Letter by Minutoli et al Regarding Article, “Reduced Myocardial 123-Iodine Meta-Iodobenzylguanidine Uptake: A Prognostic Marker in Familial Amyloid Polyneuropathy”

To the Editor:

We read with great interest the study of Azevedo Coutinho et al evaluating the prognostic value of 123Iodine Meta-iodobenzylguanidine (123I-MIBG) scintigraphy in patients with transthyretin (TTR) familial amyloid polyneuropathy (FAP). The authors evaluated 143 patients with TTR-FAP comparing time to all-cause death with late heart-to-mediastinum MIBG uptake ratio (H/M). Median follow-up was 5.5 years. Of 143 patients, 32 (22%) patients died. Five-year mortality rate was 42% and 7.4% for patients with late H/M <1.60 (the estimated lower limit of normal) and H/M ≥1.60, respectively, reaching a high statistical significance (hazard ratio, 7.19; P<0.001). Late H/M was found to be an independent prognostic predictor of survival. More interestingly, the authors reported that patients with late H/M <1.60, even if at higher risk of unfavorable outcome, were found to benefit from liver transplantation. In fact, compared with neurophysiological score-matched controls, patients with liver transplantation (53 patients were submitted to liver transplantation) had a significant lower long-term mortality (hazard ratio, 0.32; P=0.012). It could be hypothesized that this finding may be attributable to a reduced TTR deposition because liver transplantation, determining removal of the source (liver) of the amyloid precursor protein (mutated transthyretin), would stop progression of the disease, or even to a regression of amyloid deposits given that long-term observations of patients with liver transplantation have clearly shown the histopathologic regression of amyloid deposits. Similar considerations are also valid for drug therapy, including the novel drug tafamidis, a small-molecule inhibitor that binds selectively to TTR in human plasma and kinetically stabilizes the tetrameric structure of both wild-type TTR and a number of different mutants. Indeed, clinical trials indicate that tafamidis slows disease progression in patients with TTR-FAP and reduces the burden of disease.

99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) is a sensitive and specific tool in the evaluation of TTR-FAP; namely, it is more sensitive than echocardiography and more specific than 2D feature strain echocardiography in diagnosing cardiac involvement attributable to TTR-FAP. More interestingly, it is able to reveal TTR cardiac deposition earlier than MRI and to demonstrate a larger cardiac involvement than that demonstrated by MRI, which often reveals only focal areas of delayed enhancement. It has been demonstrated that 99mTc-DPD myocardial uptake is correlated with disease severity and is a prognostic determinant of cardiac outcome in patients with TTR-FAP. Such observations raise interest on further integration of diagnostic techniques, which explore different morphological, functional, and molecular features of patients with FAP. Namely, the possible interaction of the evaluation of sympathetic innervation status by 123I-MIBG imaging and of the amyloid burden by 99mTc-DPD scintigraphy may allow a better understanding of the natural history of TTR-FAP, a more accurate prognostic stratification of patients with FAP, and a better management of the available therapeutic options.

Disclosures

None.

References


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