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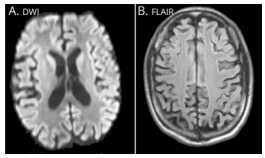
Abstracts

Articles appearing in the August 2018 issue

Impaired transmissibility of atypical prions from genetic CJD^{G114V}



Objective To describe the clinicopathologic, molecular, and transmissible characteristics of genetic prion disease in a young man carrying the *PRNP*-G114V variant.

Methods We performed genetic, histologic, and molecular studies, combined with in vivo transmission studies and in vitro replication studies, to characterize this genetic prion disease.

Results A 24-year-old American man of Polish descent developed progressive dementia, aphasia, and ataxia, leading to his death 5 years later. Histologic features included widespread spongiform degeneration, gliosis, and infrequent PrP plaque-like deposits within the cerebellum and putamen, best classifying this as a Creutzfeldt-Jakob disease (CJD) subtype. Molecular typing of proteinase K–resistant PrP (resPrP^{Sc}) revealed a mixture of type 1 (~21 kDa) and type 2 (~19 kDa) conformations with only 2, rather than the usual 3, PrP^{Sc} glycoforms. Brain homogenates from the proband failed to transmit prion disease to transgenic Tg (HuPrP) mice that overexpress human PrP and are typically susceptible to sporadic and genetic forms of CJD. When subjected to protein misfolding cyclic amplification, the PrP^{Sc} type 2 (~19 kDa) was selectively amplified.

Conclusions The features of genetic CJD^{G114V} suggest that residue 114 within the highly conserved palindromic region (113-A**G**AAAAGA-120) plays an important role in prion conformation and propagation.

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Axon reflex–mediated vasodilation is reduced in proportion to disease severity in TTR-FAP

Objective To evaluate the area of the vascular flare in familial amyloid polyneuropathy (FAP).

Methods Healthy controls and patients with genetically confirmed FAP were prospectively examined, on the upper and lower limbs, for thermal sensitivity (Medoc TSA-II thermal analyzer) and for axon reflex–mediated flare. The latter was induced by iontophoresis of histamine on the forearm and leg on 2 different visits. We used laser Doppler imaging (LDI) to measure the flare area (LDIflare).

Results Six patients had FAP of variable severity; 1 had generalized analgesia secondary to leprosy (used as a positive control). The median Neurologic Impairment Score–Lower Limbs (NIS-LLs) was 6 (0–27). The warmth detection thresholds in the feet were higher in patients (median 43°, interquartile range 39.0°–47.6°) compared with controls (37.4°, 35.3°–39.2°), indicating small fiber impairment. On the leg, LDIflare was smaller in the patients on 2 consecutive visits (controls: median 13.0 and 13.3 cm^2, interquartile range 9.7–22.8 and 8.3–16.9; patients 6.9 and 8.0 cm^2, 2.6–10.8 and 6.4–12.1; $p = 0.011$). LDIflare on the leg was correlated with NIS-LL (Spearman rank correlation 0.73, $p = 0.09$ on the first visit; Spearman rank correlation 0.85, $p = 0.03$ on the second visit).

Conclusions Our study underscores that histamine-induced axon reflex–mediated vascular flare on the leg is reduced in proportion to disease severity in patients with FAP.

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E. Harris, C.L. Bladen, A. Mayhew, et al. 2016;2:e89. doi.org/10.1212/NXG.0000000000000089