Dear Editor,

We thank de Boer et al. for their valuable comments to our article and for drawing attention to the early manifestations and pre-manifest subjects in retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations (RVCL-S). In our article, we reported phenotypic variability in three related cases and analyzed their large genealogy. The genetic testing identified 15 additional TREX1 gene mutation carriers, who in the neurological evaluation conducted at that time did not show evident clinical symptoms of RVCL-S, including Raynaud’s phenomenon (authors’ Fig. 1). The mean age of these pre-manifest relatives was 27.2±7.0 years (median = 25; range = 18-40 years, and 60% aged 18-27 years) thus, most of them had not reached the typical age of onset. Due to financial constraints, no neuroimaging or neuroophthalmological clinical studies were performed; therefore, we could not ascertain the absence of vascular retinopathy or subclinical brain signs in some of the older pre-manifest carriers. Vascular retinopathy in RVCL-S becomes apparent in the fourth or fifth decade of life, soon followed by clinical manifestations of progressive focal and global brain disease, and according to Stam et al., the mean age at diagnosis is 42.9±8.3 years. Regarding the follow-up of pre-manifest carriers, we agree with de Boer et al., and medical care was offered to all of them at our institution. Since a brain biopsy should only be considered in cases with uncertain imaging findings and negative family history, the molecular test is definitely the gold standard for RVCL-S diagnosis. Finally, in relation to withholding a diagnosis to pre-manifest mutation carriers, the pre-symptomatic diagnosis was offered to at-risk persons, although only 11 relatives accepted. Until now, merely one out of three pre-manifest carriers returned to our hospital to receive his genetic results; in the remaining carriers, delivery of their results was postponed due to depression, highlighting that few people wish to know their genetic status. Since this is a personal decision, we considered ethical to respect the subjects’ autonomy, and their right to not to know.

REFERENCES


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