

Cardiac ^{123}I -metaiodobenzylguanidine Scintigraphy in a Patient with Familial Parkinsonism with *Parkin* Gene Mutation

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A decreased cardiac ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) uptake has been used as a powerful tool to identify Lewy body disease, such as idiopathic parkinson's disease (IPD). We performed cardiac ^{123}I -MIBG scintigraphy in patient with autosomal recessive juvenile parkinsonism (ARJP) with *parkin* gene mutation (PARK2). The findings showed normal cardiac ^{123}I -MIBG uptake. Therefore, although the clinical features of ARJP are sometimes quite similar to those of late-onset IPD, cardiac ^{123}I -MIBG scintigraphy may be used as a valuable tool to identify patients with IPD and to distinguish them from patients with other parkinsonian syndromes.

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Cardiac ^{123}I -metaiodobenzylguanidine (MIBG) scintigraphy has been investigated as a useful tool to distinguish Parkinson's disease (PD) from atypical Parkinsonism.¹ This feature corresponds to the presence of myocardial postganglionic sympathetic dysfunction as part of the neurodegenerative process in PD. This impairment occurs early in the course of the disease, and its severity depends on disease progression and treatment. *Parkin* disease (PARK2; OMIM 602544) is the most frequent monogenic early-onset parkinsonism (EOP), accounting for approximately 49% of familial EOP.¹ Pathological features of *parkin* disease resemble those of idiopathic Parkinson's disease (IPD) in that they show degeneration of neurons in the substantia nigra pars compacta and in the locus coeruleus², and occasionally Lewy bodies.^{2,3} The typical clinical phenotype shows early onset of parkinsonian features, usually before the age of 40, benign clinical course, dystonia at onset, increased tendon jerks, sleep benefit, early motor fluctuations, and susceptibility to levodopa-induced dyskinesias. Recently, it has been suggested that cardiac ^{123}I -MIBG scintigraphy could be used as a tool to estimate Lewy body pathology and to distinguish IPD from this disorder. Study about cardiac ^{123}I -MIBG uptake in a patient with *parkin* disease was not established yet in the Korean population. Thus, we herein report the cardiac ^{123}I -MIBG scintigraphy findings of a patient with Korean familial *parkin* disease.

Case

This family was briefly described as having familial *parkin* disease by Kim et al.^{4,5} (Figure 1). The present patient (II-4, born 1954) noticed a bilateral resting tremor at 38 years of age. When bradykinesia and gait disturbance developed later, she was diagnosed with PD. The disease progressed slowly, affecting both sides of the body.

She was treated with 750 mg levodopa/carbidopa, which resulted in marked improvement in her parkinsonian features. The Hoehn and Yahr stage on state was I. She additionally

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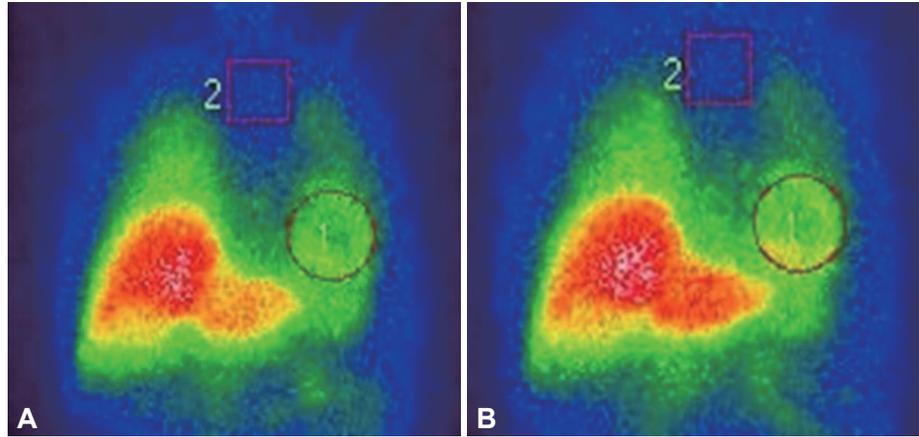


Figure 1. Cardiac ¹²³I-metaiodobenzylguanidine scintigraphy in this patient. All of early (A) and delayed images (B) reveal normal cardiac ¹²³I-metaiodobenzylguanidine uptake. The H/M ratio is 1.94 in the early image and 1.99 in the delayed image. H/M: heart to mediastinum.

