

## Brain Histopathology of Cynomolgus Monkey (*Macaca fascicularis*) with Memory Impairment Indicated by Alzheimer Type Neurodegenerative Disease.

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### INTRODUCTION

The study is about the degenerative lesion found in nine cynomolgus monkeys that showed decline cognitive function during their old age life. In previous studies, the brain of these cynomolgus monkeys has been tested positive for amyloid deposits by using the ELISA test.

### MATERIALS AND METHODS

The paraffin blocks from nine individual of cynomolgus monkey brains are accepted in the pathology division, in the process for making HE stained histopathology slide. The lesions found were to be matched with Alzheimer's disease literature in humans in other journal.

### RESULT AND DISCUSSION

Some neurons lesion are clearly seen using HE staining are predominantly the neurofibrillary tangle (NFT) sediment deposits inclusion, granulovacuolar disease (GVD), neuron necrosis or apoptosis and amyloid senile plaque (SP). Those lesions are recognized as a marker characteristic of Alzheimer's neurons in humans.

NFT is a pile of proteins found first by Alois Alzheimer in the Alzheimer's neurons. The neurofibrillary tangle consists of abnormal accumulations of abnormally phosphorylated tau within the perikaryal cytoplasm of certain neurons. When the neurofibrillary tangle occurs within a neuron with a more rounded configuration, the inclusion appears as interweaving swirls of fibers, and here it is called a globoid neurofibrillary tangle (Perl 2010).

Granulovacuolar degeneration involves the accumulation of large, double membrane-bound bodies within certain neurons, which suggested that the bodies are related to autophagic organelles (Funk *et al.* 2011)

Apoptosis and necrosis can be discriminated by a number of morphological characteristics of shrink neuron. To describe the specific mechanisms of cell death occurring during neurodegenerative disorders, such as Alzheimer's

disease many investigations, have attempted to label the particular pathway of cell death either as apoptosis or as necrosis (Behl 2000).

The senile plaque consists of a central core of beta-amyloid, a 4-kD peptide, surrounded by abnormally configured neuronal processes or neuritis (Perl 2010).

The findings of lesions analyzed with qualitative and semiquantitative methods with the aid of image J software. Lesions namely level 0 if no lesions are found, I if there are <25% lesion, II if there are 26-50% lesion, III if there are 51-75% lesion, and IV if there are 76-100% lesions (Gibson-Corley *et al.* 2013).

The *neurofibrillary tangle* observations on 100 of neuron cells show there are two individuals at level 0, five individuals at level I and two individuals at level II. Whereas, in observing the hippocampal region of two individuals, both show severity at level II, there are two individuals at level 0, five individuals at level I and two individuals at level II. Meanwhile, in observing the hippocampal region of two individuals, which show severity at level II.

The *granulovacuolar* disease lesion analysis results in the mediotemporal region with the semiquantitative method of ordinal type are two individuals at level 0, and seven individuals at level I. Observations on two individuals are observed in the hippocampal region, namely both at level I. The granulovacuolar disease lesion analysis results in the mediotemporal region with the semiquantitative method of ordinal type are two individuals at level 0, and seven individuals at level I. Observations on two individuals are observed in the hippocampal region at level I.

Lesion *necrosis / apoptosis* which only found in one individual based but the lesion reaches the degree of level IV (95%).

Only one individual showed lesion resembled *Senile Plaque* in humans. The lesion is found in the mediotemporal region as diffuse subtype of circled of eosinophilic area surround some neurons.

## CONCLUSION

Since many lesion similarities between humans and monkeys cynomolgus, the study can be a hint of the use of monkeys that are subjected to naturally degenerative brain lesions as a model of research on degenerative diseases in humans.

## REFERENCES

- [1] Behl C. 2000 Apoptosis and Alzheimer's disease, *J Neural Transm (Vienna)*. 107(11):1325-44.
- [2] Funk KE, Mrak RE, Kuret J. 2011 *Neuropathol Appl Neurobiol*. 37(3): 295-306.
- [3] Gibson-Corley KN, Olivier AK, Meyerholz DK. Principles for valid histopathologic scoring in research. 2013. *Vet Pathol*. 50(6).
- [4] Perl DP. 2010 Neuropathology of Alzheimer's Disease, *Mt Sinai J Med*. 77(1): 32-42.