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Research Article

Retinal Examination in Lewy Body Dementia

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Abstract

Aim: To detect Alpha- synuclein and Lewy bodies in the retina of patients with Lewy Body Dementia (LBD).

Methods: 5 patients with probable LBD were examined with fundus autofluorescein (FAF) and optical coherence tomography (OCT). FAF revealed hypo and hyperfluorescent lesions. OCT was performed through these lesions to detect abnormal accumulations. Also, 5 age-matched healthy controls were examined.

Results: Alpha- synuclein and Lewy bodies were detected in 4 patients. No lesions were observed in the control group.

Conclusion: Retina examination by OCT and FAF reveals aggregations exactly similar to the histopathological images of Alpha- synuclein and Lewy bodies in live patients with LBD.

Keywords: *Retina; Lewy Body Dementia*

Introduction

Lewy body dementia (LBD) is a kind of an umbrella term for two related diseases. It refers to both Parkinson's disease (PD) dementia and dementia with Lewy bodies. Some symptoms of these two diseases differ, but reflect the same underlying pathological changes in the brain. In the long term, people with both diseases will develop very similar cognitive and behavioral symptoms [1,2]. Patients with LBD have Lewy bodies in the mid-brain region (similar to those with PD) and in the cortex of the brain. They may also have the plaques and tangles of the brain that characterize Alzheimer's disease (AD). Because of this overlap, many patients with Lewy body disease are misdiagnosed as having either PD or AD [1,2].

Patients with LBD have cognitive problems similar to those that occur in AD. Motor problems are less severe compared to PD ; most commonly an impairment in walking and then muscle stiffness are observed. Tremor is less common. Visual hallucinations and delusions are frequently described [3].

Pathophysiology of LBD

LBD is characterised by eosinophilic intracytoplasmic neuronal inclusion bodies (Lewy bodies) in the brainstem and neocortex. A Lewy body is composed of the protein alpha-synuclein along with ubiquitin, neurofilament protein, alpha B crystallin, and glucocerebrosidase (Goker-Alpan., *et al*. 2010). Pathologically, Lewy bodies are present in a pattern more widespread than usually observed in PD. Also, alpha-synuclein aggregates by unknown mechanisms, but it is hypothesized that overproduction of alpha-synuclein and abnormal forms of other proteins lead to abnormal aggregation [4]. Retinal pathologies in the LBD and PD groups were attributed to alterations in the photoreceptor cells, which were accompanied by an increase of 'pale inclusions' in the inner plexiform layer. Immunocytochemical staining in postmortem eyes revealed that the distribution of alpha-synuclein was diffuse in LBD, but mostly in inner plexiform and nuclear

layers plus ganglion cell layer. As a result of these accumulations, optical coherence tomography demonstrated inner retinal thinning in patients with PD and LBD 5).

Material and Methods

We examined 5 patients diagnosed preliminarily with probable LBD at a neurology institute . The mean age was 71 (range between 64 and 78). All patients had fundus autofluorescein (FAF) and optical coherence tomography (OCT) examinations. The regions with hyper and hypo- fluorescence were examined by OCT to find the layer of the lesions. Also, 5 age- matched healthy controls were observed by FAF and OCT.

Results

In 4 patients we were able to find alpha-synuclein and Lewy bodies by OCT (Figures 1, 2). The lesions were detected in the hyper or hypofluorescent regions on FAF (Figure 3). None of the controls disclosed such lesions on OCT. Alpha- synuclein extended from the outer nuclear into the inner nuclear layer while the Lewy body occupied a large portion of the retina. Autopsy of 1 patient revealed alpha-synuclein and LBs in the retina (Figures 4-6). The other patients were still alive.

