Histopathological Changes of the Hypophysis in Malnutrition in Elderly Subjects

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Abstract Major objectives in forensic gerontology are physical and mental disorders during aging, which can be caused by various factors involving nutrition and stress, often accompanied by dysfunction in the neuroendocrine systems including the hypophysis. The objective of the present study was to investigate the histopathological changes in the adenohypophysis in elderly subjects using autopsy materials. Hypophyses with a scaphoid shape (group S: 16 males and 4 females; mean age, 78.6 years) and a normal one (group C: 30 males and 20 females; mean age, 65.2 years) were compared. Incidence of the scaphoid-shaped hypophysis mildly increased with age, being 17% in the elderly over 65 years of age. The weight of the pituitary gland in group S (0.42 ± 0.1 g) was lower than that of group C (0.65 ± 0.2 g). The degree of fibrosis was higher in group S (31.6% ± 5.4%) than in group C (18.3% ± 6.3%). Immunohistochemical staining showed no significant differences in the proportion of the ACTH cells and the TSH cells between the two groups (p>0.05). However, there was an increase in the proportion of gonadotrophs, prolactin cells, and S-100-containing cells in group S and a decrease in that of GH cells (p<0.05). These findings may be associated with reduced anabolic, gonadal and hepatic functions due to malnutrition.

Key Words: human pituitary, immunohistochemistry, malnutrition, morphology, neuroendocrine.

Introduction

Retrogressive changes and reduced mental activity due to aging vary greatly among individuals. These are probably associated with individual and environmental factors. Major objectives in forensic gerontology are physical and mental disorders during aging, which can be caused by various factors involving nutrition and stress, often accompanied by functional abnormalities of the neuroendocrine system involving the hypophysis. In postmortem investigation, pituitary glands of a scaphoid shape are often observed in elderly undernourished subjects, suggesting some factors of aging depend on nutritional conditions. However, there appears to have been no investigation on the causal mechanism and endocrinological significance.

The objective of the present study was to examine the scaphoid-shaped hypophyses in elderly subjects with regard to the micromorphology and immunohistochemistry of hormone-producing cells and S-100 protein-containing cells.

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Materials and Methods

Specimens

The hypophyses from 70 autopsy cases (46 males and 24 females; 30-88 years of age; 6-48 h postmortem) were studied. Hypophyses with a scaphoid shape (group S: 16 males and 4 females; mean age, 78.6 years) and a normal shape (group C: 30 males and 20 females; mean age, 65.2 years) were compared. Both the cases with normal shaped hypophyses and the cases with scaphoid shaped hypophyses were selected from with groups the same cause of death. 10 serial frontal sections (4μm thick) of each of the anterior, middle and posterior one-thirds of pars distalis were made from formalin-fixed, paraffin-embedded specimens. These tissue sections were used for hematoxylin-eosin (H&E) staining for light microscopy, immunostaining to identify hormone-producing cells, and Azan-staining to examine fibrosis.

Immunostaining procedure for light microscopy

For immunostaining, tissue sections were incubated at 4°C overnight with the following primary antibodies: rabbit anti-human growth hormone (GH) (22K) serum (NIDDK, Maryland, USA, 1:8000), rabbit anti-human prolactin (PRL) serum (Biogenisis, New Hampshire, USA, 1:5000), rabbit anti-human luteinizing hormone (LH) serum (Scantibodies Laboratory, Inc, CA, USA, 1:7000), rabbit anti-human follicle stimulating hormone (FSH) serum (Scantibodies Laboratory, Inc, CA, USA, 1:7000), rabbit anti-human thyroid-stimulating hormone (TSH) serum (NIDDK, Maryland, USA, 1:5000), as well as rabbit anti-adrenocorticotropic hormone (ACTH) (1-24 N-terminal) serum (1:8000) and rabbit anti-human S-100 protein serum (1:5000), which were provided by the Department of Anatomy, Jikei University, School of Medicine. Immunoreactions were detected by the avidin-biotin-complex (ABC) method using the diaminobenzidine (DAB) stain to visualize the immunoreactive product, followed by counterstaining with hematoxylin.

Fractionation calculation of hormone-producing cells was measured using an Olympus SP 1000 image-analyzer (Olympus, Tokyo, Japan) following the method of Takanashi et al. Statistical analysis

The Student's t-test was used for testing statistical significance.

Results

Macromorphology and incidence

An example of scaphoid-shaped hypophysis is shown in Fig. 1. This type was found in 20 cases (58-85 years of age) among 325 subjects examined (around 6%). The incidence was increased in the elderly over 65 years of age: 38 of 221 cases (17%). The average age of the group S (78.6 years) was higher than that group C (65.2 years), although a significant difference was not noted (p>0.05). No difference was noted in Body Mass Index (BMI) between males and females (p>0.05) in both groups. The weight of the hypophysis was significantly smaller for the group S (0.42±0.1 g) compared with the group C (0.65±0.2 g) (p<0.05). A comparison of the groups C and S using BMI indicated that the group S had a significantly lower BMI than the group C, independent of gender (Table 1).

Light microscopic study

Cells containing one or two ring-shaped structures in the cytoplasm were often noted in the adenohypophysis in the group S (H&E stain, Fig. 2 and 3). Signetting in gonadotroph was immunostained weakly with anti-human LH (DAB stain, Fig4).

Fig. 1: Morphological change of the hypophysis into a scaphoid shape accompanied by undernutrition.