別添 5

III. 研究成果の刊行に関する一覧表

1: Konno T, Miura T, Harriott AM, Mezaki N, Edwards ES, Rademakers R, Ross OA, Meschia JF, Ikeuchi T, Wszolek ZK. Partial loss of function of colony-stimulating factor 1 receptor in a patient with white matter abnormalities. Eur J Neurol. 2018 Mar 6. doi: 10.1111/ene.13611.

2: Konno T, Yoshida K, Mizuta I, Mizuno T, Kawarai T, Tada M, Nozaki H, Ikeda SI, Onodera O, Wszolek ZK, Ikeuchi T. Diagnostic criteria for adult-onset leukoencephalopathy with axonal spheroids and pigmented glia due to CSF1R mutation. Eur J Neurol. 2018 Jan;25(1):142-147. doi: 10.1111/ene.13464.

3: Ikeuchi T, Mezaki N, Miura T. Cognitive dysfunction and symptoms of movement disorders in adult-onset leukoencephalopathy with axonal spheroids and pigmented glia. Parkinsonism Relat Disord. 2018 Jan;46 Suppl 1:S39-S41. doi:10.1016/j.parkreldis.2017.08.018.

4: Preethish-Kumar V, Nozaki H, Tiwari S, Vengalil S, Bhat M, Prasad C, Onodera O, Uemura M, Doniparthi S, Saini J, Nashi S, Polavarapu K, Nalini A. CARASIL families from India with 3 novel null mutations in the HTRA1 gene. Neurology. 2017 Dec 5;89(23):2392-2394. doi: 10.1212/WNL.0000000000004710.

5: Mizuta I, Watanabe-Hosomi A, Koizumi T, Mukai M, Hamano A, Tomii Y, Kondo M, Nakagawa M, Tomimoto H, Hirano T, Uchino M, Onodera O, Mizuno T. New diagnostic criteria for cerebral autosomal dominant arteriopathy with subcortical infarcts and leukocencephalopathy in Japan. J Neurol Sci. 2017 Oct 15;381:62-67. doi:10.1016/j.jns.2017.08.009.

6: Ibrahimi M, Nozaki H, Lee A, Onodera O, Reichwein R, Wicklund M, El-Ghanem M. A CARASIL Patient from Americas with Novel Mutation and Atypical Features: Case Presentation and Literature Review. Cerebrovasc Dis. 2017;44(3-4):135-140. doi:10.1159/000477358.

別添 1

New diagnostic criteria for CADASIL in Japan

Clinical criteria

#1 Age at onset (clinical symptoms #2 or white matter lesions) ≤55 years old.

#2 At least two of the following clinical findings:

a. Either of subcortical dementia, long tract signs, or pseudobulbar palsy.

b. Stroke-like episode with a focal neurological deficit.

c. Mood disorder.

d. Migraine.

#3 Autosomal dominant inheritance.

#4 White matter lesions involving the anterior temporal pole by MRI or CT.

#5 Exclusion of leukodystrophy (Adrenoleukodystrophy, metachromatic leukodystrophy, etc.).

Genetic criteria

Most pathogenic mutations in CADASIL are detected in *NOTCH3* exons 2-24 and result in the gain or loss of cysteine residues in the epidermal growth factor-like repeat domain. Cysteine-sparing variants should be carefully evaluated by skin biopsy and segregation studies

Pathological criteria

The pathological hallmark of CADASIL is granular osmiophilic material (GOM) in media of small arteries detected by electron microscopy. The finding of increased immunostaining of NOTCH3 is also useful.

Definite

CADASIL is definite when the individual fulfills

(1) White matter lesions by MRI or CT.

(2) Clinical criteria #5

(3) Genetic criteria and/or pathological criteria

Probable

CADASIL is probable when the individual fulfills clinical criteria #1-#5.

Possible

CADASIL is possible when the individual has abnormal white matter lesions (Fazekas grade ≥2) and fulfills either of

(1) ≤55 years old

(2) At least one of the symptoms in clinical criteria #2

別添 2　*CADASIL scale-J*

・高血圧なし：5 点、
・50 歳以下発症： 5 点、
・陳旧性皮質下梗塞： 3 点、
・球麻痺症状あり： 3 点、
・家族歴あり： 1 点、
・側頭極病変： 3 点

上記の総点数 15 点以上が陽性