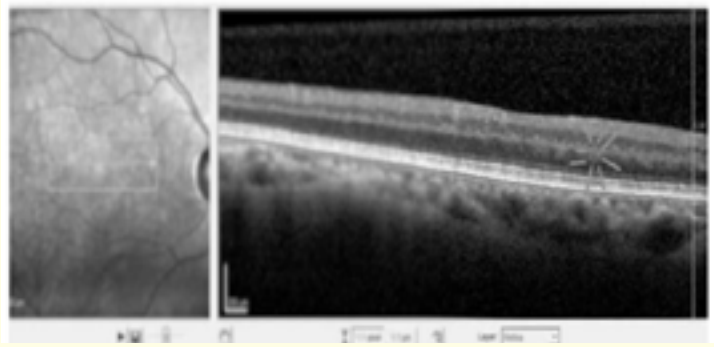

Figure 1: *OCT image of Alpha-synuclein.*

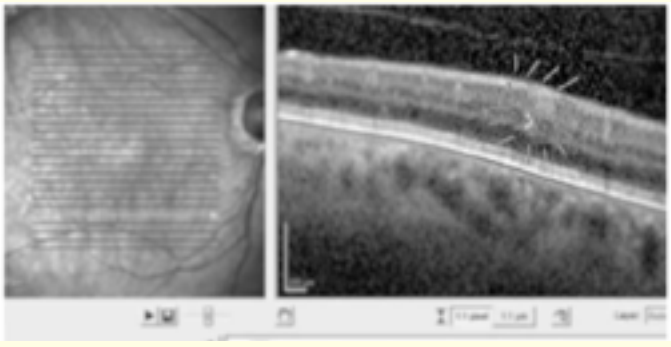

Figure 2: *OCT image of a Lewy body.*

Figure 3: *FAF image. Hyperfluorescent lesions in retina.*

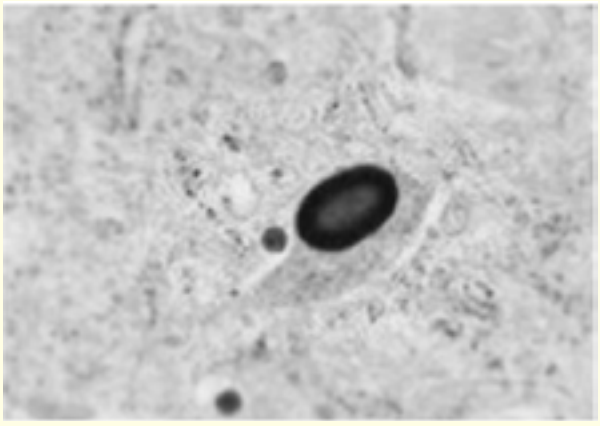

Figure 4: *Histopathological image of Alpha-synuclein.*

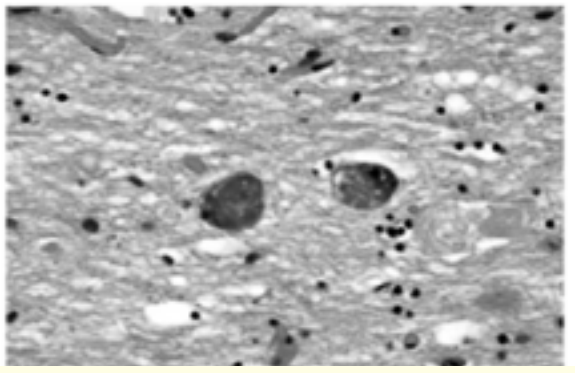

Figure 5: *Histopathological image ofa Lewy body.*

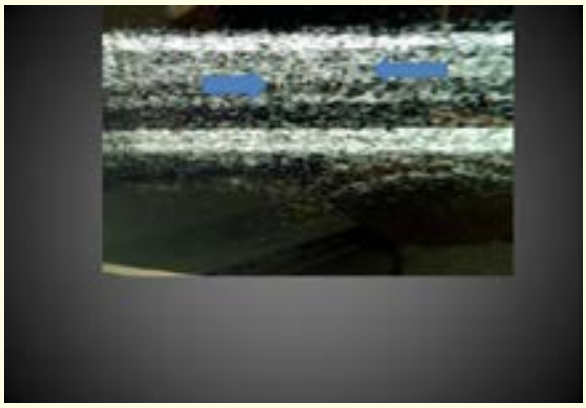

Figure 6: *OCT image of a Lewy body.*

Discussion

Prior immunocytochemical studies showed alpha-synuclein and Lewy Bodies in the retina of postmortem eyes. The presence of these misfolded proteins may explain the reason of the visual complaints in PD and LBD patients. The aggregation of alpha-synuclein is the hallmark of PD while depositions of Lewy bodies are the hallmark of LBD [6]. The exact similarity of alpha-synuclein and Lewy bodies detected by OCT in the retina with the histopathological images convinces us that it is possible to detect these misfolded proteins by retinal exam (Figure 4,5). OCT examination is easy and helpful for the confirmation of the diagnosis. There are studies that show there is spread of alpha-synuclein from neuron to neuron. Since there are no conventional synapses between amacrine cells and ganglion cells in the retina, alpha- synuclein needs another route to reach the ganglion cells and from there to brain via the optic nerve. Exosomal transport and endocytosis have been the proposed mechanisms of this transport. The fact that α-synuclein can be released in association with exosomes and extracellular vesicles strongly suggests that these might constitute the primary vehicles of cell-to-cell transmission of the protein, preserving it from degradation by extracellular enzymes and facilitating its correct targeting toward recipient cells [7]. These evidences strongly support that α-synuclein spreading could very well contribute to synaptic impairment in LBD. The detection of alpha-synuclein and Lewy bodies in the retina may be important for the early detection of both PD and LBD. Early diagnosis may allow time for important early treatment that may extend quality of life [8,9]. LBD can be difficult to diagnose, and patients with this disease are often mistakenly diagnosed as having AD or sometimes vascular dementia. Tests for conditions other than dementia that can cause similar symptoms also need to be carried out [1]. The OCT studies showed the thinning of the inner layers of the retina plus retinal nerve fiber layer damage [10]. But, the misfolded proteins were not shown by OCT in any studies in live patients. Our study is an important step towards the demonstration of Lewy bodies and alpha-synuclein in retina of live LBD patients which can also confirm the diagnosis.

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