

## Figure e-1 Diagnostic Evaluation

(A) A cryosection of the biopsy stained with H&E shows active myonecrosis and regeneration along with a mild degree of endomysial fibrosis, atrophy, hypertrophy, and increased internal nuclei. Immunofluorescence studies performed in cryosections show normal dystrophin (B), reduced alpha-dystroglycan glycoepitope in some fibers (IIH6 VIA4-1 stain), and normal beta-dystroglycan. Muscle fibers labeled #1 and #2 are the same fibers in adjacent sections stained for dystrophin and alpha-dystroglycan. The scale bar is approximately 100  $\mu$ m. C-H) Muscle MRI –showing mild increased T1 hyperintensity in patient P1 (images C-D) and in patient P3 (images G-H); moderate increased signal in muscle in patient P2 (images E-F) with increased muscle bulk in the medial gastrocnemius. (I-K) Brain MRI in patient P1. (L-M) Brain MRI in patient P2. There are no abnormalities of the brainstem or cerebellum seen in either patient.