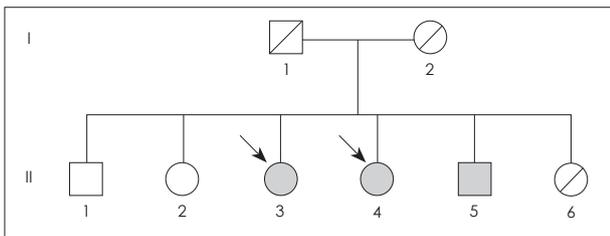


Figure 2. Pedigree of family. Circle indicate women, squares indicate men and arrows indicate the affected individuals. Black symbols represent persons with homozygous mutations. Hatched symbols denote deceased subjects.

showed only mild dysarthria on neurological examination at 47 years of age, but the brain magnetic resonance imaging was normal finding. However, right foot and trunk dyskinesia (peak dose dyskinesia) was marked at 50-years of age, and we reduced dose of levodopa/carbidopa to 500 mg.

The older sister (II-3, born 1950) noticed a gait disturbance at age 44 and was diagnosed with Parkinson disease. The younger brother (II-5, born 1958) presented with paresthesia of the lower extremities and twisting sense in the left toe at the age of 34, but he did not exhibit any parkinsonism during 10-years follow up period. Another brother (II-1, born 1939) was normal. The PCR amplification of the family members revealed a homozygous deletion of exon 4 in the *parkin* gene (II-3, II-4 and II-5) (Figure 1).

The cardiac ¹²³I-MIBG scintigraphy of the patient was performed with an intravenous injection of 111 MBq of ¹²³I-MIBG using a dual-head camera (Siemens, Germany). Data of early and delayed phases was obtained 30 minutes (early) and 4 hours (delayed) after injection. The values of the heart to mediastinum (H/M) ratio in the early and delayed phases were 1.94 and 1.99, respectively (Figure 2). These ratios were significantly higher than the 2SDs calculated from 50 PD patients (early; 1.343 ± 0.251 , delayed 1.258 ± 0.242) and were within 2 SDs of the normal mean (early; 2.342 ± 0.214 , delayed; 2.418 ± 0.231).

Discussion

A reduced cardiac uptake of MIBG, which indicates cardiac sympathetic denervation, may occur even during the early stage and offers a sensitive tool with which to differentiate PD and diffuse Lewy body dementia (DLB) from other disorders with akinetic rigid symptoms and dementia.³ All of IPD, DLB and pure autonomic failure have Lewy bodies as a common pathologic feature and are considered to be 3 phenotype of single disorder that may be called Lewy body disease (LBD).² Whereas, neuropathological studies have revealed the generalized loss of neurons with no Lewy bodies in the substantia nigra and locus ceruleus of most case of *parkin* disease. Our patient showed normal cardiac uptake of ¹²³I-MIBG. The present findings and previous reports, even considering the limited number of patients, strongly suggest that cardiac uptake of MIBG is a useful diagnostic marker to differentiate *parkin* disease from PD.

The present data raise the issue whether normal cardiac sympathetic innervation is a feature of *parkin* disease. In previous study, Mashiko et al.⁶ reported that myocardial MIBG scan was normal in Japanese autosomal recessive juvenile parkinsonism patient caused by *parkin* gene. Although involvement of cardiac sympathetic nerve system in *parkin* disease is unknown, to our knowledge, this is the first report of cardiac ¹²³I-MIBG scintigraphy finding in Korean familial *parkin* disease. Therefore, we think normal cardiac uptake of ¹²³I-MIBG might be of potential diagnostic value to indicate the absence of Lewy body pathology, resulting in distinguishing LBD, such as IPD and DLB, from other diseases without Lewy body pathology, including *parkin* disease.

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