Progressive Myoclonus Epilepsies – State of the Art

Preface

The progressive myoclonus epilepsies (PMEs) are 'progressive', because they worsen with time and are generally fatal. They are 'myoclonus', because these patients generally have frequent, often constant, myoclonus, which is commonly, though not invariably, cortical. They are 'epilepsies', because in addition to the myoclonus the patients suffer convulsive and other types of seizures, which are soon intractable, and which in many cases precipitate death in status epilepticus. But the PMEs are in most cases more. They are often associated with blindness, because the retina is nervous tissue, and what is wrong with that nervous tissue is what is wrong with the brain itself, namely neurodegeneration. The PMEs are therefore also ataxia, and dementia, and general demise of the brain. The PMEs are yet more. They are children who are born and grow and go to school and love and are loved, before they are struck. They are therefore not static early tragedies that families adjust to from the get-go, but are children with whom the family has grown and who are slipping daily a little bit more into greater pain, towards greater intellectual and emotional separation, and towards death. And yet that death does not come fast in most cases, because these are children generally with otherwise healthy bodies. They and their families therefore suffer for years, sometimes decades before the end.

Yet again the PMEs are something more. Almost all are monogenic diseases. As such, however horrible, they are genetically simple. As such, and because each has an open window of health prior to significant neurodegeneration, they will be among the first brain diseases to be treated by interventions such as gene replacement therapy. Also, because they are genetically simple, they will be understood ahead of genetically complex neurological disorders.

We are therefore dealing with the worst and best of all neurological worlds. This series of chapters reviews the PMEs and provides the most up-to-date knowledge of their basic mechanisms. It concludes with an outlook at upcoming gene knowledge empowered therapies. It is hoped that the next book written on this subject will include real examples of available cures, and a dream shared by all neurologists, that when they see a family with a PME they would be able to say: 'This is what you have. Take this'.

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A word of appreciation is due to all the leaders and teachers in the field of PMEs over the decades. We are certainly forgetting many, but these names include the team from the Montreal Neurological Institute, Drs. Eva and Fred Andermann, Samuel Berkovic now in Australia, previously trained with the Andermanns, and Guy Rouleau; the group in Helsinki led by Anna-Elina Lehesjoki; the Marseille group (the late Dr Joseph Roger and his team: Charlotte Dravet, Pierre Genton and Michelle Bureau); and the Los Angeles group (Antonio Delgado-Escueta and his trainee now a leader in Spain, Jose-Maria Serratosa).

Finally, the greatest thanks go to each and every child we have all seen, who taught us so much about the brain generally, for the sake of countless future patients, and all the families who teach us every day what humanity is at its best.

Berge A. Minassian, Pasquale Striano, Giuliano Avanzini