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RAPID COMMUNICATION

Focal Reduction in Cardiac ^{123}I-Metaiodobenzylguanidine Uptake in Patients With Anderson-Fabry Disease

Saori Yamamoto, MD, PhD; Hideaki Suzuki, MD, PhD; Koichiro Sugimura, MD, PhD; Shunsuke Tatebe, MD, PhD; Tatsuo Aoki, MD, PhD; Masanobu Miura, MD, PhD; Nobuhiro Yaoita, MD, PhD; Haruka Sato, MD; Katuya Kozu, MD; Hideki Ota, MD, PhD; Kentaro Takanami, MD, PhD; Kei Takase, MD, PhD; Hiroaki Shimokawa, MD, PhD

Background: It remains to be elucidated whether cardiac sympathetic nervous activity is impaired in patients with Anderson-Fabry disease (AFD).

Methods and Results: We performed ^{123}I-meta-iodobenzylguanidine (MIBG) scintigraphy and gadolinium-enhanced cardiovascular magnetic resonance (CMR) in 5 AFD patients. MIBG uptake in the inferolateral wall, where wall thinning and delayed enhancement were noted on CMR, was significantly lower compared with the anteroseptal wall. The localized reduction in MIBG uptake was also noted in 2 patients with no obvious abnormal findings on CMR.

Conclusions: Cardiac sympathetic nervous activity is impaired in AFD before development of structural myocardial abnormalities.

Key Words: Anderson-Fabry disease; Cardiomyopathy; Cardiovascular magnetic resonance; MIBG scintigraphy

Anderson-Fabry disease (AFD) is a multisystem, X-linked, lysosomal storage disorder caused by a mutation in the α-galactosidase A (GLA) gene.[1] The cardiac abnormality of AFD first appears as left ventricular hypertrophy followed by cardiac dilatation, fatal arrhythmias and death.[1,2] In AFD patients, cardiac fibrosis and wall thinning are localized to the inferoposterior wall, although the mechanism remains unclear.[2,3] In the present study, we used ^{123}I-meta-iodobenzylguanidine (MIBG) scintigraphy to examine whether cardiac sympathetic nervous activity is impaired in patients with AFD.

Methods

(See **Supplementary File 1**.)

Results

The 5 patients' characteristics are shown in **Table S1**. Benidipine, which could interfere with MIBG uptake, had been administered in only 1 patient. Early and late heart-to-mediastinum (H/M) ratios were significantly lower, and washout ratios significantly higher in the AFD group than in the control group (early H/M ratio, 2.02±0.11 vs. 2.49±0.05, P=0.003; late H/M ratio, 1.86±0.07 vs. 2.68±0.07, P<0.001; washout ratio, 21.4±3.9 vs. 12.6±1.0, P=0.004). **Figures 1A,C** is representative images of a AFD patient showing reduced MIBG uptake in the inferolateral wall, where wall thinning and delayed enhancement were noted on CMR as compared with the anteroseptal wall. Moreover, localized reduction in MIBG uptake was noted in a patient with no obvious wall thinning or delayed enhancement on CMR (**Figures 1B,D**). The ratio of MIBG uptake in the inferolateral wall to that of the anteroseptal wall was significantly lower in the AFD group than in the control group (**Figure 2**).

Discussion

In the present study, reduced MIBG uptake was confined to the inferolateral wall in the AFD patients. Spinelli et al reported a reduced H/M ratio in AFD patients, but did not show localization of the reduced MIBG uptake.[4] A possible explanation for this observation is regional differences in cardiac innervation. The inferior wall, as compared with the anteroseptal wall, is predominantly innervated by parasympathetic nerves and less innervated by sympathetic nerves.[5] Thus, it is conceivable that sympathetic nerves in the inferior wall are more easily depleted in the early stage of AFD which is progressive in nature. Another explanation is a partial volume effect. In the

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Department of Cardiovascular Medicine (S.Y., H. Suzuki, K.S., S.T., T.A., M.M., N.Y., H. Sato, K.K., H. Shimokawa), Department of Radiology (H.O., K. Takanami, K. Takase), Tohoku University Graduate School of Medicine, Sendai, Japan
Mailing address: Koichiro Sugimura, MD, PhD, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan. E-mail: ksugimura@cardio.med.tohoku.ac.jp

