Studies on changes in diagnostic markers for metabolic disorders in healthy cats with aging

Summary of doctoral thesis

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In our country, super-aging society is expanding at a speed that is so fast that we don't see it in the world. Non-communicable diseases (NCDs) such as obesity, diabetes and cancer have increased with progress of super-aging society. It is difficult to cure NCDs completely, so that preventive medicine is useful for these diseases. In recent years, the life span of dogs and cats has significantly extended, and the number of animals over 15 years old is increasing. The number of age-related diseases of animals as well as human is increasing, and it is necessary to respond from a different viewpoint from conventional veterinary medicine.

In this story, we investigated changes in body weight and body condition score (BCS) and blood biochemical diagnostic markers with aging in healthy cats visited for a medical examination. We attempted to create especially standard values for each age for diagnostic markers related to lipid metabolism. Preventive medicine, especially early diagnosis is necessary to establish the appropriate diagnostic markers, so that the standard values for each age is useful for early diagnosis of animal diseases.

1. In recent years, the average life span of cats has extended significantly. The development of veterinary medicine and changes in food environment and breeding environment are main factor of extended life span of cats. The average life span of cats is considered to be 14.2 years, so it has extended 0.5 years (6 months) during 10 years from 2008 to 2017. But the extended life span of cats has occurred new problems. It is increase of various diseases with aging. We think that the incidence of chronic kidney disease, tumors, motor organs disease and dementia may increase with aging, and the number of cases requiring care also may increase. Animals as well as owners are aging. A new problem that older people have provided care for older pets occurs. In our country, the birthrate is decreasing and the population is aging rapidly, and the quality of medical care required by society is

changing significantly. The incidence of NCDs such as obesity, diabetes, and cancer is increasing, so that it is a major social problem in countries around the world. In recent years, the number of dogs and cats over 15 years old at home has increased remarkably, which is equivalent to 75 years old of human, and the number of NCDs with aging also has increased because of the extension of life span due to the progress of veterinary medicine and changes in lifestyle. Early diagnosis and treatment are useful for these diseases. Therefore, the new animal medical systems that the preventive medical care for animals for individuals by early diagnosis and treatment is marked. Obesity is a model for this system. It is necessary to develop appropriate diagnostic markers for the early diagnosis with aging. It is necessary to investigate changes in diagnostic markers in healthy cats with aging because these markers change with aging.

2. In dogs and cats, there is no appropriate index like a human's body mass index (BMI: body weight kg ÷ height m^2). Instead, the body condition score (BCS) is used. In this chapter, we examined changes in body weight and BCS of healthy cats with aging. The animals were divided into 5 groups with age: New born (≤1 years), Young (1 ～ ≤5 years), Middle (5 ～ ≤10 years), Old and Old-thin (10 years ～). Comparing the average of Young group and Old group, age was 2.7 ± 0.2 years and 12.1 ± 0.4 years, weight was 4.1 ± 0.2 kg and 4.8 ± 0.3 kg, and BCS was 5.5 ± 0.2 and 6.6 ± 0.3. It was clarified that the blood lipid concentration of the healthy cats increases with increase of the weight and BCS with aging. Cats are more likely to be obesity than dogs, and the rate of obesity has increased in various regions in recent years. The incidence is 30-40% and tends to increase all over the world. This survey found that 31.3% of the total were overweight and obese. However, it is expected that the ratio of obesity in the actual visiting animals will be higher because the subjects are the animals taking

medical examinations who are interested in health care. Obesity is a risk factor for NCDs involving in the causes of death in many people. It is difficult to cure NCDs completely, so that "not obesity" is most effective. In other words, appropriate early diagnosis is necessary to quickly respond to NCDs such as obesity.

3. We investigated changes in glycolipid metabolites, hormone concentrations and enzyme activities in healthy cats in general veterinary clinic. So, glucose (GLU), triglyceride (TG), albumin (ALB), malate dehydrogenase/lactate dehydrogenase (M/L) ratio, serum amyloid A (SAA), AMP activated protein kinase (AMPK) in serum changed with aging. TG concentrations (mean $\pm$ SE) in serum of Old group (108.2 $\pm$ 28.8 mg 100 mL^{-1}) were statistically significantly higher than those of Young group (40.7 $\pm$ 7.1 mg 100 mL^{-1}). SAA concentrations in serum of Old group (84.7 $\pm$ 38.4 ng mL^{-1}) were higher than those of Young group (22.5 $\pm$ 10.9 ng mL^{-1}) but there was no statistically significant difference. Adiponectin (ADN) concentrations in serum of Old group (4.7 $\pm$ 1.0 μg mL^{-1}) were lower than those of Young group (5.3 $\pm$ 0.9 μg mL^{-1}) but there was no statistically significant difference. It is suggested that healthy cats decrease energy metabolism on lipid metabolism with aging, which reflects the result of the previous chapter. Obesity and obesity diseases have involved in various factors by individual such as gene, nutrition, and lifestyle. In the veterinary field, the number of elderly animals is increasing as well as humans and NCDs such as diabetes, kidney disease and obesity are increasing, it is necessary to respond them. From this result, GLU, TG, ALB, M/L, AMPK, SAA, and ADN were useful markers for detecting early small changes in metabolic diseases. In addition, it is important to find the early stage of obesity by doing regularly physical examinations and using of these

markers because obesity increases the risk of various metabolic diseases such as diabetes and cancer.

It is necessary to be changed standard value of the marker with aging because energy metabolism changes with aging. We attempted to establish standard value with aging for TG, ADN, SAA, and M/L ratio related to lipid metabolism by study so far. For TG concentrations, the upper limit is set to 45 mg / 100 mL for Young group, 70 mg / 100 mL for Middle group, and 120 mg / 100 mL for Old group, and it is possible to diagnose early for hyperlipidemia if the value exceeding 50% is used as the standard for hyperlipidemia. It is possible to diagnose early various diseases with obesity if the standard values of adiponectin and SAA respectively define 2.0 µg mL^{-1} as low limit value and 200 ng mL^{-1} as upper limit value for Old group because it is a diagnostic standard for dyslipidemia that increases with aging. In addition, AMPK activity is also one of the markers to attend in the future that decreases with aging and lead to an extension of lifespan.

In the future, it will be necessary to set more accurate standard values by accumulating various data and to attend other markers such as immunity, so it is possible to apply this initiative to human with a declining birthrate and an aging population.