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Nephrocalcinosis and retinal dystrophy, rare manifestations of MPV17-related mitochondrial depletion syndrome? ☆

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Letter to the Editor

With interest we read the article by Kim et al. about four pediatric patients with hepato-cerebral mitochondrial depletion-syndrome(MDS) due to MPV17-mutations who all died from hepatic failure a few months after birth [1]. We have the following comments and concerns.

Nephrocalcinosis is an uncommon phenotypic manifestation of MPV17-mutations. Only in a single patient with MDS due to a RRMB2 mutation has nephrocalcinosis been reported [2]. Are there indications that nephrocalcinosis was due to causes other than the MPV17-mutation? Was the family history positive for nephrocalcinosis? Was there hyperparathyroidism, heart failure, prolonged hypercalcemia, placenta previa, placenta abruptio, or schock in patient-1?

Another not yet reported manifestation of a MPV17-mutation is retinal dystrophy [1]. Which type of retinal dystrophy was diagnosed? Retinitis pigmeentosa, Best's disease, or Stargadt's disease? Were causes other than the MPV17-mutation excluded as cause of reatinal dystrophy?

Cardiac manifestations are also a rare clinical manifestation of the MPV17-mutation. Was any of the four investigated for cardiac disease? Was there cardiomyopathy, arrhythmias, or conduction defects? Was the individual or family history positive for palpitations, syncope, heart failure, or sudden cardiac death?

Contrary to nephrocalcinosis, retinal dystrophy, and cardiac disease, polyneuropathy is a common phenotypic feature of MPV17-mutations [3,4]. Neuropathy in MPV17-mutation carriers is usually of the axonal sensory-motor type [4]. Were other causes of polyneuropathy excluded in patient-1?

What about the family history of these four patients? Did any of the first-degree relatives of them also carry the MPV17-mutation? Which were the clinical characteristics of the mutation carriers? The mutation p. Val66Glu can be regarded as pathogenic only if a conserved region was affected and if the mutation segregated with the phenotype through the generations.

Overall, these interesting case series merits an in-depth discussion and exclusion of alternative causes of rare clinical manifestations and a thorough work-up of the familial background.

References

[1] J. Kim, E. Kang, Y. Kim, J.M. Kim, B.H. Lee, K. Murayama, G.H. Kim, I.H. Choi, K.M. Kim, H.W. Yoo, MPV17 mutations in patients with hepatocerebral mitochondrial DNA depletion syndrome, Mol. Genet. Metab. Rep. 8 (2016) 74–76.
[2] V. Stojanovic, J.A. Mayr, W. Sperl, N. Barišić, A. Doronjski, G. Milak, Infantile peripheral neuropathy, deafness, and proximal tubulopathy associated with a novel mutation of the RRM2B gene: case study, Croat. Med. J. 54 (2013) 579–584.
[3] C.L. Karadimas, T.H. Vu, S.A. Holve, P. Chronopoulou, C. Quinzii, S.D. Johnsen, J. Kurth, E. Eggers, L. Palenzuela, K. Tanji, E. Bonilla, D.C. De Vivo, S. DiMauro, M. Hirano, Navajo neurohepatopathy is caused by a mutation in the MPV17 gene, Am. J. Hum. Genet. 79 (2006) 544–548.
[4] E.L. Blakely, A. Butterworth, R.D. Hadden, I. Bodi, L. He, R. McFarland, R.W. Taylor, MPV17 mutation causes neuropathy and leukoencephalopathy with multiple mtDNA deletions in muscle, Neuromuscul. Disord. 22 (2012) 587–591.

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