Magnetic resonance imaging of Fabry disease cardiomyopathy in patients receiving oral chaperone therapy

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Background: Fabry disease is a lysosomal storage disorder with multiple organ involvement. Renal and cardiac symptoms can lead to dialysis and myocardial hypertrophy with fibrosis, responsible for heart failure with preserved ejection fraction (HFpEF). Enzyme replacement therapy (ERT) is available for all patients with Fabry disease since 2001, requiring infusions every other week. Since May 2016, the chaperone migalastat represents a novel form of specific therapy as the first oral therapy available for certain Fabry patients. Through this molecule the function of the mutated enzyme α-galactosidase A can be restored. Recent trials have shown positive cardiac effects of chaperone therapy using echocardiography; however, MRI investigations further evaluating these findings are not available yet.

Objective: To evaluate cardiac effects of migalastat therapy in patients with amenable α-galactosidase A mutations in the prospective monocentric HEAL-FABRY registry (NCT03362164).

Methods and results: Comprehensive clinical investigations including serial MRI were conducted at baseline before initiation of migalastat therapy and at least one year thereafter in all patients without contraindications such as pacemakers or ICDs. Out of 29 patients included in the study (mean age at start of therapy 52.8±14 years, total range 20–74 years), until then 12 patients with MRI data completed the 1-year follow-up. At 1 year, enzyme activity in leucocytes increased from 0.06 to 0.21 nmol/min/mg protein (p=0.001). Distinctive changes over time were observed not only in diastolic but also systolic parameters. The systolic myocardial mass index was reduced by 2.39% (p=0.10). In the AHA segment number 5, most important for classification of severe myocardial damage in Fabry patients, late gadolinium enhancement was reduced by 8.58% in all 5 patients with verified progressive fibrosis (p=0.14). One patient stopped migalastat therapy due to personal reasons. No significant side effects were observed.

Conclusion: These preliminary MRI data show positive effects of migalastat therapy in patients with Fabry disease and cardiac involvement. Compared to echocardiography, MRI has the potential to allow for comprehensive additional analyses regarding both cardiac morphology and function.

Analysis of LGE (systolic phase)
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