発見．全経過（自然経過）9年．

【病理所見】脳重900g．肉眼的に，全体は脳は小ぶりで，小脳と橋底部が高度に萎縮．大脳割面では，基底核が萎縮性で被殻では外側，後方部が褐色調．脳幹部では，橋底部，中小脳脚が萎縮性．黒質と青斑核の色素は脱落している．組織学的には，線条体，中脳黒質，青斑核，橋核，オリーブ核，プルキンエ細胞の高度の神経細胞脱落とグリオーシスをみとめた．中枢神経系には明らかなレビー小体は認めなかったが，交感神経節には，多数のレビー小体様構造物が認められた．さらにシヌクレイン免疫組織染色にて，上記の変性部位に加えてより広範なグリア細胞質内封入体（GCI）の出現を認め，その密度は大脳脚がもっとも高かった．

【症例のまとめ】臨床的には，高齢発症のMSAで，進行性の小脳失調，パーキンソニスム，自律神経障害を呈し，胃瘻造設や気管切開をせずに，全9年の経過で突然死に至った症例．病理所見は，高度進行期のMSAに一致していると考えられた．

7 Amyotrophic lateral sclerosis with TAF15-predominant FET pathology: clinicopathologic features of an autopsied patient

○ Bo Cui[1], Mari Tada[1], Yuya Hatano[2]
Akari Takeshima[1, 2], Tomohiko Ishihara[2]
Akihiro Sugai[2], Takayoshi Tokutake[2]
Masato Kanazawa[2], Osamu Onodera[2], and
Akiyoshi Kakita[1]

Departments of Pathology[1] and Neurology[2],
Brain Research Institute, Niigata University

【Introduction】 Patients harboring brain inclusions positive for FET (FUS, EWS, and TAF15) proteins usually manifest frontotemporal dementia (FTD), but some may exhibit symptoms of amyotrophic lateral sclerosis (ALS). In these patients with either FTD or ALS, a large proportion of these inclusions are immunolabeled for both FUS and TAF15. Here we describe the clinicopathologic features of an autopsied patient with ALS in whom TAF15 inclusions greatly outnumbered FUS inclusions.

【Clinical summary】 A 77-year-old female patient complained of left-hand weakness, followed by gradually worsening weakness in her neck and bilateral upper limbs, dysphasia, and dyspnea. Neurological examination revealed hyperreflexia in all limbs and muscle atrophy in her neck and upper limbs. Electromyography indicated diffuse neurogenic change. Therefore, a clinical diagnosis of ALS was made. Mild cognitive impairment was also evident. She died suddenly at 81 years of age. She had no family history of neurological disorders. Gene analysis identified a novel p.Ser76Ile (c.227G>T) mutation in *TAF15*, but pathogenic effects of this mutation have been unclear.

【Pathological findings】 The brain, showing mild atrophy of the frontal lobe, weighed 1,044 g. The anterior nerve roots of the cervical and thoracic spinal cord showed severe atrophy. Neuronal loss and gliosis were evident in the motor and premotor cortex, spinal anterior horns, and brainstem motor nuclei, and were most prominent in the hypoglossal nucleus and cervical anterior horns. A few basophilic inclusions were evident in these areas. Immunohistochemistry using antibodies against FET proteins and their nuclear transport receptor transportin1 (TRN1) revealed that the numbers of both TAF15 and TRN1 inclusions were much greater than those of both FUS and EWS inclusions. Interestingly, FUS inclusions were localized in lesions with severe neuron loss.

【Discussion】 The immunohistochemical profiles of these inclusions are characteristic and may be associated with the *TAF15* mutation.