Lipomatosis of axillary lymph nodes in a cynomolgus monkey (Macaca fascicularis)

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Abstract: Lipomatosis of lymph nodes is defined as the replacement of the lymphatic parenchyma by adipose tissue which grows in the node from the hilus toward the cortical zone. In humans, it is considered as part of the normal aging process and is common in obese patients, but there are no reports in non-human primates. In this report, we describe the first case of lymph node lipomatosis in the bilateral axillary lymph nodes of a young adult cynomolgus monkey. Macroscopically, there were no apparent abnormalities in the axillary lymph nodes on either side, and their volumes were unchanged. At the cut surface, pale yellow fat-like tissue was observed in the medullary area. Histopathologically, well differentiated adipocytes replaced a large part of the lymphatic parenchyma in the area from the hilus to the medulla without any malignant findings. Based on these findings, the patient was diagnosed with lipomatosis of the lymph nodes. (DOI: 10.1293/tox.2021-0054; J Toxicol Pathol 2022; 35: 113–116)

Key words: lipomatosis, adipocytes, axillary lymph node, cynomolgus monkey, spontaneous lesion

Lipomatosis of lymph nodes is the replacement of lymphatic parenchyma by adipose tissue which grows in the node from the hilus toward the cortical zone1,2 and is regarded as a non-malignant change and a part of the normal aging process in humans3,4. Lipomatosis of lymph nodes is also called fatty infiltration1, lipomatous atrophy2,5, fatty replacement4, or fatty change5,6. Lipomatosis has been observed in the axillary lymph nodes of aging mice7, but to our knowledge, there have been no reported cases in non-human primates. Here, we describe a case of spontaneously arising lipomatosis of the axillary lymph nodes in a cynomolgus monkey.

A six year old male cynomolgus monkey (Macaca fascicularis) of Cambodian origin was purchased from Shin Nippon Biomedical Laboratories, Ltd. Blood was sampled without any test article treatment. No remarkable findings were observed in the clinical observations or blood tests from routine medical examinations, and the final body weight was 6.5 kg. At necropsy, only involution of the thymus was observed. All animal procedures were conducted in accordance with the Chugai Pharmaceutical Guide for the Care and Use of Laboratory Animals, and all experimental protocols were approved by the Institutional Animal Care and Use Committee.

All tissue sections embedded in paraffin were stained with hematoxylin and eosin (HE), and the sections of the axillary lymph nodes were stained with azan stain using standard methods. Frozen sections were used for Oil Red O staining of the axillary lymph nodes. For immunohistochemical analysis8, the sections of the axillary lymph nodes were subjected to primary antibody against Ki-67 (SP6, rabbit monoclonal anti-Ki-67, Abcam, Cambridge, UK, ab16667) to analyze the proliferative activity of adipocytes. The sections were incubated with goat anti-rabbit secondary antibody (Dako, Glostrup, Denmark, E0432) followed by incubation with avidin-biotin-peroxidase complex (ABC peroxidase standard staining kit, Thermo Fisher Scientific, Waltham, MA, USA). The reaction was visualized using 3,3-diaminobenzidine tetrachloride. Finally, the sections were counterstained with Mayer’s hematoxylin.

On microscopic examination, the medullary lymphatic parenchyma was replaced by adipose tissue-like structures, and the medullary area, including the hilus, expanded in both the axillary lymph nodes (Fig. 2a, 2b). Adipose tissue-like structures were composed of Oil Red O positive well-differentiated adipocytes, with a single large fat droplet in the cytoplasm and peripherally located nuclei (Fig. 2c). The

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adipose tissue that mainly occupied the area from the hilus to the medulla was focally located adjacent to the paracortical area, but the adipocytes did not show invasive growth and cellular atypia (Fig. 2d). There were few morphological changes in the cortical area, except for the vague formation of germinal centers (Fig. 2e). The periphery of the axillary lymph node was covered with a fibrous capsule, and intranodal adipocytes did not infiltrate the adjacent adipose tissue beyond the capsule (Fig. 2f). Immunohistochemically, Ki-67 expression was detected in lymphocytes of the lymphoid follicles, but the increased number of adipocytes were negative for Ki-67 (Fig. 3).

In the present case, a large proportion of the medullary parenchyma of the bilateral axillary lymph nodes was occupied by adipose tissue without any malignant findings. This lesion was diagnosed as lipomatosis of the lymph nodes. To confirm whether lipomatosis appeared in other lymph nodes in this monkey, the mesenteric lymph node and pancreatic hilar lymph node were histopathologically examined. Lipomatosis was not observed in these lymph nodes (data not shown). There were no remarkable histopathological findings in other organs or tissues, except for some spontaneous changes.

The lesion in this case is a common finding in aged and obese patients and is not a malignant change. It is especially common in peripheral lymph nodes that usually receive little antigen stimulation, such as cubital, axillary, and popliteal nodes. Bilateral lipomatosis has been reported in the human axillary, cervical, and inguinal lymph nodes. Generally, in humans, adipose tissue replaces normal lymphatic parenchyma; therefore, nodal volume shows no change, but in some cases, lymph nodes may increase in volume. The axillary lymph nodes were not enlarged in the present case, but histopathologically, the adipose tissue replaced a large part of the medullary parenchyma. In cynomolgus monkeys, there are no previously reported lipomatosis cases; however, in a discussion among experts in experimental animal histopathology at an academic conference, a few specialists mentioned finding a similar lesion in the axillary lymph nodes of cynomolgus monkeys used in experimental animal histopathology at an academic conference. Reticular cells may be responsible for this lesion. In conclusion, the lymphatic parenchyma of both the axillary lymph nodes was replaced by adipose tissue without any malignant findings in a young adult cynomolgus monkey, and this lesion was diagnosed as lipomatosis of the lymph nodes. This is the first reported case of lipomatosis of lymph nodes in a cynomolgus monkey, and it is unclear whether lipomatosis is associated with aging and obesity or whether it occurs in a site-specific manner in this species.
Fig. 1. The macroscopic finding of axillary lymph node on one side. On the cut surface, a pale yellow fat-like tissue was present in medullary area. The nodal volume showed no change. Bar=2 mm

Fig. 2.

Fig. 3. Intranodal adipocytes were negative for Ki-67 immunohistochemical staining. (inner box: Lymphocytes of the lymphoid follicle were positive for Ki-67.) Bar=100 µm.
as in humans. More cases must be investigated to fully understand the etiology of lipomatosis of the lymph nodes in cynomolgus monkeys.

**Disclosure of Potential Conflicts of Interest:** The authors declare no conflicts of interest.

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