**An autopsy case report of adult-onset Krabbe disease: Comparison with an infantile-onset case**

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**Supplementary materials**

**Supplementary Figure 1** MRI images arranged in chronological order and pathological images of adult-onset case (Case 1).

(A) Magnetic resonance images (T2-weighted images) showing high intensity in the white matter along the pyramidal tract to the bilateral precentral gyrus (arrowheads) and from the triangular part to the posterior horn in the lateral ventricle (arrows); these findings do not change for 13 years. Each set of two images from the left showing 13, 7, 6, 2 and 0 years before death respectively. (B) A Globoid cell positive for CD68. (C) The degenerating pyramidal tract of the midbrain, medulla oblongata, and cervical cord exhibiting slight myelin pallor in Klüver–Barrera staining. Scale bars: 5 µm (B), 10 mm (C).

**Supplementary Figure 2** Radiological and pathological images of infantile-onset case (Case 2).

(A) Magnetic resonance images (T2-weighted images) at the age of 11 months (8 months before death) showing high intensity in the posterior horn of the lateral ventricle. (B) Globoid cells and astrocytosis (arrows). Scale bar: 5 µm (B).

**Supplementary Figure 3** Pathological images of the demyelination of adult-onset (Case 1: A–C) and infantile-onset case (Case 2: D–F).

(A) The white matter of the precentral gyrus showing myelin pallor in Klüver–Barrera staining. (B) The white matter is strongly positive for neurofilament staining. (C) Nerve fibers remaining well (white asterisks showing U-fiber). (D) The white matter showing myelin pallor in Klüver–Barrera staining. (E) The white matter showing no positivity in neurofilament immunohistochemistry with remaining of U-fibers. (F) No nerve fiber in the demyelinated lesion (left side) while U-fibers remaining (black asterisks). Scale bar: 5 mm (A, B, D, E), 20 µm (C, F). Klüver–Barrera (A, D), neurofilament immunohistochemistry (B, C, E, F).

**Supplementary Figure 4** Effect of *GALC* mutations on its transportation and protein translation.

Adult-onset mutations, such as L618S or D528N, reduce transportation of *GALC* to the lysosome, thus retaining some enzymatic activity. In contrast, infantile-onset mutations, such as 12Del3InsR515H, produce inactive or non-folded proteins.