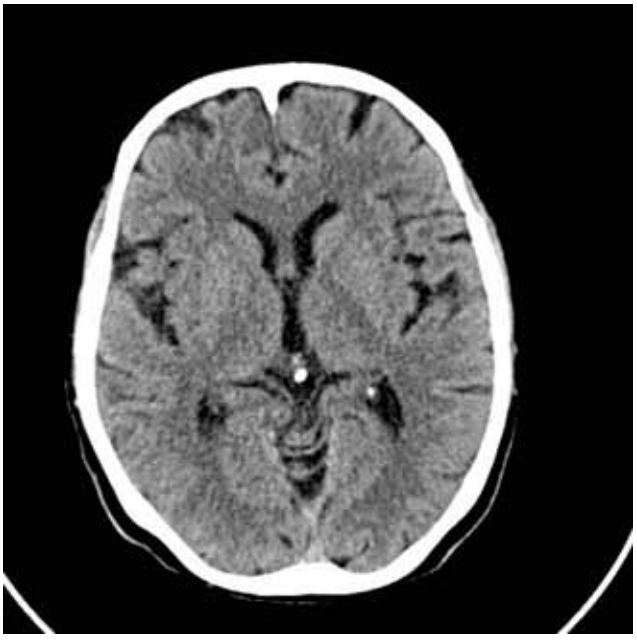

FIGURE 1. *Axial section: uniform cortical atrophy on frontal and temporal lobes*

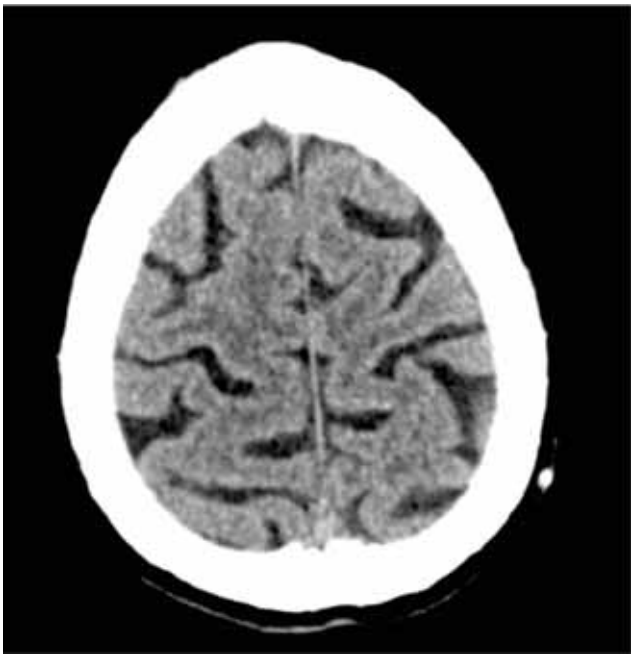

FIGURE 2. *Axial section: frontal lobe atrophy*

In January 2017, after one year after diagnosis was made, patient came in clinic for a clinical revaluation. Her outcome was very good, with few extrapyramidal signs, but persistent orthostatic arterial hypotension, persistent auditory hallucinations with religious content, but without behavioural manifestations; she have had a slight change of mood in last two months, with discrete hypomania, with hyperbulia and increased vital energy, symptoms for which is was started by the treating psychiatrist, a therapy with 300 mg sodium valproate daily. Instead, patient presented a good outcome in neurocognitive status evaluation with MMSE=25/30 and a Sunderland clock Test of 8/10.

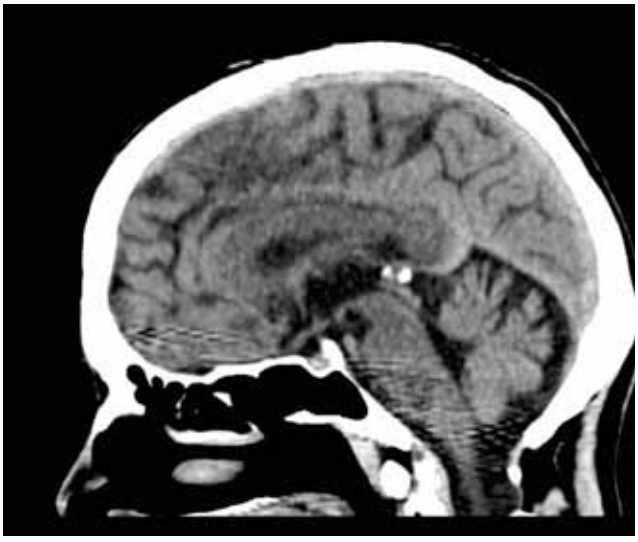

FIGURE 3. *Sagittal section: cortical and cerebellar atrophy*

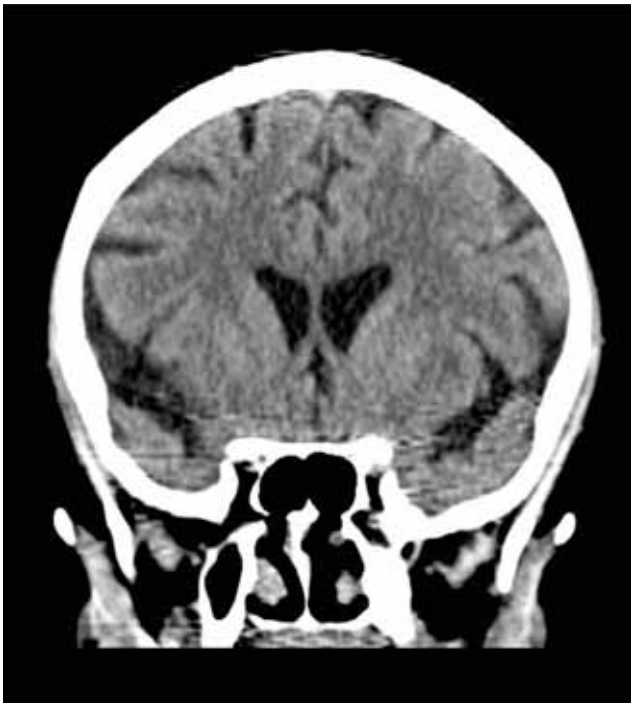

FIGURE 4. *Coronal section: symmetrical cerebral atrophy*

We performed a control CT scan which revealed global cerebral and cerebellar atrophy in contrast of the biological age, without other pathological features. Despite good clinical neurological and psy-

chiatric evolution, it was not possible to perform a cerebral MRI, because our patient refused this kind of investigation, based on her mood changes.

CONCLUSIONS

Probable disease was established because we had two core features of the disease: recurrent visual hallucinations and spontaneous features of extrapyramidal syndrome. At the same time temporal sequence of symptoms occurred in a concurrently way, first neurocognitive troubles and afterwards parkinsonism.

Dementia with Lewy Body is an under-diagnosed disease, as clinical thinking is of priority, there are no biomarkers yet available for diagnosis and at least in our country, single-photon emission computed tomography (SPECT) perfusion and MRI morphometric imaging even though are useful to distinguish DLB, corticobasal syndrome (CBS), Creutzfeldt Jacob Disease from Alzheimer Disease (9), are not of applied use, because of low practical availability and high costs. Any psychiatric symptoms in old age patients must be carefully investigated and monitored, as purely psychiatric disorders are extremely rare in this age. Almost in all cases there are underlying pathologies.

At the same time, dementia type is important because of long term management, especially of behaviour and psychiatric symptoms difficult to assess in certain condition, with a great impact on caregivers.

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