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Madelung's Disease is Not Uncommon in MERRF Patients

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Letter to the Editor

In a recent article, Gilson et al. reported about a 57 years old female with the clinical diagnosis of MERRF syndrome who also presented with Madelung's lipomatosis (multiple symmetric lipomatosis) [1]. The authors regarded the association of Madelung's disease with MERRF syndrome as unique [1]. We have the following comments and concerns.

The first shortcoming of the report is that the genetic cause of MERRF syndrome was not provided. In about 90% of the cases, MERRF syndrome is due mutations in the *tRNA(Lys)* gene [2]. Since MERRF syndrome in the presented family obviously followed a maternal trait of inheritance, it is quite likely that all affected individuals carried the same *tRNA(Lys)* mutation. Since a targeted approach for *tRNA(Lys)* variants is today an easily available issue, the report would profit significantly from discovering the underlying genetic defect.

Since the diagnosis of MERRF syndrome was established exclusively upon the clinical presentation, it is essential that the patient fulfils the clinical diagnostic criteria. The diagnosis of MERRF syndrome is clinically established upon the presence of four canonical features, such as myoclonus, generalised epilepsy, cerebellar ataxia, and a ragged-red fiber myopathy [2]. Additionally, MERRF patients may present with migraine, intellectual decline and dementia, stroke-like episodes, polyneuropathy, optic atrophy, pigmentary retinopathy, hearing impairment, cardiomyopathy, arrhythmias, gastrointestinal dysmotility, including vomiting or dysphagia, diabetes, hypothyroidism, short stature, or focal or generalized lipomatosis [2]. Presence of phenotypic features in addition to the canonical ones implies that MERRF plus is present. The patient obviously did not present with epilepsy. A more detailed description of the patient's phenotype and the detailed presentation of all affected relatives could be helpful in this respect.

We do not agree that alcohol is a trigger for the development of Madelung 's disease [1]. Chronic alcoholism is rather the consequence of the defacing, cosmetic problem than the trigger of the disease. Since millions of people are alcohol-addicted worldwide, we should expect a significantly higher prevalence of Madelung's disease than 1 in 25000 [3]. Accordingly, Madelung's disease should be particularly prevalent in countries with excessive alcohol consumption such as France or Italy, which is definitively not the case. Madelung's disease is most likely not an independent disease but rather a particular manifestation of a MERRF mutation [2]. The prevalence of MERRF mutations in MERRF patients is most likely much higher if patients with Madelung's disease would have been systematically investigated not only for the m.8344A>G variant but also for the other 19 variants associated with MERRF. Sixteen of them are definitively pathogenic and three classified as possibly pathogenic according to the modified Yarham score [2].

Overall, we suggest that the pesented patient is genetically investigated, that the patient and his affected relatives are thoroughly screened for clinical manifestations of MERRF syndrome, and that Madelung's disease should be regarded rather as a feature of MERRF syndrome than as a distinct entity.

References

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