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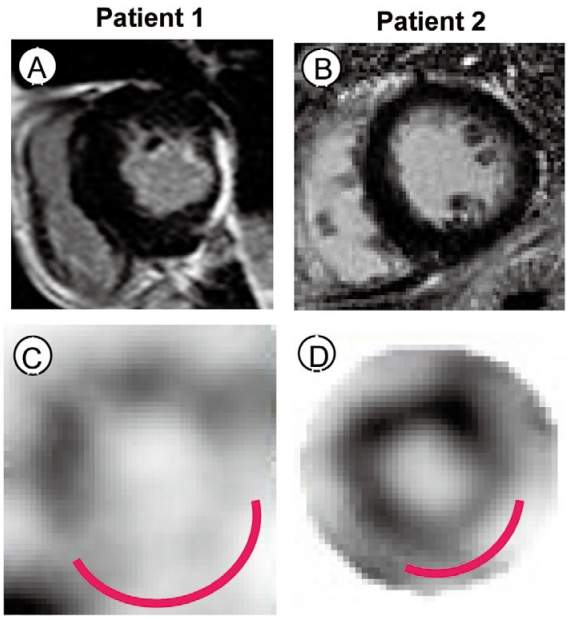

Figure 1. Representative images of gadolinium-enhanced CMR (**A**,**B**) and MIBG scintigraphy (**C**,**D**) in AFD patients. MIBG uptake in the infero-lateral wall, where wall thinning and delayed enhancement was observed in CMR (**A**), was lower than that in the anteroseptal wall (**C**). Localized reduction in MIBG uptake was also observed in a patient without obvious wall thinning and delayed enhancement in CMR (**B**,**D**). (**A**,**C**) Patient 1, (**B**,**D**) patient 2 (see **Table S1**). AFD, Anderson-Fabry disease; CMR, cardiac magnetic resonance; MIBG, ^{123}I-meta-iodobenzylguanidine.

present study, the region with reduced MIBG uptake coincided with that with wall thinning. A thin wall might hamper the actual estimation of MIBG uptake in the inferoposterior wall. However, localized reduction in MIBG uptake was noted in the inferoposterior wall of a patient who had no obvious wall thinning or delayed enhancement on CMR, suggesting that degenerative changes in cardiac sympathetic nerves precede cardiac fibrosis. Thus, the reduction in MIBG uptake in AFD patients was not attributable to nonspecific changes. AFD may be underdiagnosed because the manifestation is limited to the heart in some cases.[3,6,7]

The present results indicate that MIBG scintigraphy could detect cardiac abnormalities in AFD patients before the development of structural myocardial abnormalities, suggesting its usefulness for early detection of the disease.

Disclosures

None.

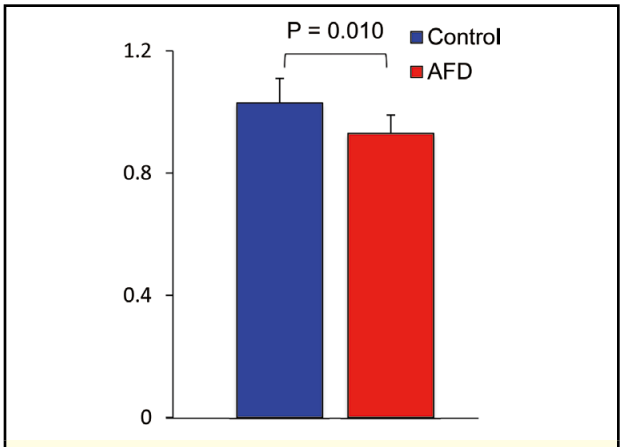

Figure 2. Ratio of MIBG uptake in the inferolateral wall to that of the anteroseptal wall in the AFD and control groups. AFD, Anderson-Fabry disease; CMR, cardiac magnetic resonance; MIBG, ^{123}I-meta-iodobenzylguanidine.

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Supplementary Files

Supplementary File 1

Methods

Table S1. Baseline patient characteristics

Please find supplementary file(s);
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