Supplementary Online Content


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This supplementary material has been provided by the authors to give readers additional information about their work.
**eFigure 1. Grading of Neuropathological Changes in the Spinal Anterior Horns**

Neuronal loss and gliosis in the anterior horns are graded as follows (A-H): (A, E) Grade 0 (none). The neurons are sparse in number without glial proliferation. (B, F) Grade 1 (mild). Occasional loss of neurons with mild gliosis is noted. (C, G) Grade 2 (moderate). Moderate loss of neurons associated with evident astrocytosis is observed. (D, H) Grade 3 (severe). Neurons have almost completely disappeared, and glial proliferation is marked. Aggregations of macrophages in the anterior horns are graded as follows (I-L): (I) Grade 0 (none). Aggregations of CD-68 positive macrophages are not observed in the all fields of the specimens. (J) Grade 1 (mild). Aggregations of macrophages are occasionally found. (K) Grade 2 (moderate). Aggregations of macrophages are moderate and found in the almost all investigated fields. (L) Grade 3 (severe). Aggregations of macrophages are abundantly and diffusely found. (A-D) Hematoxylin-eosin staining, (E-H) Klüver-Barrera staining, and (I-L) anti-CD-68 immunohistochemistry. Scale bars = 100μm.
eFigure 2. A TAR DNA-Binding Protein of 43 kDa (TDP-43)–Positive Inclusion in a Control Material

Phosphorylated TDP-43 aggregates within a glial cytoplasm of the lumbar anterior horn of a 79-year-old male with no history of neurodegenerative disease. Immunohistochemistry using anti-phosphorylated TDP-43 antibody. Scale bar = 50 μm.
eFigure 3. Ubiquilin 2–Positive Structures in Patients Enrolled in the Present Study

Ubiquilin-2-positive dystrophic neurites in the temporal cortices (A-B, F-H) or cytoplasmic inclusions in the hippocampal dentate neurons (C-E) were occasionally found in 8 patients. The lesions that are associated with the most abundant inclusions are shown here. (A-B) are type A patients, (C-E) are type B patients, and (F-H) are type C patients. Ubiquilin-2 immunohistochemistry. Scale bars = 50 μm.