MM1

History of clarifying pathogenesis of neurodegenerative disease and development of neuropathology

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In this lecture, I would like to talk about the role of neuropathology in nearly 50 years of effort in clarifying pathogenesis of neurodegenerative disease. After graduating from medical school in 1969, I majored in neurology and had been engaged in research and education of neuropathology thereafter. I would like to talk about 4 diseases in particular, i.e., spinocerebellar degeneration, Lewy body disease, progressive supranuclear palsy (PSP), and amyotrophic lateral sclerosis (ALS), in regard to the changes within the history of disease concepts, neuropathological features, and the history of clarifying pathogenesis.

As for spinocerebellar degeneration, I'd like to address the themes ranging from the historical descriptions of sporadic olivo-ponto-cerebellar atrophy, striatonigral degeneration, and Shy-Drager syndrome to disease concept proposal of multiple system atrophy, and discovery of glial cytoplasmic inclusion and of α-synuclein as a causal protein. Also, for hereditary case, I'd like to review disease classification by identifying causal genes, understanding of triplet repeat disease, and the significance of intranuclear inclusion.

As for Lewy body disease, I'd like to review the history of Parkinson's disease, which began from the description of Lewy body, establishment of concept of dementia of Lewy body disease as dementia, α-synuclein deposition, development of intracerebral lesions, and pathological changes of whole body organ.

As for PSP, I'd like to talk about the history of PSP and corticobasal degeneration, neuropathological characteristics, development of neuropathological staining technology, establishment of roles of glial cell, and 4R tauopathy.

For ALS, I'd like to talk about the characteristics of classic ALS, ALS with dementia (ALS-D), frontotemporal degeneration with ubiquitin positive inclusion (FTLD-U), TDP-43 discovery, importance of frozen brain and brain bank, a new classification of frontotemporal degeneration (FTLD).

Lastly, I would like to emphasize the importance of neuropathology to young generations who are studying neuropathology. Looking back at the historical transition of neurodegenerative diseases, understanding of neuropathology is essential for the establishment of disease concept, interpretations of images such as magnetic resonance imaging (MRI), association with clinical neurological symptomatology, and clarification of molecular biological genetic research.

MM2

Developmental Neuropathology

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In the process of normal brain development, cascade of molecular as well as structural alterations take place. The formation of the brain is very complicated process. It is quite astonishing to learn how precisely normal developmental process proceed. Any deviation from the normal development results in a formation of "abnormal brain". The resulting brain contains basic components of the normal brain but assembled in an abnormal way. Depending on the extent of deviation, the brain may show uniquely specific pathological outcome, regardless of the specific etiologic factors. Etiologic factors that initiate molecular and structural abnormalities are variable and the timing of the insult on the developing brain is important determining factor on the outcome of the pathological phenotype. In my lecture, I would like to review the basics of neuropathology in the pediatric age-group.

For the matter of convenience, I will select 4 major stages (periods) of brain development and discuss the pathological changes. The 1st stage is the stage of neurulation (neural tube formation), The 2nd is the stage of ventral induction (prosencephalon formation and midline patterning). The 3rd stage is the period of the brain growth, cellular proliferation and migration. The 4th stage is the 2nd half of fetal life to postnatal years and period of cerebral cortical organization. Deviation from the normal developmental pattern during the 1st, 2nd and 3rd period results in the uniquely and grossly abnormal brain but pathologic changes during the 4th period may be very subtle on routine morphological examination of the brain.

Reference:
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Adle-Biassette H, Harding, B.N, Golden, J.A.: Developmental Neuropathology, 2nd edition (Willey Blackwell)
Suzuki, K. Neuropathology of Developmental abnormalities. (Review Article) Brain and Development 29 (2007) 129-141.

MM3

What I have learnt from muscle research

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1) Back ground

When I graduated Kumamoto University Medical School around 50 years ago, most of patients with muscular dystrophies had stayed in home with no education and no medical care. There was very heavy discrimination against muscular dystrophies. Then our Government started to establish special muscle disease units in 27 National Sanatoria Hospitals where small children had education and rehabilitation. I worked in one of the hospital and tried to establish a small diagnostic laboratory.

2) Muscle histochemistry

A. Fixation for frozen sample

Dip the sample quickly in isopentane cooled by liquid nitrogen or in mixed solution of dry ice and acetone; SHAKE the tissue in solution for 1 min.

B,. ATPase staining

Try pre-incubation solution at various pHs (pH 10.5, 10.6, 10.7, 10.8 10.9 and 11.0) , (pH 4.7, 4.6, 4,5, 4.4, 4,3 and 4.2) and select the best differentiated one

C. PAS (periodic acid Schiff) staining for glycogen

Since glycogen particles are washed out during staining for frozen section, please use epoxy resin 1μm section in Schiff solution for 1 hour.

3) Electron microcopy (EM)

An important way to know pathogenetic mechanism (!) ,

Electro-cytochemistry (cytochrome C oxidase: COX EM) is also available

4) Muscle imaging

Muscle CT/MRI is useful to know disease distribution and to select the best muscle for biopsy. There are many disease specific neuro-imaging features.

5)-Muscle tissue repository

For future research works and gene counseling all muscle biopsies must be kept

In deep freezers at -80 degrees in centigrade.

MM4

History of brain tumor classification

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Tumors developed in the cranial cavity are called brain tumors. Their cells of origin are multiple, including neuroepithelial cells, meningothelial cells, nerve sheath cells, mesenchymal cells and so on. Accordingly, there are many tumor types and subtypes: for example, more than 160 tumors are listed in the current WHO classification. It is, therefore, essential to classify correctly these tumors for the management of patients as well as for basic investigation. More than a century ago, brain tumors were classified according to their macroscopic and microscopic features. These schemes are called “morphological classification”. In the early 20th century, neuropathologists became to classify tumors based on their cells of origin and cellular developmental stage. This kind of scheme is called “histogenetic classification”. The representative one is a classification published by Bailey and Cushing in 1926. In the mid-20th century, the concept of grading was introduced in the brain tumor classification. Grading of tumor became popular among clinicians and general pathologists. Meanwhile, the international classifications, particularly those planned and published by WHO, are now a standard of brain tumor classification, and have been used worldwide. The first edition of WHO's was published in 1979, and several revisions have been made until now. The latest edition is characterized by the inclusion of genetic abnormalities in the nomenclature of tumors. Advancement of pathologic methods was another important driving force for the development of classification. Lastly, the future perspectives of brain tumor classification will be presented.