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PREFACE

A solved puzzle: Familial adult myoclonus epilepsy is a new expansion repeats disorder

On the 27th–28th of May 2022, the International Workshop on Familial Adult Myoclonus Epilepsy (FAME) was held in Naples, Italy (Figure 1). The event was endorsed by the International League Against Epilepsy and supported by a European Joint Programme on Rare Disease grant. More than sixty international researchers gathered together to discuss this unusual and interesting epileptic disorder. This supplement reports the clinical and experimental characteristics of this condition described over the past 30 years under different acronyms (BAFME: benign adult familial myoclonic epilepsy; ADCME: autosomal dominant cortical myoclonus and epilepsy; FCMTE: familial cortical myoclonic tremor and epilepsy),[1] which were presented and discussed during the workshop. For consistency, we will use the acronym "FAME" throughout the supplement.

The prevalence is not established yet, as this condition is often underrecognized, but it is estimated to be <1/35 000.[2] Its diffusion and disease history across the world have been reviewed by Berkovic et al.[3] This condition is transmitted in an autosomal dominant manner and is characterized by the occurrence of cortical myoclonic tremor, overt myoclonus, and rare bilateral tonic–clonic seizures. FAME is considered a neurodegenerative condition, although it is relatively slow in progression, as discussed by Giraldez et al.[4] The diagnosis is based on specific neurophysiological testing, namely jerk-locked back-averaging, somatosensory evoked potentials, long-latency reflex, and motor evoked potentials, among others. A review of the neurophysiological findings has been discussed by Dubbioso et al.[5] Imaging data, including functional magnetic resonance imaging, indicates a cortical origin of the cortical myoclonic tremor and decreased cerebellar activation.[6] Interestingly, cerebellar changes indicating changes in Purkinje cells emerged from few neuropathology reports, in patients from isolated pedigrees. These data have been reviewed by Van Rootselaar et al.[7] The differential diagnosis may be challenging and should consider some forms of genetic generalized epilepsy and progressive myoclonus epilepsies. This topic is discussed by Baykan et al.[8]

The genetic cause of FAME has long remained elusive, but recently it has been identified for the four main geographical aggregates and consists of an intronic repeat pentameric expansion occurring in different genes and still causing an overlapping phenotype across the world. Although their protein products have different functions, the underlying pathogenic mechanism is likely the same. These aspects are discussed by Corbett et al.[9] and Silveira et al.[10]

FAME treatment is so far symptomatic and often elusive, as discussed by Coppola et al.[11] Elucidating the

FIGURE 1 Participants in the 2022 International Workshop on Familial Adult Myoclonus Epilepsy.

pathogenesis of this condition is essential to provide further insight into therapeutic options aiming at precision medicine that would not be possible otherwise.[12]

We heartily thank Dr. Mike Sperling, Editor of *Epilepsia*, for the generous offer to publish this supplement issue, which may serve as a helpful guide for epileptologists as well as for medical students and residents who want to learn more about the pathophysiology, epidemiology, and potential treatment of this intriguing epileptic disorder.

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CONFLICT OF INTEREST STATEMENT

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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